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Editorial

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Head and Neck Cancers: Problems and Perspectives

Head and neck cancers are one of the commonest malignancies encountered in our country. More than one-third of patients registered in our institute are of head and neck malignancies. In males, about half of patients are in this category. Tobacco and gutka chewing are the major etiological factors for these malignancies and now we see increasing incidence of head and neck cancers in young adult.

Oral Cancers

They are commonest among head and neck cancers. Surgery followed by adjuvant radiotherapy and/or chemotherapy is primary line of treatment. Radiotherapy is required in all the patients as either curative/adjuvant/palliative treatment. Postoperative radiotherapy (PORT) is indicated in more than 80% operated cases and major indication is depth of invasion in pathological specimens. This is a very tricky problem and improper handling of specimen may lead to fallacy in the determination of depth of invasion.

In case of carcinoma anterior two-third of tongue, nearly all patients need postoperative radiation due to muscle invasion in pathological specimen, hence proper selection of patients before doing surgery may save patients from getting extra morbidity from postoperative radiation.

A good plastic surgery is mandatory in case of oral cancers because defective anatomical contours lead to improper dose distribution giving to unusual side effects and inadequate doses to the area being treated. It is very essential to keep the edges of remaining mandible after hemimandibulectomy and restoring proper blood supply to mandible during surgery as these short comings may lead to postradiation mandibular necrosis in future.

Use of intensity modulated radiation therapy/ three-dimensional conformal radiation (IMRT/ 3DCRT) therapy should be encouraged in treatment of head and neck malignancies to minimize cumbersome late radiation effects like xerostomia, dysphagia and spinal cord damage. Dental care is of utmost importance before, during and after radiotherapy. All the loose teeth should be removed during oral surgery and dental procedures like root canal treatment, scaling should be properly done before starting radiotherapy. Usually a gap of 4-6 weeks is given between surgery and radiotherapy so proper treatment of all dental problems should be attempted during this period because no dental manoeuvre is allowed 8-10 months post radiotherapy.

Chemotherapy is required in cases of positive margins, positive lymph nodes with extracapsular extension. Chemoradiation may lead to increased local toxicity about which patient should be informed well in advance.

Brachytherapy alone or in conjunction with teletherapy can be a good alternative to surgery in early cases of oral cancers. Such type of treatment gives 100% local control with practically no disfigurement of face and neck.

Oropharynx

Most of the cases are detected in advanced stages. Surgery has practically no role in management and worldwide accepted treatment is chemoradiation. Present schedule of giving chemotherapy is on weekly or 3 weekly basis, commonly used drugs are platinum analogues and few other drugs like taxanes can be tried in moderate doses as radiosensitizers.

IMRT is the choice of treatment as it effectively reduces late morbidities of the treatment. HPV is now supposed to be causative agent in many oropharyngeal cancers and such type of patients have better prognosis and require less doses of radiation with/without chemotherapy. HPV testing is still not a common practice in our country. Many targeted therapy have been tried in these cancers and these therapies may replace cytotoxic chemotherapy in future.

Nasopharynx

They also usually present in advanced stages. Neoadjuvant chemotherapy (NACT) is effective in reducing the bulk of disease and can be followed by chemoradiation. Such types of treatment are very toxic and all efforts should be done to reduce morbidity. All the patients should be treated by IMRT as far as possible.

Paranasal Sinuses (PNS)

Surgery is the mainstay of treatment. In advanced stages a good maxillofacial surgery team is needed for proper removal of tumour. Preoperative radiation can be used to downstage the tumour before surgery.

Larynx and Hypopharynx

Laryngeal preservation should be tried in all stages using chemoradiation except in the presence of gross cartilage invasion. Hypopharyngeal tumours like carcinoma pyriform fossa usually respond nicely to radiation but in cases of small primary with a large node, a neck dissection may be tried before giving curative radiotherapy. Post cricoid cancers are usually seen in young females and are resistant to radiation. Surgery can be better treatment in such cases.

There are nice articles in this issue on head and neck cancers. Excellent demographic data are presented by community oncology department. Retrospective studies using newer targeted therapy and hypofractionated radiotherapy show results at par with international data. Paediatric nasopharyngeal carcinoma is a serious problem and need proper uniform treatment policy. Article on use of nerve block on pain management is technically sound but further elaborated results are needed.

Editorial

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Changing Face of Head and Neck Cancer

Head and neck squamous cell carcinoma forms 25% of all cancers in male and 10% of all cancers in females in India. Predominant prevalence is also seen in France and Brazil. There is a rapid progression in diagnosis and multimodality treatment approaches, giving long survival, less morbidity and good aesthetic and functional results. It is a team approach of surgical, medical and radiation oncologists with maxillofacial prosthetics and pathologist. Treatment has been well streamlined for last 2 decades with emphasis on organ preservation.

The most interesting facet is the **Human papilloma virus** related oropharyngeal cancer. HPV strains 16 and 18 have now emerged as strong causative factors in nontobacco chewers. Tobacco and alcohol consumption are the well-knownfactors, which are, and will remain the causative factors wherever the use is rampant. The HPV related squamous cell carcinoma of oropharynx is unique in a way that it is found in younger age group, responds well to almost all treatment modalities and carries a better prognosis. The HPV infection is sexually transmitted and is increasing due to changing sexual behaviour. Some groups have shown incidence of HPV positive cancer up to 70 %. Since 2010, most centres in USA treating head and neck cancer test for HPV with IHC (immunohistochemistry) and ISH (in situ hybridation). These tests are costly. The viral DNA being incorporated in lymphoepithelial tissue of oropharynx produces E6 and E7 proteins and P16 surrogate protein at different stages. These proteins are detected in tumor tissue by ISH. Detection of HPV in any head and neck cancer does not affect treatment but it only prognosticates the outcome.

PET CT has emerged as a new and effective modality to stage the disease and detect residual or recurrent disease after organ preservation therapy of chemo-radiation, with possibly early salvage surgery where indicated.

Micro vascular free flaps to reconstruct surgical defects in oral cancer have come up in a big way using autologus soft tissue and bone. This gives aesthetic and functional results and every comprehensive cancer care centre has a reconstructive team.

Advances in **radiotherapy** units like Intensity Modulated Radiation Therapy **(IMRT), Cyber knife high dose radiotherapy** with utmost precision have reduced the radiation toxicity and other related side effects. **Targeted agents** like Erlotinib are used with radiotherapy for better response. Minimally invasive surgery for laryngeal and oropharyngeal cancer has revolutionized the treatment outcomes in organ preservation with least morbidity. It started with Endoscopic LASER and now there is even a far better modality-**TORS**-Trans Oral Robotic Surgery.

With all these strides, the prime goal for head and neck cancer care giver remains prevention and early detection. This requires training of dentists and ENT surgeons. Head and neck cancer has now been recognized as a speciality in some centres across India, which offer special 3-year course in the subject.

Primary prevention is the potential strategy for long-term disease control and early detection and treatment may have limited potential to improve mortality in short term.

Shri R. J. Kinarivala Research Oration Award 2012-2013

Professor Atul Mehta
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Progress in the Treatment of Myeloma

Multiple myeloma is a malignancy of plasma cells which affects more than 30,000 sufferers and their families in the UK. Myeloma comprises 15% of all lymphoid malignancies and 2% of all malignancies. It is twice as common in blacks as in whites, commoner in males than females, and has a median age at diagnosis of 71 years. The incidence is rising, and the disease is increasingly seen in younger individuals. It is a challenging problem for Oncologists across the world – but also a dramatic illustration of the progress that has been made over the last 15 years.

It remains true that most – nearly all – patients who are diagnosed with myeloma will die of it. However, the average interval between diagnosis and death has risen from 2-3 years to 4-6 years.[1] This significant improvement is a result of improved treatments at induction, relapse and the use of maintenance strategies.

Treatment

A range of new treatments have been evaluated. Thalidomide and its analogues are front line agents despite their teratogenic effects; indeed, the molecular mediators of teratogenicity appear to play a crucial role in the susceptibility of plasma cells to the cytotoxic effects of these agents. The proteosome is a novel target for chemotherapeutic agents and myeloma protocols utilise the efficacy of not only first generation, but subsequent generation inhibitors. Histone deacetylase inhibitors, modulators of the function of chaperones such as Hsp 90, and new alkylators and anthracyclines have all been developed and are in trial protocols for the treatment of myeloma Autologous SCT is the standard of care for myeloma patients <60 years. Studies have evaluated the role of 'double' auto transplants and demonstrated that intensive approaches can dramatically improve survival in selected patients. The role of allogeneic and 'mini – allo' procedures remains controversial, however, because of high relapse rates.

Supportive Care

Lytic bone lesions occur in 70-80% of myeloma patients. It is known that these lesions occur in close relation to MM cells, and are due to increased osteoclast activity associated with reduced osteoblast (bone-forming) activity. Strategies for preventing bone disease have now been shown to improve survival; and new antibody – based bone protection strategies are being developed. Monoclonal antibodies are in trial which not only improve supportive care, but also increase recruitment of the immune system against plasma cells as well as demonstrate direct cytotoxicity to plasma cells.

There is also an increasing commitment to involving patients and their families in the choice of treatment, and in making information and psychosocial support available to patients and carers.

Future Challenges

Myeloma is a common disease and delay in diagnosis is frequent; this delay impacts in a negative fashion on survival. There is a need to increase awareness of myeloma among general physicians, general practitioners and orthopaedic surgeons. Successful treatments come at a cost – a financial cost for society and for the health care system but a cost in terms of increasing side effects for patients. The advances in myeloma over the past 2 decades have, however, changed the outlook for patients so that it can now be considered a chronic disease with multiple treatment options at relapse.

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Dr. T.B. Patel Oration Award 2012-2013

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Options for Breast Cancer Early Detection and Control in Low and Medium Resource Countries

Breast cancer incidence rates have been steadily increasing in low- and middle-income developing countries (LMICs), with an annual percentage increase ranging between 1% and 2%. In the absence of specific primary prevention strategies for reducing breast cancer incidence, early detection and prompt treatment is the major control option to improve survival and quality of life and to reduce suffering and premature deaths from it. The 5-year breast cancer survival rates in most developing countries vary between 9.5% and 66.0% which are significantly lower than in high-income countries. The poor survival reflects the limited breast cancer awareness among women and primary care practitioners, advanced clinical presentation and limited capacity for early diagnosis and effective multimodality treatment and a significant proportion of breast cancer patients not accessing care or not completing treatment due to poorly developed and poorly accessible health care services or socioeconomic barriers.

Organised mammography screening is not feasible in LMICs. There is no evidence yet to support implementation of organised clinical breast examination (CBE) based screening in routine health services and results from two randomised trials evaluating the effectiveness of CBE screening in India are anticipated in the near future. On the other hand, observational data support the effectiveness of improving breast cancer awareness among women and health care professionals, the skills of primary care practitioners in clinical suspicion of breast cancer and prompt referral and the efficiency and infrastructure of health services for diagnosis and prompt treatment in improving breast cancer outcomes and preventing premature deaths from it. Improving capacity for diagnostic imaging, histopathology and hormone receptor testing will result in accurate staging and appropriate treatment choices. Development of appropriate referral pathways for women suspected with breast cancer and improving access to early diagnosis (clinical examination, diagnostic imaging and fine needle aspiration cytology/ biopsy), basic multimodality treatment and follow-up care are equally important in this context. The substantial progress in breast cancer outcomes before the implementation of wide spread mammography screening in high income countries indicate the utility of improving breast awareness and health system approach for breast cancer control in low and high income countries. Political commitment and planned and phased investment of national resources in creating community breast awareness, appropriate health care financing mechanisms to limit out of pocket health care expenditures and in strengthening diagnostic and treatment infrastructure and resources are vital to improve breast cancer outcomes in the overall context of cancer control in LMICs.

Quality of Life (QoL) in Head and Neck Cancer (HNC) Patients - A Palliative Care Perspective

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Summary

The term Quality of Life (QoL) refers not only to the impact of disease and treatment, but to the recognisation of the patients as an individual and also as a whole person, body, mind and spirit. Pain and Palliative Care Out Patient Department is the right place to address their problem and pain interventions. A true picture of various issues of QoL in Head and Neck Cancer (HNC) is described.

Keywords: Quality of life, Palliative care, Head and neck cancer

Introduction

The term Quality of Life (QoL) has been increasingly used in medical and philosophical literatures for the past four decades.[1] Health related QoL focuses on the impact health status has on QoL. It is very relevant to measure HRQoL in chronic illness like cancer in general and Head and Neck Cancer (HNC) in particular, as impact of the disease and its treatment is very much evident.

QoL is defined as satisfaction and well being that a patient experiences on a daily basis.[2] It is a multidimensional concept that minimally includes broadly defined assessment of the Physical, Mental, Emotional and Social domains of functioning.[3] At the same time QoL is an individual perception and must take into account many aspects of life. It is a matter of concern in patients of HNC right from the stage of diagnosis, during the course of various treatments and even after prolonged disease free survival.

A formal Pain and Palliative Care Out Patient Clinic became functional on International Hospice and Palliative Care Day of 2010, in afternoon hours at our institute. We started seeing HNC patients proportionate to institutional load. Out of total 2059 new patients referred to Pain and Palliative Care services, 970 patients were of HNC in last 2 years.

Initially, we were just concentrating on management of pain and other symptoms of these patients. Their chief complains were narrated by their relation or caregivers, as patients kept sitting with hands on their head, the most painful part in HNC patients. Slowly we started evaluating their nutritional status, ability to communicate, ugly tumors (most of the time covered by scarf / towel), wounds and scars and psycho-social-spiritual issues through a questionnaire designed by our counselor.

The various domains affecting QoL in our patients are listed in Table 1. These effects are ongoing, mostly in post treatment phase. Few of these domains like dryness of mouth and shoulder pain are also present in few of our patients who are "disease free survivals" at the end of two years.

Table 1: Various domains of QoL in HNC

- Appearance and cosmoses
- Chewing, swallowing and loss of taste
- Breathing
- Speech and other disability
- Dryness of mouth or excessive salivation
- Poor oral hygiene and halitosis
- Pain
- Fungated tumors and wounds
- Socialization, sexual life
- Financial aspect, loss of job, etc
- Psychological well being, loss of self esteem

The first and foremost dimension, appearance and cosmoses were least attended and least complained domain in our patients. Lack of awareness, education, advanced stage of disease and poor socio-economic background are few of the factors responsible for it. Most of them, 70 patients out of 970 HNC, smartly covered the area with scarf or cloth. The least we could do for these patients is to teach them to do dressing of their wounds at home with Metrogyl for local application.

We found although loss of speech is disabling and laryngectomy is disfiguring, only minority of patients reported speech or appearance being more than "somewhat important" to their overall QoL. List et al[4] reports that patients priorities lie in achieving cure, followed by survival as long as possible then followed by QoL issues. In spite of this, QoL considerations assume particular importance when choosing between treatment options, new technology e.g. Intensity Modulated Radiation Therapy and clinical trials of new treatment modalities.

The second important issue was difficulty in swallowing even liquids. Two hundred and twenty five patients had difficulty in swallowing. They were advised about Ryle's Tube or Percutaneous Endoscopic Gastrotomy. More than 50% patients

refused for any type of tubes however, repeated sessions of counseling were ended up in successful insertion of tube in 108 patients. Their caregivers were educated about cost effective homemade liquid/ semisolid preparations through brochure. Lack of prior information, fear of uncertainty and anxiety are the factors for refusal of tubes for feeding purpose. Evidence suggests that providing patients with effective information regarding their condition, course of treatment and consequences, patient satisfaction and QoL is improved and their anxiety reduced.[5] Personalization of the information should be provided on disease and prognosis. Early interventions are effective at increasing nutritional intake and improving some aspects of QoL in patients with cancer who are malnourished or are at nutritional risk but do not appear to improve mortality.[6]

Severe pain was common domain in almost all patients as unrelived pain in spite of NSAIDs and weak opioids is one of the reasons for reference to Pain Clinic. Un-interrupted supply of Oral Morphine in our center is boon for these patients. Constant efforts on education of caregivers and patients on round the clock medication, refilling of prescription, assurance, change in diet and water intake to cope up with side effects, watch on stock of Morphine (with patient as well as pharmacist) are few of the solutions for effective cancer pain management. References for other modalities of pain management like radiotherapy, chemotherapy and interventional techniques for nerve blocks have its own role to play.

Most of our patients have post surgical chronic pain syndromes, loss of taste or dryness of mouth, as they have undergone combination therapy for their advanced disease stage at the time of diagnosis. The total score of QoL have been noted in literature to be significantly worse in advanced tumors than early stage tumors. Use of combined treatment is also noted to have the greatest negative impact on QoL scores.[7,8] The burden of head and neck cancer is often manifested in psychosocial dysfunction, which can have a negative impact on quality of life. We have intervened in this issue to a great extent by addressing the need of care givers, role of family members, assistance in cost of treatment, financial assistance from government and our institute etc. Insomnia, depression, anxiety, fear of death are few of the symptoms noted in our patients. But we need to overcome communication and cultural barriers of not sharing emotions and sufferings, increase patient load, difficulties in follow up and constraints due to lack of resources before having an impact on this issue. To date, there is evidence to suggest that psychosocial interventions generally provide an overall positive effect. There are several distinct categories of interventions that have been employed for patients with cancer, namely, education, emotional support, and psychotherapy. Fawzy suggested that psychosocial interventions provide an overall positive effect on quality of life, although some interventions have failed to achieve the desired results.[9]

The light at the end of this gloomy, dark tunnel is "follow up" of patients attending Palliative Care. At the end of repeated written and verbal instructions, building up trust, phone calls and home visits, 80% patients are followed up till death. We do not have studies for assessment of QoL of these patients, but it is certain that they had good pain relief, adequate control of symptoms, clean wounds, nutrition support and bereaved caregivers during their last days of life. We are also carrying out pre-treatment counseling and helping patients to choose from various treatment options, for the patients who are referred to our clinic well in advance.

Finally, let me state that whatever we have initiated and achieved so far is just a drop in ocean; there is much left to do. A planned, multidisciplinary approach, matching with our Palliative Care theme "Sharing the Care" is need of time. A systematic study of QoL assessment, translation of questionnaire, its application and audit can elucidate meaningful directions for future research and clinical care of our patients.[10] We also need to address delayed reference in nearly terminal stage, when life expectancy is less than six months. There is unmet demand to bridge the gap of number of patients on palliative treatment in institute and number attended by palliative care team. Early intervention is critical in area of nutrition, pain management and education of patients and care givers.

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Solution to Crossword Puzzle-II

Answers:

ACROSS:

1: INHIBIN
7: TAMOXIFEN
9: HPV
12: CISPLATIN
14: LEGS
16: CHORIOCARCINOMA
18: OSTEOCARCINOMA
22: ANGIOSARCOMA
23: CALCITONIN
25: LEEP
26: APML
29: IMATINIB
34: EWING
35: ANDROBLASTOMA

DOWN:

1: INSULINOMA
2: ITP
3: COLA
4: VILI
5: RET
6: FIBROADENOMA
8: AFP
9: HCGASTRIN
10: VIPoma
11: ENDOCERVIX
13: TIA
15: GASTRIN
16: CLONEI
17: CKIT
19: EI
20: CONIZATION
21: KRUKENBERG
23: CEA
24: CML
27: NIGRO
28: XRAY
30: MRSA
31: GIST
32: MRI
33: SLE

Congratulations to the Winner:

Dr. Vaishakhi Chaudhary
Resident, Gynecological Oncology

Retrospective Analysis of Hypofractionated Radiotherapy for Palliation of Locally Advanced Head and Neck Cancers

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Summary

A retrospective study of the fifty locally advanced head and neck cancers patients treated with palliative hypofractionated radiotherapy at Gujarat Cancer and Research Institute was carried out to find out efficacy and toxicity profile of the treatment schedule. Fifty patients without curative treatment options were treated with 45 Gy in 15 fractions, 3 Gy per fraction in 3 weeks. Endpoints of the study were response rates, toxicity, disease-free survival overall survival at one year. Ninety eight per cent of patients were male, more than 26% had oropharyngeal cancer and all were stage IV disease. Complete response and partial response rates were 22% and 46%, respectively. Overall response rate of 68% was achieved. Twenty four percent had stable disease, and 8% progressed during or directly after completion of treatment. Disease-free survival and overall survival were 32% and 54% at 1-year, respectively. Acute grade III skin and mucosal toxicities were observed in 4% and 10% of patients, respectively. In conclusions, our hypofractionated radiotherapy scheme is an effective, well-tolerated and safe palliative schedule in locally advanced head and neck cancers patients who are unsuitable for curative treatment options and it achieved excellent palliation with acceptable response rates, symptomatic improvement and acceptable toxicity profile.

Keywords: Hypofractionated radiotherapy, Head and neck cancer, Efficacy and toxicity, Squamous cell

Introduction

Head and neck cancers (HNC) include mainly malignant tumors arising from base of skull to the clavicle. Eighty five percent of them are squamous cell carcinoma (SCC) and their variants.[1] Sixty per cent of them are locally advanced at the time of presentation and they pose exceptionally difficult management problems even in current era of the modern oncology practice as the 5-year overall survival rate remains essentially unchanged at 50% over the past several decades.[2-4] They have also significant impact on the quality of life of the patient causing different morbidities related to the function (nutrition, breathing), cosmetics, psychological and social aspects (self esteem, communication and social integration). Out of these locally advanced cancer patients many are not candidates for the curative treatment due to disease status or poor performance status of the patient. These patients need effective palliative option to symptomatic relief and decrease disease burden as early as possible. Hypofractionated radiotherapy has long been used for palliation in many different cancer sites (bone metastasis, brain metastasis, lung, esophagus, head and neck, etc) with different schedules. Palliative care is instrumental for these patients in providing pain control, autonomy and dignity for the remainder of their lives. Palliation usually refers to alleviation of symptoms when life expectancy is limited. The goals of ideal palliation include optimal symptomatic relief, tumor response, low toxicity and minimization of the time spent in a health care facility or treatment centre. Therefore this retrospective study was performed to examine the impact of hypofractionated radiotherapy in palliation of locally advanced head and neck cancers (LAHNC) with regards to the overall response rate, overall survival, symptoms and toxicities.

Materials and Methods

A retrospective study of the fifty untreated locally advanced head and neck cancers patients registered at Gujarat Cancer and Research Institute, treated from June 2011 to September 2012 were enrolled for the study. Thorough clinical examination, examination under anaesthesia, direct endoscopic examination of pharynx and larynx was done. CT scan or MRI was done in selected patients. Patients with tumors involving oral cavity, oropharynx, hypopharynx and/or larynx were included. Due to either advanced disease and/or poor performance status they were unsuitable for radical treatment with surgery or chemoradiotherapy. Therefore, they were treated with palliative intention in order to achieve a maximal durable locoregional and symptom control. Patients who did not complete their treatment were excluded from the study.

Radiotherapy (RT)

Patients were immobilized in a supine treatment position with acrylic mask prepared in the mould room. Simulation was done on conventional 2D simulator(Ximatron-Varion). Patients were treated with conservative portals which encompass the gross disease (primary tumor and nodal disease) with a 1 cm margin. Two parallel opposed bilateral fields were mostly used. RT schedule was of hypofractionated radiotherapy with total dose of

45Gy in 15 fractions, 3Gy per fraction. Patients were treated on Co-60 machine (Th-780 and Bhabhatron-II) at 80 cm source-skin distance (SSD). Treatment was delivered five days a week for three weeks.

End points of the study were response rates (complete response [CR], partial response [PR], and overall response rate [ORR]) (ORR=CR+PR), disease-free survival (DFS), overall survival (OS), toxicity (RTOG criteria).[5] The treatment response was evaluated after 4 weeks of completion of RT and was done by clinical examination. It was recorded as CR, when both primary and nodal disease disappeared completely, as PR, if there was any residual disease (locally or regionally). Patients in whom the disease did not respond to RT were recorded as stable disease (SD), while patients who progressed during or directly after the treatment were recorded as progressive disease (PD). Patients with CR and/or PR were given additional 20 Gy in 10 fractions with conventional fractionation if general condition of the patient permitted. Following completion of treatment, patients were followed up monthly for the first six months and thereafter at an interval of 2 months.

Results

Median age was 53 years (range: 26-72 years); 98% of patients were males. Thirty eight were between 50-59 years. All patients were histopathologically SCC with stage IV disease. Table 1 shows the distribution of patients by primary tumor site. Oropharynx was the main site involved. In patients were ≥2 primary sites were involved, oropharynx and larynx were main sites.

Table 1: Distribution according to primary tumor site

Site	No.
Oropharynx	13
Hypopharynx	6
Larynx	4
Oral cavity	2
Primary site not found	2
≥2 region involved	23
Total	50

Eleven patients (22%) had CR and 23 patients (46%) had PR, resulting in an ORR of 68%. Twelve patients (24%) had SD and 4 patients (8%) had PD during or after the RT. Total 21 patients were given additional RT of which nine were CR and twelve were PR. Four patients had received chemotherapy while 25 patients were followed up with only symptomatic treatment. At the end of one year, 16 patients were alive without disease and 11 were alive with disease thus DFS and OS at 1 year in our study group was 32% and 54%, respectively.

None of the patients died because of acute radiation toxicity. Grade III skin desquamation and grade mucositis were reported in 2(4%) and 5(10%) patients, respectively. Eight patients (16%) experienced acute grade III dysphagia. Main acute toxicities were of grade I and II. No grade IV acute toxicities were observed. There was no treatment break due to acute side effects of treatment. Exact number of late toxicities were not noted, but no grade IV late toxicities were seen.

Before starting radiotherapy 78% patients had complaint of pain (headache, earache and pain in neck) and needed strong analgesic; 28% with dysphagia, with solid and semisolid food, needed feeding tube and 40% with hoarseness of voice. One month postradiotherapy symptoms and clinical evaluation was done. All patients had significant pain relief, swallowing improvement and quality of voice improvement. Only 24% patients who had persistent pain postradiotherapy were referred to pain clinic. Swallowing with solid and semisolid food was achieved in all patients where as only 14% patients needed Ryle's tube feeding. Quality of voice was near normal to fair in communication except 14% patients were having poor quality of voice and some patients need tracheostomy.

Discussion

Patients with untreated advanced stage head and neck squamous cell carcinoma (HNSCC) have a median survival of approximately 100 days.[6] Historically, patients with unresectable advanced HNSCC treated by RT alone have loco-regional control rates between 50 and 70% and 10-20% 5-year survival rates.[7-9] Most of these patients die of loco-regional disease progression. Addition of chemotherapy in a curative setting has improved disease control and long-term survival.[7,8] However, patients who are inoperable and/or unable to tolerate curative chemoradiotherapy, as was the case in our study population, still require some form of palliative treatment to control their locoregional disease and to alleviate symptoms. The information about the optimal palliative regimen for incurable HNSCC in the current literature is scanty. The optimal palliative RT schedule should provide worthwhile regression of the tumor and local symptoms within a short time with minimal toxicity. From radiobiological, economic and logistical points of view, a hypofractionated schedule would be the most suitable option. Short treatment time has radiobiological advantage against accelerated repopulation in tumor and it is also necessary because these patients are usually of age, have a poor performance status and significant co-morbidities. Less number of treatment fractions allows more efficient use of resources which is also an important factor in developing countries like India.

Because of the above advantages of a hypofractionated treatment schedule, we treated this group of HNSCC unsuitable for curative treatment options with 15 fractions of 3Gy. We have achieved an excellent response rates (CR 22% and ORR 68%), reasonable DFS-rates (32% at 1 years) and reasonable OS-rates (54% at 1years) with low rates of acute toxicities and acceptable late toxicity profile.

Hypofractionated radiotherapy has been used for palliation in LAHNSCC with doses ranged from 3-6Gy per fraction. There is no uniform guideline or criteria regarding which fractionation schedule would be appropriate for particular patient of LAHNSCC. Different studies achieved overall response rate from 53% to 83%. We achieved overall response rate of 68% after one month of completion of RT. CR rate was 22% which was lower than the reports of other studies (45% and 39%).[10,11] Moreover, in the present study the PR rate was 46% which was comparatively higher than that reported by Al-mamgani et al (28%),[10] Kancherla et al (33%)[11] and Mohanti et al (37%) studies.[12] Further, Al-mamgani et al (40%)[10] and Kancherla et al (42%)[11] have reported a lower overall survival rate compared to the present study (54%) at 1 year. On the other hand the achieved DFS (32%) at 1 year was observed to be similar to the report of Al-mamgani et al study.[10] Other studies have observed wide range of toxicities. Al-mamgani et al, [10] had observed acute grade ≥III skin and mucosal toxicities in 45% and 65% of patients, respectively. In Hypo trial,[13] grade III mucositis and dysphagia were experienced in 26% and 11%, respectively while Mohanti et al[12] observed only dry desquamation and patchy mucositis, which healed over one month. Chen et al[14] in their review noted that 9% of those 47 treated with the RTOG regimen developed grade III+ toxicity compared with 37% among those treated with other schedules. In the present study we observed acute grade III skin and mucosal toxicities in 4% and 10% of patients, respectively.

Conclusion

This study proves the efficacy and safety of this hypofractionated schedule 45Gy in 15 fractions in 3 weeks used at our institute in a palliative setting for HNSCC patients who are unsuitable for curative options. Fifty four per cent patients have survived beyond 1 year after the treatment; with 32% were disease free. Treatment was well tolerated with improvement in symptoms and no treatment breaks. Because of these encouraging results and its radiobiological, economic and logistical advantages, this hypofractionated scheme has been adopted by our institution as palliative RT-scheme for patients with HNSCC who are unsuitable for curative treatment options as surgery or chemoradiotherapy.

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Crossword Puzzle-III

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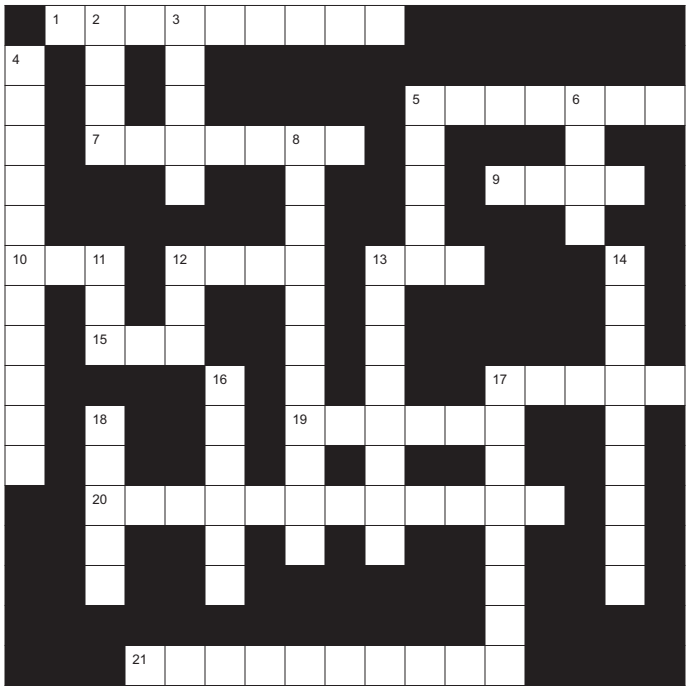

ACROSS:
1. Sibling _____ is essential in patients of Retinoblastoma (9)
5. _____ with tobacco increases risk of head neck cancers (7)
7. 30% reduction in sum of longest diameter of target lesion is _____ response (7)
9. 'School of ____' appearance in Fibromatosis coli; aquatic (4)
10. Plasmablastic lymphoma is seen in patients with ___ infection (3)
12. Nimotuzumab is IgG1 antibody against _____ (4-abbrv)
13. Syndrome; Plural of man (3)
15. Malignant potential on PET scan; Type of car (3- abbrv)
17. Indian Congress President got operated at _____ Kettering Hospital (5)
19. Commonest head neck cancer in males is of _____ (6)
20. Cinalacet is a _____ drug (12)
21. Commonest symptom of retinoblastoma is ____ (10)

DOWN:
2. Standard chemotherapy regimen for lymphoma (4-abbv)
3. _____ cranial metastasis is rare in patients of GBM due to absent lymphatics (5)
4. Hypercalcemia is a feature of _____ carcinoma (11)
5. Mr Steves with pancreatic malignancy was CEO of_____ (5)
6. Most sensitive technique for diagnosing retinoblastoma (4- abbrv)
8. Commonest glioma (11)
11. Pain scoring system (3-abbrv)
12. Virus causing nasopharyngeal carcinoma (3-abbrv)
13. Commonest malignancy in Ppregnancy (8)
14. _____ psitacci is a likely infective cause of orbital lymphoma (9)
16. Sun sign after Gemini (6)
17. Indian cricket vice captain had mediastinal _____ (8)
18. Gene linked with aggressive prostate malignancy (5)

Magnitude of Head and Neck Cancer in Patan District, Gujarat

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Summary

This study reports the magnitude of head and neck cancers amongst the population of district Patan, Gujarat. All new cases of head and neck cancers diagnosed between 1st January to 31st December, 2011, in the defined area of Patan district were included in this study. Apart from the Gujarat Cancer and Research Institute (GCRI) which is the base institution, data were also obtained from various other sources such as government, private hospitals, nursing homes, pathological laboratories, private consultants and death registration units of Patan district as well as other than Patan district. A total of 171 head and neck cancers were reported which accounted for 36.23% of total cancers. Among males, 147 cases (47.42%) and among females, 24 cases (14.81%) were head and neck cancers. Majority of the subjects were in the age range of 35-64 years. Cancer of tongue was the commonest site in both sexes. Head and neck mortality was more prevalent in the age group of 70-74 years for males and above 75 years for females. The study helped in understanding the possible behavior patterns in head and neck cancers. Since, tobacco and alcohol are the most common risk factors for head and neck cancers; the study implies an urgent need for taking appropriate preventive measures for cancer control among the population of Patan district.

Keywords: Magnitude, Head and neck cancers, Population based cancer registry, Patan district

Introduction

Cancer is a leading health problem in India, with approximately 1 million cases occurring each year. Over 200,000 cases of head and neck cancer (HNC) occur each year in India versus 30,000 for USA. Cancer accounts for 8% of the deaths in India.[1] HNC are the sixth most common cancers and are a major cause of cancer morbidity and mortality worldwide. In India and South East Asia, oral cancer incidence accounts for up to 40% of all malignancies.[2] The most common risk factors associated with HNC are tobacco and alcohol use with significant interaction observed between the two.[3] The prevalence of cancer is often strikingly dissimilar in different groups of population, varies greatly from one community to another, and differs in different communities in the same geographic location, depending on the practices and lifestyle of the people in that location. To identify and quantify the etiological profile that might be implicated in a selected population, it is essential to determine the behavioral patterns, habits, customs and environmental background of the group under study. An attempt was made here to study the magnitude of head and neck cancers occurred among the population of Patan district. It will give the scientific basis for the planning and organization of cancer control in Patan district.

Materials and Methods

In the study, active registration of cancer cases done from the Patan district covered 7 talukas: Patan, Sami, Harij, Chanasma, Sidhpur, Radhanpur, and Santalpur having 524 villages with population of 11,82,709 as per census 2001. For this study more than 100 sources were covered for cancer registration. The Gujarat Cancer and Research Institute (GCRI) is a regional cancer center in Gujarat and contribute a major share. At the time of registration at GCRI, trained staff filled the core performa by direct interview with patient or relative. They also visited various sources of registration in coverage area of all government and private hospitals, nursing homes and diagnostic laboratories besides base institution (GCRI) and death registration units in defined area and actively pursued and collected information on cancer cases reported.

Usually the sites lip, tongue, mouth, salivary gland, tonsil, oropharynx, nasopharynx, hypopharynx, pharynx, nose and sinus, larynx and thyroid are considered as head and neck cancers.[4] Data collection, data entry, coding and analysis have been done as per the National Cancer Registry Programme, (ICMR).[5] The sites of HNCs were classified on the basis of ICD-10 for topography coding.[6] Third edition of the International Classification of Disease for Oncology had been used for morphology coding.[7]

All new cases of HNCs diagnosed during the year 2011 (1st January to 31st December) in the defined area of Patan district formed the incident cases and thus included in the study. The inclusion criteria was those patients who lived in the defined area of Patan district for a minimum period of one year at the time of first diagnosis.

The percentage of males and females HNCs from total cancers were calculated. Age group and gender wise distribution for HNCs incidence and mortality were also calculated. In this study analysis of Crude Incidence Rate (CIR), Age Specific Incidence Rate (ASpR) and Age Adjusted Incidence Rate (AAR) were calculated. CIR is calculated by dividing total number of new cases registered during a year by corresponding population of that year and

Table 1: Number (n), percentage (%) and Age Adjusted Incidence Rate (AAR) for head and neck cancer in Patan district - 2011

ICD Codes	Site	Male			Female		
		n	%	AAR	n	%	AAR
C00	Lip	0	0	0	0	0	0
C01-02	Tongue	44	29.93	8.92	8	33.33	1.36
C03-06	Mouth	34	23.13	6.14	7	29.17	1.29
C07-08	Salivary Gland	02	01.36	0.38	1	04.17	0.16
C09	Tonsil	08	05.44	1.65	1	04.17	0.19
C10	Oropharynx	04	02.72	1.08	0	0	0
C11	Nasopharynx	01	00.68	0.24	1	04.17	0.19
C12-13	Hypopharynx	23	15.65	5.41	1	04.17	0.22
C14	Pharynx	12	08.16	2.54	0	0	0
C30-31	Nose & Sinuses	01	00.68	0.24	0	0	0
C32	Larynx	15	10.20	3.17	1	04.17	0.22
C73	Thyroid	03	02.04	0.54	4	16.67	0.68
	Total	147	100	30.31	24	100	4.31

Table 2: Number (n) and percentage (%) of head and neck cancer cases by broad age group and gender

Age group (In Years)	Head and Neck Cancer cases					
	Male		Female		Total	
	n	%	n	%	n	%
15-34	010	06.8	04	16.67	014	08.19
35-64	104	70.75	14	58.33	118	69.01
65+	033	22.45	06	25.00	039	22.81
Total	147	100	24	100	171	100

multiplying the result by 1,00,000. ASpR refers to the rate obtained by dividing the total number of cancer cases by the corresponding estimated population in that age group and multiplying by 1,00,000. As age increases, the incidence of cancers also increases, therefore, with an increase in the median age of population the cancer incidence also increases in the community. In order to make rates of cancer comparable between two populations or countries, the five year age distribution of the world standard population are taken into account to obtain the age AAR.[8]

Results

During the year 2011, a total of 472 cancer cases (310 males and 162 females) were registered in Patan district. Out of them, 171 (36.23%) were HNC cancers. Out of 171 HNC, 147 (86%) were males and 24 (14%) were females. It shows the higher male preponderance in HNCs. The CIR per lac population in males was 20.8 and in females 3.68. The corresponding AAR was 30.31 and 4.31. Male/Female ratio was 6.13:1. Gender wise distribution of HNC is given in Table 1. The most common sites of cancer in both males and females were tongue (29.93 and 33.33%) and mouth (23.13 and 29.17%). This was followed by hypopharynx (15.65 and 4.17%), larynx (10.20 and 4.17%), thyroid (2.04 and 16.67%), tonsil (5.44 and 4.17%), salivary gland (1.36 and 4.17%), nasopharynx (0.68 and 4.17%). The first five leading sites of HNC for males and females are represented in Figure 1 and 2.

Table 3: Number (n) and percentage (%) of head and neck cancer deaths by gender in Patan district – 2011

Site	Male		Female		Total	
	n	%	n	%	n	%
Tongue	4	14.81	2	50	6	19.35
Mouth	5	18.52	1	25	6	19.35
Tonsil	3	11.11	0	0	3	09.68
Hypopharynx	7	25.93	1	25	8	25.81
Pharynx	4	14.81	0	0	4	12.90
Nose & Sinuses	1	03.70	0	0	1	03.23
Larynx	3	11.11	0	0	3	09.68
Total	27	100	4	100	31	100

Percentage of HNC by broad age group and gender are shown in Table 2. Majority of HNC cases (69.01%) were found in 35-64 year age group in both the genders (male-60.82%, female-8.19%). Incidence of HNC cases was 22.81% above 65 years of age group, 8.19% cases for 15-34 years of age group and none in pediatric age group.

Figure 3 illustrates age specific incidence rates (ASpR) with five year age group in both the genders. The age specific rates were found to follow the general pattern of increase with age. The age specific incidence rates of HNC showed the peak incidence in 70-74 years in males and above 75 years in females. Except in the age group of 25-29, the age specific incidence rates for females were found to be generally lower than males.

Distribution of number and percentage of HNC deaths by gender is depicted in Table 3. Total 31 HNC deaths were found in this study out of which 27 in males and 4 in females. Hypopharynx (25.93%) and mouth (18.52%) were common sites in males where as tongue, hypopharynx and mouth sites were found in females.

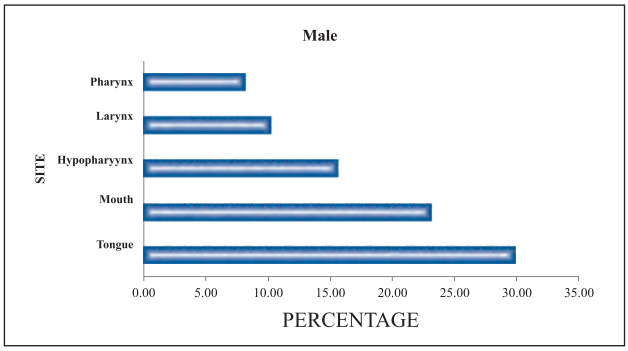

Figure 1: Leading sites of head and neck cancer for male in Patan district-2011

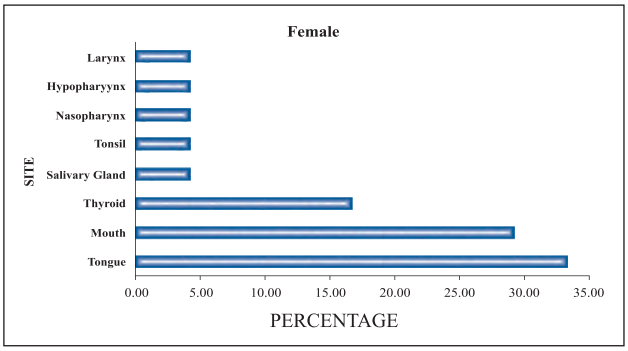

Figure 2: Leading sites of head and neck cancer for female in Patan district -2011

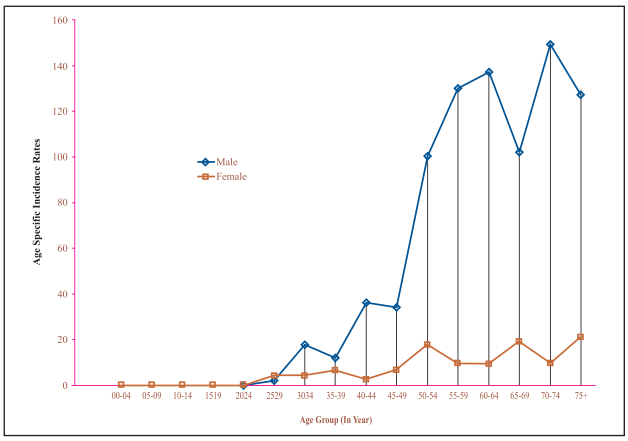

Figure 3: Age Specific Incidence Rates (ASpR) per 1, 00,000 populations with five year age group by gender

Discussion

This is a population based study which has covered Patan district of Gujarat. During 2011, a total of 171 HNC patients were registered, which contributed 36.23% of total (472) cancer cases. Higher incidence in male HNC (86%) was observed than females (14%). The age adjusted incidence rates of HNC in Patan district were 30.31 and 4.31 per 100,000 populations in men and women respectively. The commonest HNC in both the sexes were those of tongue and mouth with rates of 8.92 and 6.14 for male and 1.36 and 1.29 for female. The average age adjusted incidence rates for HNC in males and females varied from 46.1 and 54.2 in Barshi registry to 116.2 and for 125.8 Delhi registry. In males for the sites tongue and mouth, highest incidence rate was noted by Bhopal registry and lowest in Barshi. For mouth in females the highest incidence was noted in Bangalore and the lowest in Barshi (1.2).[4] Highest age specific incidence rates of HNCs observed in 70-74 years age group in males and above 75 years age group in females. Out of total 31 HNC deaths hypopharynx and mouth sites are common in male deaths and tongue, hypopharynx and mouth sites were common HNC deaths in female.

Conclusion

The data helps in understanding the possible behavior patterns in HNC patients. Hence, there is an urgent need for taking appropriate preventive strategies through common risk factor approach along with intense educational program to revert back the present scenario of such preventable disease.

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Interventional Pain Management in Head and Neck Cancer Patients

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Summary

Interventional pain management has though minimum but definitive role in cancer pain management. Incidence of head and neck cancer is 52% in our institute. These patients need pain management during various stages of their disease. This study was carried out to find the role of OPD based interventional blocks as an adjuvant to oral analgesic in head and neck cancer pain management. Head and neck cancer patients attending pain and palliative care clinic in Gujarat Cancer and Research Institute from October 2010 to October 2012 were evaluated for various intervention blocks. Out of 1997 patients, 885 patients were of head and neck cancer. They had severe pain (VAS score 8-10). They were given various types of blocks like deep cervical plexus block, superficial cervical plexus block, glossopharyngeal nerve block and interscalene block with injection bupivacaine hydrochloride 0.125% and injection methylprednisolone. More than one nerve blocks were received by 76.08% of patients. Nerve blocks were repeated in 56.4% patients. Visual analog scale (VAS) of all patients decreased significanly from 8-10 (mean 8.0+/-0.43) to 2-3 (mean3.0+/-0.3) (P<0.001) immediately after block. Mean duration of pain relief was 15.8+/- 0.23 days. Requirement of analgesic was either same or reduced in subsequent weeks. One patient had bradycardia during procedure which was treated with injection atropine. One patient had giddiness and bradycardia which was treated with injection atropine and intravenous (i.v.) fluid. No other complications were noticed. Other supportive treatment was continued. Simple interventional blocks combined with pharmalogical method improve pain relief in head and neck cancer patients.

Keywords: Head and neck cancer, Pain management, Interventional block

Introduction

Majority (70-90%) of patients of cancer pain can have satisfactory pain relief with treatment plan using WHO analgesic ladder.[1-4] Nearly 5 -10% of patients with advance cancer, who are not able to achieve adequate pain relief in spite of optimal conventional pharmacological management, can be treated with nerve blocks and other technique for pain management.[1-4] Many patients could be benefited from the use of interventional pain management techniques because it provides better pain relief with reduced dose requirement of opioids and fewer side effects.[1] Cost of the procedure is a major concern in poor patient. It made us to think about OPD based nerve blocks using surface landmark to minimize cost of treatment. It needs multidisciplinary decision making with careful consideration of the risk and benefits of technique. We present here the results of interventional block for head and neck cancer pain management which were carried out in last two year.

Materials and Methods

Head and neck cancer patients attending pain clinic from October 2010 to October 2012 were evaluated for various blocks. The inclusion criteria for study were 1) head and neck cancer patients, 2) patients with moderate to severe pain, 3) patients on oral analgesics and had inadequate pain relief, 4) patients with excessive side effects of oral medications like nausea, vomiting and constipation, 5) patients not having fungated growth in area of injection, 6) patients and relatives willing for blocks.

All patients were treated with oral analgesics according as per WHO guideline. They were on tablet morphine 60-120 mg/day, non steroidal anti inflammatory drugs, antidepressant and on other supportive treatment according as per their symptoms. Type of pain was continuous, either dull aching, throbbing, pinpricking or burning.

All patients and their relatives were explained about the procedure and complications. Informed written consent was obtained from patients and their relatives. Intravenous line was secured and 500 ml dextrose saline was started. SpO2, ECG and NIBP monitors were applied and injection glycopyrolate was given to all patients.

Superficial cervical plexus block[5,6] was given to all patients as all of them had pain either around anterior, lateral or posterior aspect of neck. They received 0.25% of 15 ml injection bupivacaine hydrochloride in fan shaped manner below midpoint of posterior border of sternocleidomastoid muscle. Deep cervical plexus block[5,6] was advised in patients who had pain in distribution of C_2, C_3 or C_4 dermatomes. A line is drawn from the tip of mastoid process to Chassaignae's tubercle of C_6 which is palpable at the level of cricoids cartilage. C_2 transverse process is commonly palpated one finger breath caudal to the mastoid process on this line and C_3 and C_4 are at similar interval 1.5 cm caudally on the same line. A needle (22 G 2.5 inch) was directed medially and caudally to hit transverse process of C_2, C_3, C_4 to obtain paraesthesia. After negative aspiration for blood or cerebrospinal fluid (CSF), 2ml of 0.125%

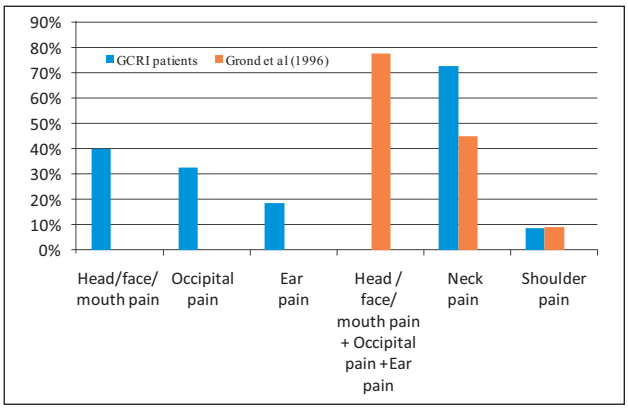

Figure1: Site of pain

Table 1: Primary information

Study duration	**October 2010-12**
No of patients who had attended PPC OPD	1997
No patients of Head and neck cancer pain	885
No of patients who had received block	92
Mean age of patients (years)	39.7
Sex M:F	14:8

bupivacaine hydrochloride with 1ml (40mg) of methylprednisolone was injected.

Glossopharyngeal nerve block[5,6] was advised in patients who had ear pain. A 1.5 inch 22G needle attached with 5cc syringe is inserted at a midpoint on a line joining the angle of mandible to tip of mastoid process of occipital bone. The needle is directed medially to locate the styloid process. After contact with bone the needle is withdrawn and walked of the styloid process posterior. As soon as contact lost, the needle is adjusted posterior to this at the same depth as the styloid process, (maximum 3 cm). After careful aspiration (reveal no blood or CSF) 2ml of 0.125% bupivacaine hydrochloride with methylprednisolone was injected. In patients who had been operated for RND, removal of sternocleidomastoid muscle places the styloid process and adjacent nerve and vessels more superficial.

Interscalene block[7] was given to patient who had shoulder pain. This block is most commonly performed at the level of C_6 vertebral body. Interscalene groove is identified. Needle is inserted slightly caudally and posterior direction. After eliciting paraesthesia injection bupivacaine hydrochloride 0.125% 10 ml with 40 mg of injection methylprednisolone was injected.

Results

Table 1 shows primary information. Total 1997 patients had attended pain and palliative care OPD. Out of this 885 patients had head and neck cancer. Ninety two patients had received interventional block along with other oral medication. Their disease status was stage III or stage IV cancer.

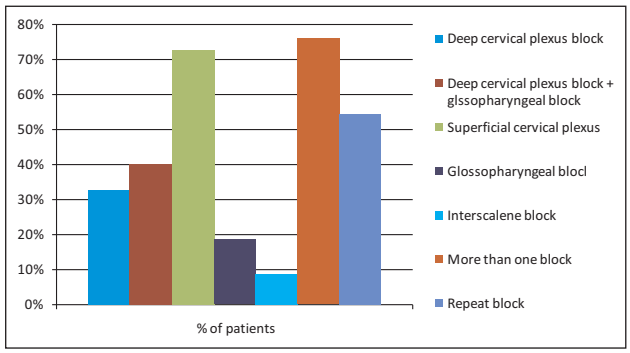

Figure 2: Different type of interventional blocks performed

Table 2 shows incidence of pain in patients attending pain and palliative care OPD. It was compared with various other studies.

Figure1 shows site of pain. In our study 40.21% patients had head, face and mouth pain, 32.60% patients had pain around occipital region and 18.47% patients had ear pain, 72.82% patients had neck pain and 8.69% of patients had shoulder pain which was comparable with site of pain in Grond et al study.[8]

Figure 2 shows names of block a patient received. Sixty-seven patients received superficial cervical plexus block, either along with Glossopharyngeal nerve block or with deep cervical plexus block. Thirty patients received Deep cervical plexus block and thirty seven patients received both deep cervical plexus and glossopharyngeal nerve block. Eight patients received interscalene block. Seventy patients received more than two blocks at a time.

Visual Analog Scale (VAS) decreased significantly from 8-10(mean 8.0+/-0.43) to 2-3(3.0+/- 0.3) ($P<0.001$) immediately following block. Mean duration of analgesia was 15.8+/- 0.23 days. Block was repeated in 54.44% patients (Table 3).

Discussion

In advance cancer, pain control is among the highest priorities for patient and for those close to them. Patients with advance head and neck cancer forms a major subgroup of patient who has attended pain and palliative care OPD, i. e. 44.31% in our institute.

Prevalence of pain in patients with head and neck cancer is highest of all cancer at 70%. Patients with brain cancer and squamous cell cancer of head and neck were amongst those with highest prevalence of pain 90% and 86% respectively. Prevalence of pain at diagnosis of head and neck cancer vary from 40 to 84%. Higher incidence of pain was noted in more advance disease i.e. in stage III and IV which was comparable with our data.[2]

Etiology of pain can be due to cancer itself, due to treatment of disease such as surgery, radiotherapy or chemotherapy or unrelated to cancer like arthritic

Table 2: Prevalence of pain in patient with head and neck cancer, various study[2]

Study	Stage of disease	Prevalence of pain
Bjordal (1992)	Not mentioned	18% quite a bit or very much
Chaplin and Morton (1998)	Newly diagnosed, curable	48% at diagnosis (8% severe) 25% at 12 months(3% severe) 26% at 24 month(4% severe)
Forbes (1997)	End stage cancer	79% in final evaluation
Talmi (1997)	Stage III and IV	77%
Saxena (1995)	Stage III and IV	84% 55% moderate to severe 50% unrelieved
Chua (1999)	60% Stage III and IV	100% at presentation 52% severe
Our study (2010-12)	Stage III and IV	44.31% 12.65% unrelieved

pain. It is noted that around 77% of patient had shoulder dysfunction and moderate to severe pain after radical neck dissection and 31% of patients develop shoulder arm syndrome after radical neck dissection.[2]

Type of pain can be nociceptive, neuropathic or mixed nociceptive and neuropathic. Nociceptive pain results from tissue damage due to any reason like tumour pressure, infiltration of surrounding tissue or due to neuroma formation. Any somatic nerve can become entrapped leading to chronic pain.[6] Neuropathic pain for head and neck cancer may involve all sensory nerves in face, skull, neck and shoulder resulting into burning pain, shooting pain or allodynia.[2] Occipital neuralgia originate as sensory branches C_2, C_3, C_4 entrapped causing pain in occipital region which may extend to top of head. In our study site of the pain was comparable with site of pain in Grond et al study[8] (Figure 1). All patients were on pharmacological management of pain according to WHO guideline. The three steps WHO Analgesic ladder for cancer pain recommends the use of opioids for management of moderate to severe cancer pain. But the fact is that around 5-10% of patients will not have adequate pain relief according to WHO guideline and need to incorporate additional strategies for provision of pain relief that is interventional pain management.[1-4] In our study, 12.65% of patients had not achieved satisfactory pain relief with pharmacological management of pain and out of that 10.39% of patients were given various interventional blocks (Figure 2).

Interventional blocks are indicated in chronic, intractable terminal pain that are not responding to WHO step 3 ladder for cancer pain management.[2,3] It has advantages like longer duration of analgesia without long term hospitalization and reduces frequency of visits to pain clinic. Patient can remain at home pain free even in area where medical help is scarce. Cancer pain in distribution of a peripheral nerve or nerve plexus can be moderated by performing nerve block with local anaesthetic agent or neurolytic agent. Neurolytic peripheral nerve blocks provide good initial pain relief, but development of neuritis shortly thereafter makes it less appropriate in majority of patients.[1]

Patients with cancer often have more than one distinct pain syndrome or more than one location, as sensory innervations in head and neck region arise from multiple cranial or cervical nerves. So it was not possible to relive pain with single nerve block. In patients with cancer of head and neck, block of trigeminal, glossopharyngeal, laryngeal or cervical plexus either alone or in combination can often provide excellent pain relief.[4] In our setup we provided interventional block as per dermatome distribution of pain requirement and around 76.08% of patients required multiple or more than one block (Table 3). Occipital nerve blockade with local anaesthetic can provide pain relief and if it is combined with steroid it may provide prolonged analgesia.[9] Interscalene or axillary brachial plexus block using continuous infusion of local anaesthetic has been used for intractable neuropathic pain of upper extremity associated with carcinoma of breast or lung.[7]

Table 3 : Effects of interventional block (Visual Analog Scale-VAS)

Mean VAS before block	8+/- 0.43
Mean VAS after block	3+/-0.3
Mean duration of analgesia	15.8 days
Complications	Bradycardia-in 1 patient Bradycardia and hypotension in 1 patient

Peripheral nerve blocks using continuous infusion of local anaesthetic agent with or without opioids provide good pain relief and persistent analgesia has been provided even after cessation of infusion. It is not possible to completely abolish the

need for analgesic administered oral, systemic or parenteral with single intervention block.[1] However, the dose requirement may change drastically with major improvement in analgesic or avoidance of side effects of opioids. As observed in our study duration of analgesia was of few days but their pain was manageable with oral medication.

Applying regional blocks to head and neck cancer is safe procedure. However injection of local anaesthetic into this part of body can be associated with an incidence of syncope, damage to adjacent structure or spread of drug to central nervous system.[5] Use of image guidance will provide more precision and increase safety of technique.[10]

Conclusion

Simple OPD based intervention block combined with pharmacological method provides better pain relief and reduce opioids requirement in cancer patients.

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"I was very shy as a kid. I spent my childhood pretty much as a nature nerd, and I spent a lot of time outside by myself. But I developed a sense of focus, an ability to see the patterns in the natural world."

Janine Benyus,
Biologist, Educator, Author of "Biomimicry"

Imaging of Retinoblastoma

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Summary

Even after multiple awareness programmes, retinoblastoma still presents late in developing country like India where major crowd is still uneducated. Most of the patients present at advanced stage when eye / vision preserving treatment has no role and enucleation becomes essential. In this pictorial study we have tried to show various features of retinoblastoma on imaging modalities with its complication and its differential diagnosis. We have also discussed role of imaging in post treatment patients. Imaging features of retinoblastoma may help doctors to diagnose retinoblastoma earlier thus help the patient to opt for eye/vision preservating treatment options.

Keywords: Retinoblastoma, USG, CT, MRI, Ocular, Childhood

Introduction

The most common primary ocular malignancy of childhood is retinoblastoma. It is highly malignant tumor. In 1970, Tso and colleagues established that the tumor arises from photoreceptor precursors.[1] Common incidence of retinoblastoma is 1 case per 18,000-30,000 live births. In developed countries retinoblastomas are detected early while in developing and underdeveloped countries, they are often detected after they have invaded the orbit or brain. High-resolution sonography (HRSG) is highly sensitive method for diagnosing small intra-ocular retinoblastoma. Computerized Tomography (CT) and MRI are good modalities to determine local extension of lesion, distal metastasis and to demonstrate post treatment residual /recurrent lesion or complication.

Material and Methods

We studied 100 patients of retinoblastoma over period of 3 years from year 2009-2012. Out of 100 cases, 40 were females and 60 were males. Age was between 2 months to 8 years. We have performed USG of orbit on SIEMEN G50 machine and LOGIQ P5 machine using 7.5-10 MHz linear probe. CT scan was performed on six slice Siemens Somatom machine and MRI was performed on Hitachi Aperto system. The images shown in this article are representative cases of our study.

Discussion

The most common presenting sign of retinoblastoma is leucocoria, accounting for about 56.1% of cases. Retinoblastoma can cause secondary changes in the eye, including glaucoma, strabismus, retinal detachment, and inflammation secondary to tumor necrosis. Proptosis is a more common presenting symptom in most underdeveloped countries while leucocoria is common presenting symptom in developed country.

Most retinoblastomas are quite advance at the time of diagnosis hence enucleation or external beam radiotherapy (EBRT) remains the only therapeutic option in such cases. Laser ablation, photocoagulation, and cryotherapy are newer modalities of treatment. Early diagnosis of retinoblastoma is necessary because if it is diagnosed early enough, it can be managed with new treatment modalities without enucleation or any form of irradiation. It is apparent that if all retinoblastoma could be recognized either in utero or shortly after birth, most of them could be treated promptly by the aforementioned methods, thus saving the child's life and salvaging vision.[2] Routine clinical screening of all parents and sibling of retinoblastoma patient is recommended to provide early detection of retinoblastoma and treatment at presymptomatic disease stage.[3]

HRSG is a prime imaging modality for superficial and small parts scanning. Excellent tissue details with anatomical landmarks are the hallmark of the technique. The prerequisite for HRSG is high frequency transducers ranging from 5 MHz to 15 MHz with short focus. The advantages of HRSG are that it is a noninvasive, cost effective and rapid investigation. No specific preparation or sedation is required. USG is very useful for the detection and differentiation of intraocular masses and in diagnosis of retinoblastoma.[4]

Intraocular Retinoblastoma -patterns of tumor growth

Endophytic growth

Endophytic growth occurs when the tumor breaks through the internal limiting membrane. Small Retinoblastoma is smooth, dome shaped and shows homogenous hypoechoic echopattern (Figure 1) however, large tumors are highly irregular and heterogeneous in texture. Usually it arises from retina and fills the posterior segment (Figure 2,3). But in rare case, tumor involving all the surfaces of retina can be found on HRSG known as retinoblastoma circumference. Calcification is typical feature of retinoblastoma and is accompanied with acoustic shadowing. The presence of intraocular calcium in children under three years of age is highly suggestive of retinoblastoma (Figure 4). Rarely calcification is absent (Figure 5).[5] Effected eye may show normal or

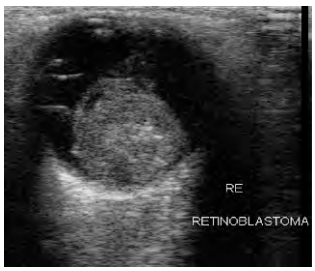

Figure 1: A 3 years old boy with endophytic retinoblastoma in right eye. USG shows well-defined hypoechoic mass in vitreous cavity forming acute angle with retina and showing few echogenic calcified spots

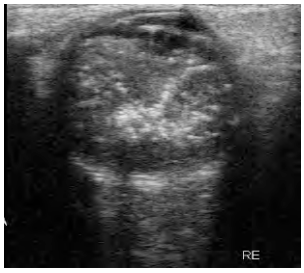

Figure 2: Huge retinoblastoma in right eye. USG showing hetero-geneous echopattern mass lesion almost completely filling vitreous cavity with internal dense calcification. Anterior chamber appears normal

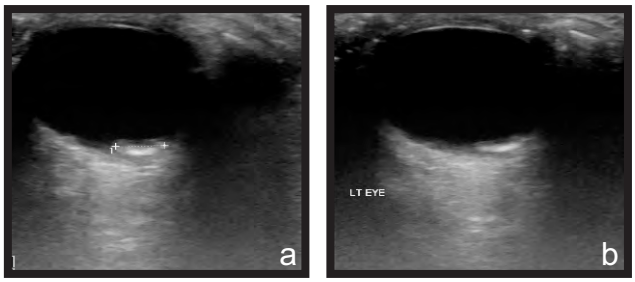

Figure 4: A 3 years old male child presented with complain of diminished vision in both eyes. USG of right eye showed presence of 6 mm sized calcification (a) and 8 mm sized calcification in left eye (b)

higher than normal axial length. Retinoblastoma in microophthalmic eye is extremely rare. HRSG can also tell about the extra-ocular extension of the tumor. The eye is usually of normal size or larger than normal.[6] Retinoblastoma may be unilateral or bilateral (Figure 6, 7), focal or multifocal (Figure 6).[7]

Endophytic tumor growth pattern can be associated with vitreous seeding. Here small fragments of tissue are separated from the main tumor. In some instances, vitreous seeding may be extensive allowing tumor cells to be visible as spheroid masses floating in the vitreous and anterior chamber. Secondary deposits or seeding of tumor cells into other areas of the retina may be confused with multicentric tumors. Differentiation between multifocal lesion and tumor seedling may be difficult.[7] Vitreous seedling produces vitreous echogenic debris on HRSG. Vitreous echogenic debris may also results from hemorrhage or increased globulin content.

Retinoblastoma can extend to involve anterior chamber. On HRSG few solid and cystic nodules can be seen. Tumor can be discovered posterior to iris, on the lens capsule and over ciliary process. Other HRSG findings include angle closure related to iris, neovascularization and uveal thickening.[8]

Retinoblastoma can locally extend and involve retro bulbar space (Figure 8) and optic nerve (Figure 9)**.** CT is better modality to see intra-lesional

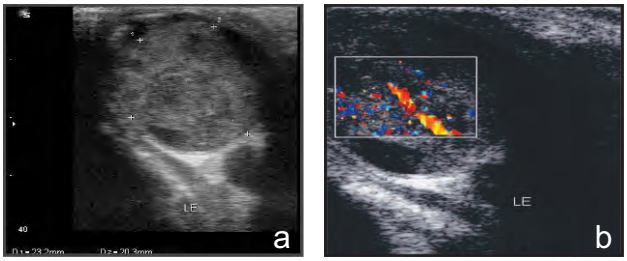

Figure 3: USG showing huge retinoblastoma in left eye with thickened optic nerve suggestive of optic nerve involvement (a), Doppler study of lesion shows high vascularity within mass suggestive of high grade malignant nature (b)

calcification (Figure 10), widening of optic canal (Figure 11) and local bony erosion (Figure 12)**.** MRI is modality of choice to detect optic nerve involvement (Figure 13)**.**

Retinoblastoma can lead to metastasis at different site. Cases have been reported with metastasis to cerebrum (Figure 14), dura matter (Figure 15), leptomeninges (Figure 16), cerebellum (Figure 17), brain stem (Figure 18), liver (Figure 19), ovary,[9] skin (Figure 20), bone (Figure 21, 22) and lung (Figure 23). MRI is modality of choice for metastasis in brain and dura matter.[10] The vascularity indicates tumor activity-hypervascular and active lesion. Vascularity regresses with treatment.[11] Echography is also useful in monitoring size of tumor and complication in post chemotherapy or radiotherapy status. In most instances, tumors that recur or continue to grow after radiotherapy tend to exhibit low to medium reflectivity and do not show calcification. Tumor tends to outgrow their blood supply resulting in areas of necrosis.[7,12]

Large size retinoblastoma and retinoblastoma located at macular region responses more to chemotherapy. While lesion less than 2 mm in size and in patient less than 2 months of age responses less to chemotherapy.[13] If the tumor extends beyond the lamina cribrosa even if the cut end of the nerve is free of tumor cells, chances of survival decrease to 60%. If the tumor cells are found at the surgical transection sight, chances of survival rates decrease to less than 20%. Intracranial extension of tumor can lead to death.[13]

Exophytic growth

Exophytic growth occurs in the subretinal space. This growth pattern often is associated with subretinal fluid accumulation and retinal detachment (Figure 24). The tumor cells may infiltrate through the bruch membrane into the choroid and then invade either blood vessels or ciliary nerves or vessels. Tumor may grow outside eyeball. Typically retinoblastoma growing outside eyeball does not show presence of calcification (Figure 25).

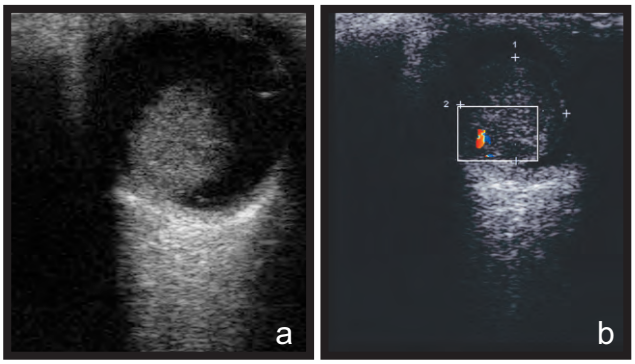

Figure 5: A 2 years old girl presented with complain of Leucocoria in right eye. USG examination revealed large well-defined homogenous hypoechoic lesion in vitreous cavity without presence of calcification which is forming acute angle with retina (a), Color doppler study of lesion showed presence of vascularity within (b)

Diffuse infiltrating growth

It is a rare subtype that comprises 1.5% of all retinoblastoma. There is relatively flat infiltration of the retina by tumor cells and without a discrete tumor mass. It exhibits slow growth pattern. It typically lacks calcification, seen in older patient and readily stimulate inflammatory or hemorrhagic process.[8,12]

Reese and Ellsworth have developed a generally adopted classification system for intraocular retinoblastoma that has been shown to have prognostic significance.

Group I: very favorable for maintenance of sight

1. Solitary tumor, smaller than 4 disc diameters, at or behind the equator
2. Multiple tumors, none larger than 4 disc diameters all at or behind the equator

Group II: favorable for maintenance of sight

1. Solitary tumor, 4-10 disc diameters at or behind the equator
2. Multiple tumors, 4-10 disc diameters behind the equator

Group III: possible for maintenance of sight

1. Any lesion anterior to the equator
2. Solitary tumor, larger than 10 disc diameters behind the equator

Group IV: unfavorable for maintenance of sight

1. Multiple tumors, some larger than 10 disc diameters
2. Any lesion extending anteriorly to the ora serrata

Group V: very unfavorable for maintenance of sight

1. Massive tumors involving more than one half the retina
2. Vitreous seeding

Retinocytomas are rare tumors that are composed entirely of benign-appearing cells. Genetic implications of retinocytoma are the same as that of retinoblastoma. Family members of patients with retinoblastoma should be closely examined for retinocytoma and if positive, they are followed for rest of their lives.[14]

Trilateral retinoblastomas are cases of bilateral retinoblastoma associated with an ectopic intracranial retinoblastoma usually involving the pineal gland or the parasellar region. Trilateral retinoblastomas contribute significantly to the overall mortality in patients with hereditary retinoblastoma in the first decade of life accounting for approximately 50% of deaths. To reduce the mortality of trilateral retinoblastoma, screening efforts should be made in patients who have bilateral or multifocal disease and those with a positive family history. Patients and their siblings should be assessed periodically for any signs of developing retinoblastoma.

Standard therapy comprises enucleation for unilateral disease and radiation therapy with or without enucleation for bilateral disease. However, contemporary treatment for retinoblastoma is transitioning to front-line chemotherapy to improve disease control while preserving vision and minimizing adverse sequel of enucleation and

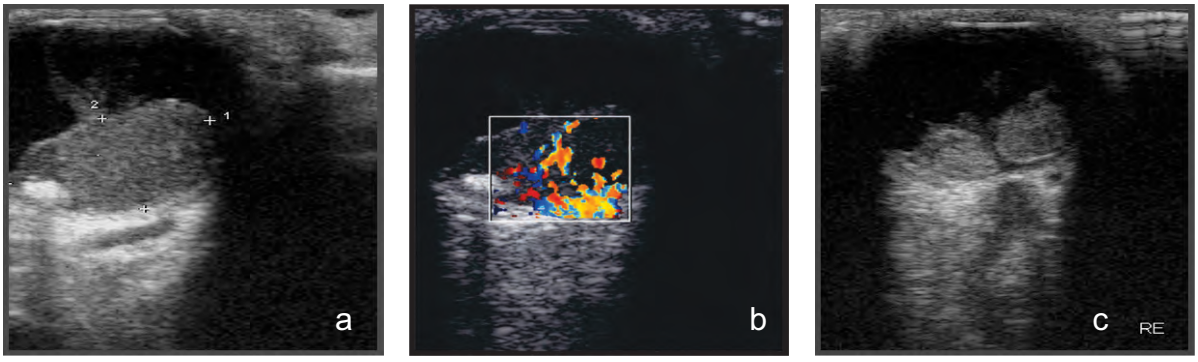

Figure 6: A 5 years old male patient presented with complain of bilateral loss of vision for 3 months. USG of left eye showed presence of large well-defined homogenous hypoechoic mass with presence of dense calcified area (a), Color Doppler study of lesion showed presence of high vascularity within, suggestive of high grade malignancy (b), USG of right eye also shows presence of large retinoblastoma with thickening of optic nerve (c)

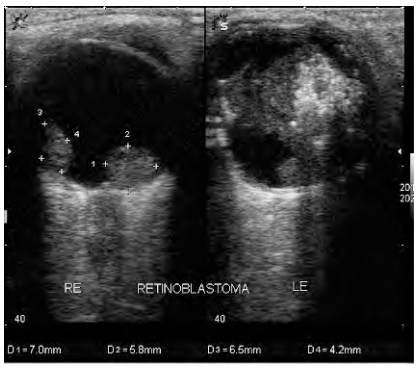

Figure 7: USG of both eyes in 4 years old boy shows presence of large calcified mass lesion in left eye with two small hypoechoic noncalcified mass lesions in right eye suggestive of bilateral multiple retinoblastomas

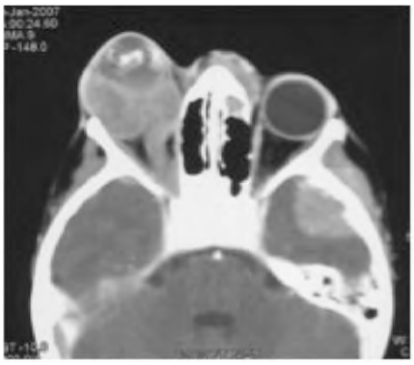

Figure 8: Axial CT scan at level of orbit shows mass in right orbit with extension into retrobulbar space

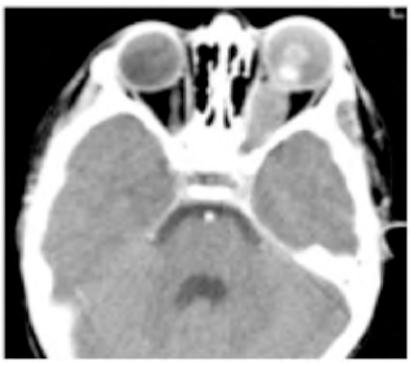

Figure 9: Axial CT scan at level of orbit shows mass in left eye-ball with thickened left optic nerve

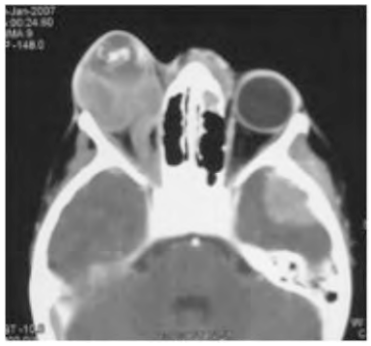

Figure 10: Axial CT scan at level of orbit shows mass in right eye-ball extending into right retrobulbar space with thickened right optic nerve. Intra-ocular component shows calcification spot within

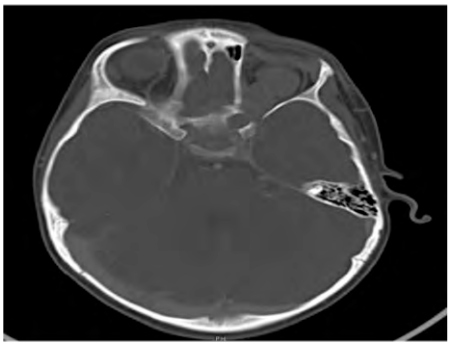

Figure 11: Patient with left eye retinoblastoma, bone window image of CT scan shows widening of left optic canal

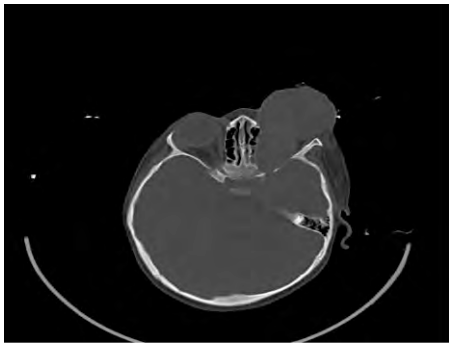

Figure 12: Patient with left eye retinoblastoma, bone window image of CT scan shows thinning of greater wing of sphenoid

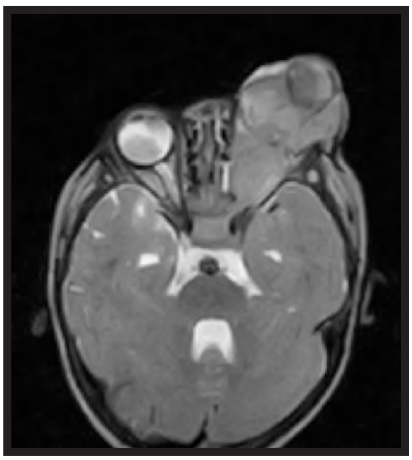

Figure 13: Patient with bilateral retinoblastoma, MR T2w image shows thickened liftt optic nerve. Left optic nerve appears hyperintense, suggestive of retroocular extension of lesion

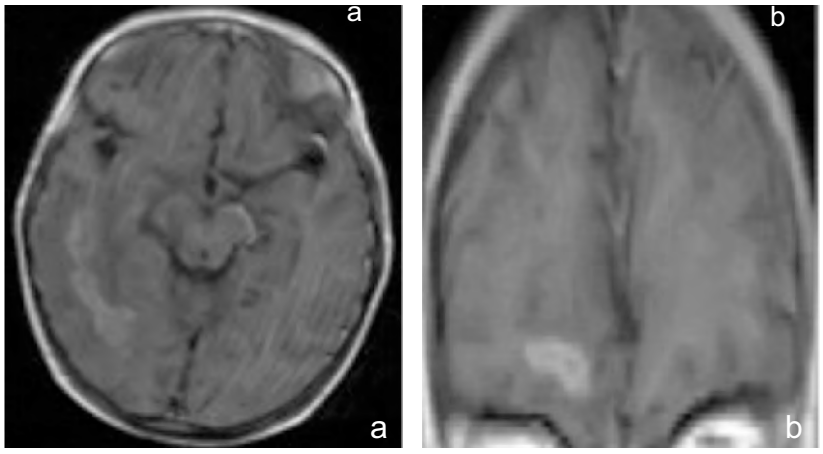

Figure 14: A 6 year old male child with retinoblastoma of right eye. MRI brain T1w post contrast axial image shows few well-defined nodular enhancing lesions in right parietal lobe (a), Coronal section of MRI brain shows similar metastasis in right temporal lobe

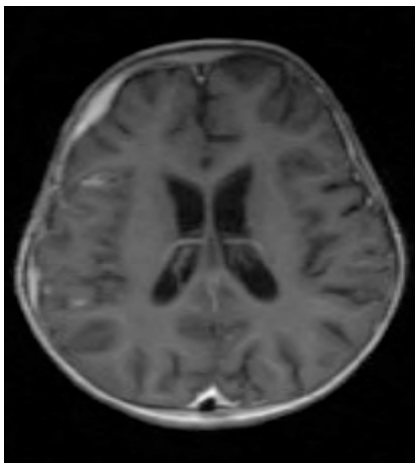

Figure 15: A 9 year old male child with retinoblastoma of right eye. T1w post contrast image of MRI brain shows dural based enhancing lesions along right frontal lobe and parietal lobe

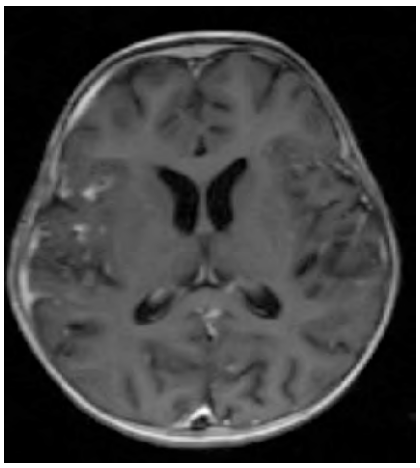

Figure 16: A 9 year old male child with retinoblastoma of right eye, T1w post contrast image of MRI brain shows focal leptomeningeal enhancement along right parietal lobe

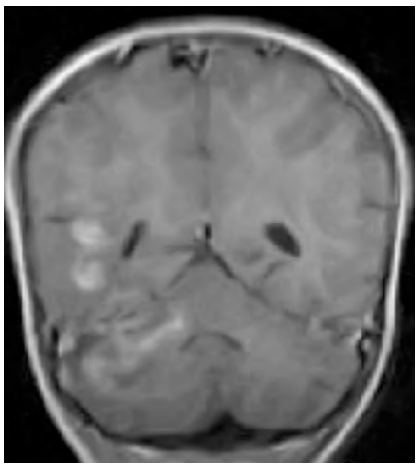

Figure 17: A 6 year old male child with retinoblastoma of right eye. T1w post contrast axial image of MRI brain shows few well-defined nodular enhancing lesions-metastasis in right cerebellar hemisphere

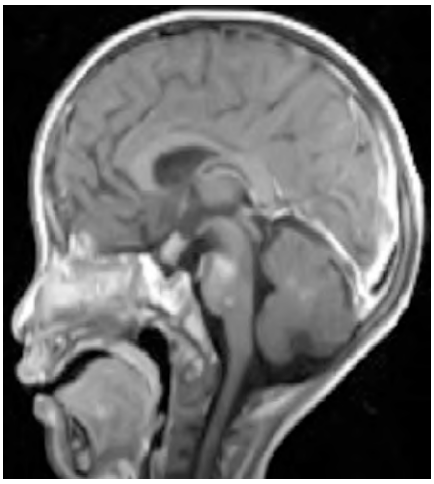

Figure 18: A 6 year old male child with retinoblastoma of right eye. T1w post contrast axial image of MRI brain shows few well-defined nodular enhancing lesions-metastasis in brain stem

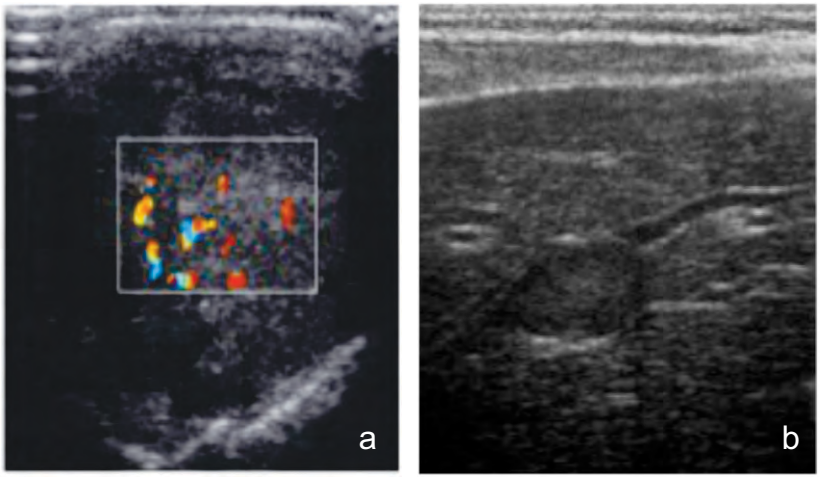

Figure 19: A 3 years old boy presented with leucocoria in left eye. USG revealed exophytic retinoblastoma in left eye with internal vascularity (a), USG of liver shows presence of hypoechoic liver metastasis (b)

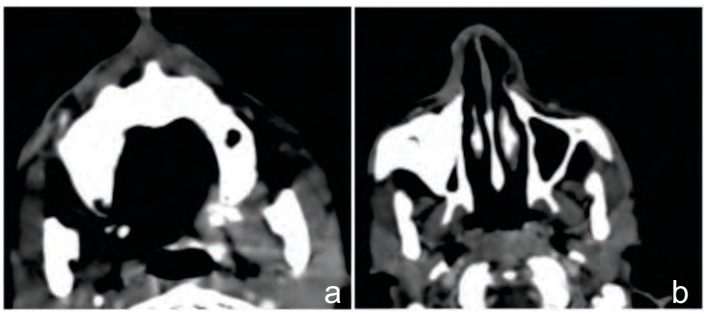

Figure 20: A 12 years old boy had right eye retinoblastoma. Enucleation surgery was performed. After 2 years he presented with swelling over nose (a, b). Biopsy confirmed metastasis

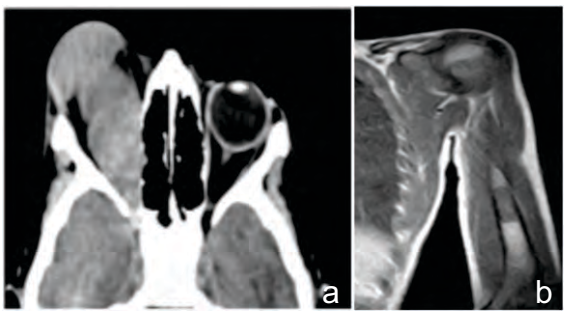

Figure 21: A 5 years old girl with right eye retinoblastoma, MRI shows retrobulbar extension of lesion with involvement of right optic nerve (a) and metastasis in left humerus (b)

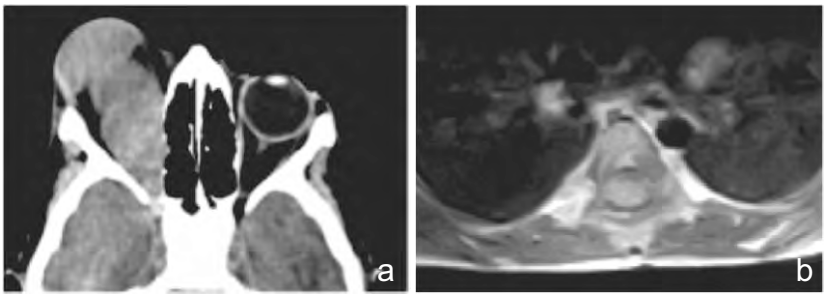

Figure 22: MRI images of 10 years old boy presented right eye retinoblastoma (a) and vertebral body metastasis (b)

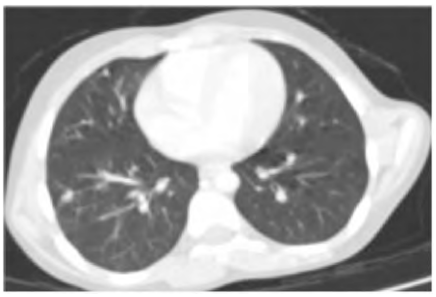

Figure 23: CT scan of 7 years old male child with retinoblastoma, lung window images show few well-defined metastatic lung nodules

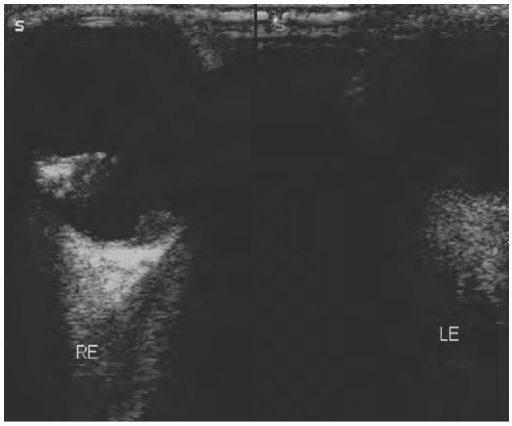

Figure 24: USG of both eyes shows presence of two small hypoechoic mass lesions in right eye with presence of dense calcification in one of the lesion. Single small hypoechoic lesion is also noted in left eye, suggestive of bilateral multiple retino-blastoma

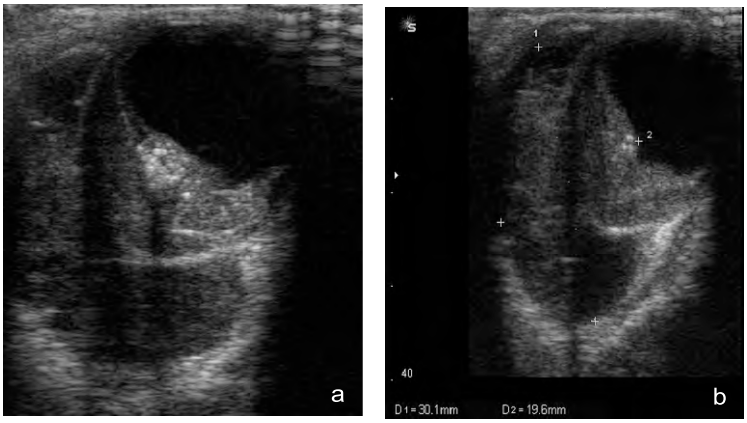

Figure 25: A 3 years old boy presented with complains of exophthalmous in right eye. USG revealed exophytic calcified retinoblastoma in right eye with large extra-bulbar component. The extrabulbar component typically doesn't show presence of calcification (a), measuring 30X19 mm (b)

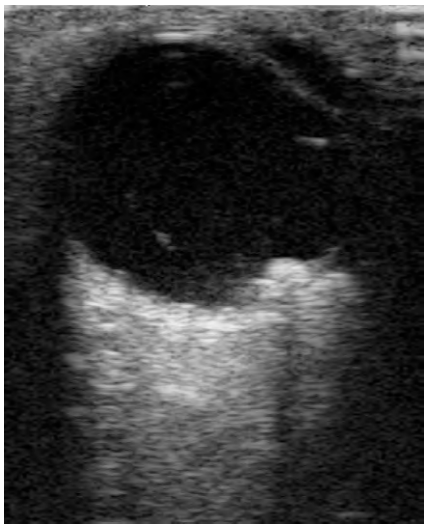

Figure 26: Known case of bilateral retinoblastoma with enucleation of right eye. Patient was also given concurrent radiotherapy. After completion of radiotherapy, USG of left eye was performed. It showed calcified residue of retinoblastoma

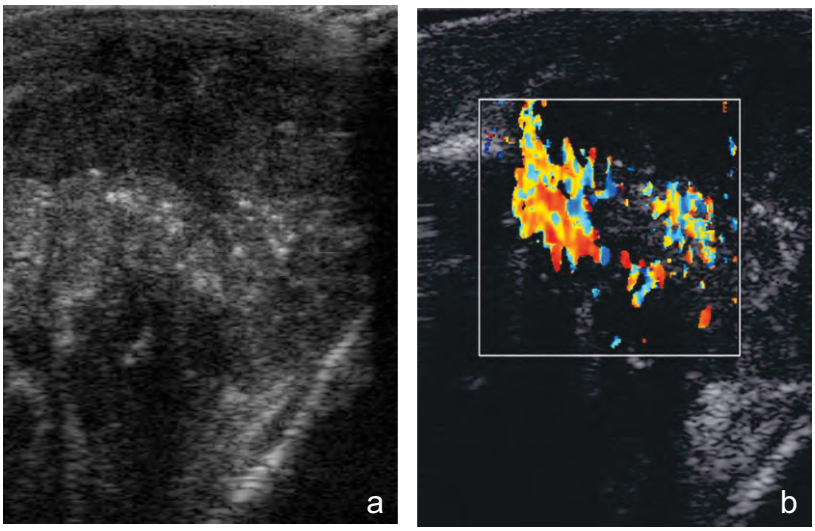

Figure 27: Known case of right eye retinoblastoma - post enucleation status. Patient presented with swelling in right orbit. USG showed presence of large hypoechoic lesion in orbital cavity with internal calcification (a), Color doppler study showed high vascularity of lesion (b). All findings suggestive of recurrent retinoblastoma in same side

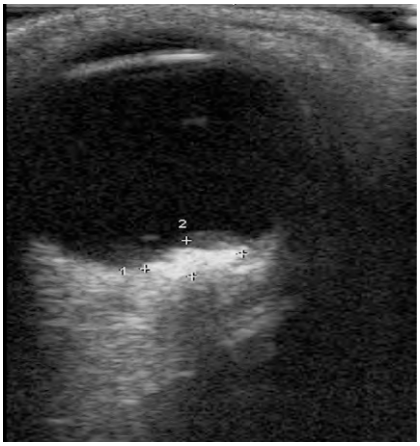

Figure 28: Old case of retinoblastoma of left eye - post enucleation status. Follow up USG showed presence of small calcified lesion in right eye, suggestive of development of retinoblastoma in opposite eye

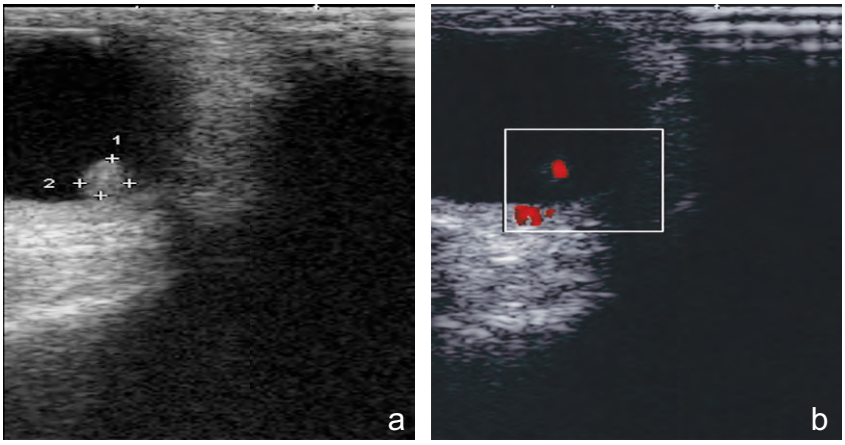

Figure 29: Treated case of right eye retinoblastoma. Follow up USG revealed small hypodense lesion in left eye without calcification (a), Color doppler study showed vascularity within the lesion (b). Findings are suggestive of retinoblastoma in opposite eye

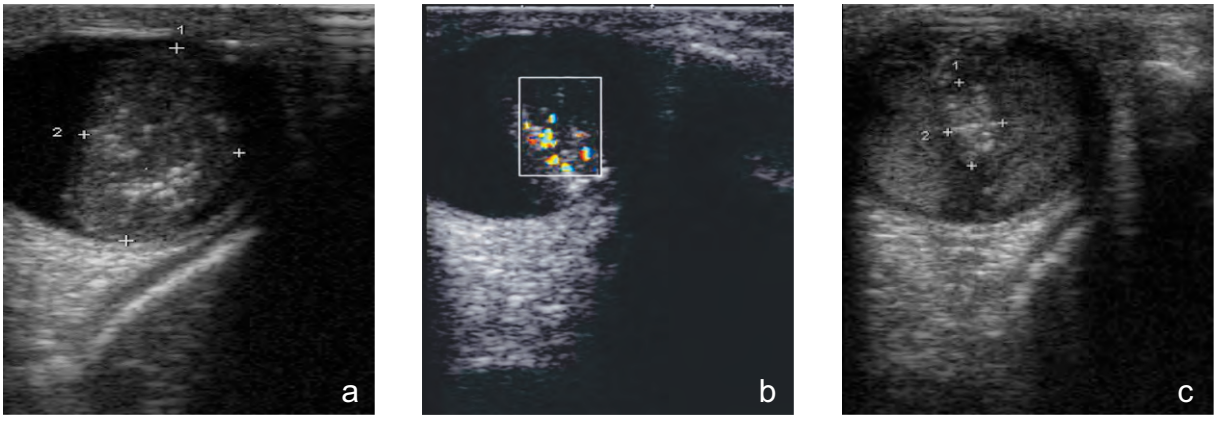

Figure 30: A 4 years old girl presented with complain of leucocoria in left eye. USG of left eye shows presence of large heterogeneous echopattern mass lesion with internal calcification, suggestive of retinoblastoma (a), Color Doppler study revealed presence of vascularity within the lesion (b). Patient was given two doses of chemotherapy. Post chemotherapy USG orbit showed complete retinal detachment with subretinal echoes. Residual mass is seen as small heterogeneous echopattern lesion with calcification. Size of mass is reduced as compared to previous USG (c)

radiation therapy. Retinoblastoma contracts, calcifies, and becomes hypovascular in response to therapy.[15] Long term follow up is essential for managing retinoblastoma after eye preserving conservative therapy.[15]

Imaging of retinoblastoma after treatment is major concern. Post conservative treatment, the size of tumor decreases, with ultimately calcified spot, fibrosis remains as residue of previous treatment (Figure 26). In post enucleation status, USG is very sensitive modality to detect residual/recurrent mass on the same side (Figure 27) or development of tumor in opposite eye (Figure 28, 29, 30).

EBRT can lead to various complications. Radiation can lead to cataract formation in 18 months to 3+ years. Hypoplasia of bone and soft tissue structures after treatment with radiation doses exceeding 3500 cGy may occur. The maxillary molar tooth buds located high in the maxilla just inferior to the posterior apex of the orbit may become irradiated with treatment. Numerous reports of failure of tooth eruption have been noted in patients with retinoblastoma treated with irradiation.

Secondary monocular tumors can develop in survivors of retinoblastoma, in order of decreasing frequency: osteosarcoma[16,17](Figure 31), various soft tissue sarcomas, malignant melanoma, various carcinomas, leukemia and lymphoma, and various brain tumors.[17] Patients treated with EBRT appear to be at a much greater risk of developing second tumors. Dunkel et al demonstrated that by age 40 years 6% of those patients who did not receive EBRT had developed second primary malignant neoplasms as compared to 35% for those who did receive EBRT.

Differential diagnosis of retinoblastoma includes PHPV, retinopathy of prematurity, coat's

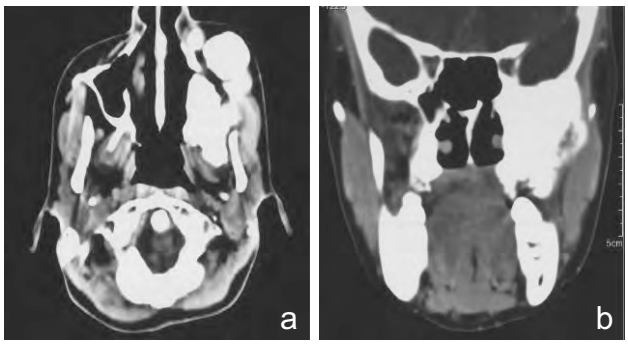

Figure 31: Known case of retinoblastoma post radiotherapy status. Axial CT (a) and coronal CT (b) scan shows sclerotic lesion involving maxilla suggestive of sclerotic variety of osteosarcoma

disease, retinal astrocytoma, toxocariasis and optic nerve head drusen.

Conclusion:

Retinoblastoma is curable intra-ocular childhood malignancy if it is diagnosed at an early stage. Various radiological modalities help in early diagnosis and staging of disease. In follow up cases during post treatment period, imaging modality help to rule out any residual or recurrent lesion.

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Pattern of Head and Neck Cancers in Regional Cancer Centre, Gujarat

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Summary

The overall aim of this retrospective study was to describe the pattern of head and neck cancers registered at The Gujarat Cancer and Research Institute (GCRI), Regional Cancer Center (RCC) from January 2001 to December 2005. During that period a total of 17824 head and neck cancers patients were registered for this study. Demographic profiles along with diagnostic and treatment information were obtained from Medical Record Department. Out of a total of 17824 cases, 14632 (82.09%) were males and 3201 (17.91%) were females which shows higher male preponderance. Male: female sex ratio was 4.57:1. Most of the cancers were in the age group of 35-64 years. Head and neck cancers were classified based on the International Classification of Diseases-Oncology (ICD-O) edition III. The most prevalent was cancer of head and neck in males was tongue (26.42%) and in females it was oral cavity (29.05%). Squamous cell carcinoma was the commonest histological type in both the sexes. The high prevalence of head and neck cancers observed at our institute shows a serious concern about the occurrence of the disease and risk factors related to these cancers. Tobacco is a major risk factor for head and neck cancers. So this study reveals an urgent need for tobacco control and other preventing measure such as cancer awareness programmes at community level.

Keywords: Pattern, Head and neck cancers, Regional Cancer Centre, Hospital Based Cancer Registry

Introduction

Head and neck cancer is the sixth most common malignancy and is a major cause of cancer morbidity and mortality worldwide.[1] In India and South East Asia, oral cancer incidence accounts up to 40% of all malignancies.[2] The most common risk factors associated with head and neck cancer are tobacco and alcohol use with significant interaction observed between the two.[3] In South Asian countries, the risk of head and neck cancer is further aggravated by smoking of bidi, [4] reverse smoking, chewing tobacco, betel quid and areca nut.[5]

The Gujarat Cancer and Research Institute (GCRI) is a Regional Cancer Centre (RCC) recognized by Department of Health and Family Welfare, Government of India. GCRI provides multi-disciplinary super specialty comprehensive cancer care under a single roof in western part of India. It is running Hospital Based Cancer Registry (HBCR) since 1972 as per the standards and norms prescribed by the National Cancer Registry Programme (NCRP) of the Indian Council of Medical Research (ICMR). Cancer Registration System is active and only the patients who are diagnosed to have cancer are included in the HBCR. Therefore, a retrospective study on pattern of head and neck cancers was conducted in the department of Community Oncology and Medical Records, GCRI.

Materials and Methods

GCRI being a RCC, various medical institutions and private practitioners refer the patients here. In this study, all the new patients who attended the out patient department were interviewed and their socio-demographic information such as age, gender, habits etc along with details of medical reports given by the referring doctors were computerized. Diagnostic and therapeutic details were abstracted from the hospital records and computerized. During the period from 2001 to 2005, a total 59,000 cancer patients registered, amongst them 17824 (30.21%) were head and neck cancer patients. Out of them 14,632 (82.09%) were males and 3201(17.91%) were females.

Classification and coding of head and neck cancer was done as per WHO Manual.[6] International Classification of Diseases for Oncology (ICD-O-III) was followed for coding of microscopically verified reports of pathology.[7] The anatomical sites included in head and neck cancers were lip, tongue, mouth, salivary gland, tonsil, oropharynx, nasopharynx, hypopharynx, pharynx, nose and sinus, larynx, and thyroid.[8] Only pathologically confirmed cancers cases were included in cancer registry database.

Statistical Analysis

The data was analyzed by using SPSS version 17 and Epi Info version 5. Chi Square test was performed to access the association of gender with age groups and primary morphology. P value of <0.05 was considered to be statistically significant.

Results

A total of 17824 cases of head and neck cancers were reported during the study period. Increase in trend of head and neck cancers had been observed from year 2001 to 2005 (Figure 1).

In both males and females, highest cases of head and neck cancers were seen within age group of 35-64 years. In all age groups, there was a highly significant male multitude ($p<0.000$). Sex ratio for male: female was 4.57:1 (Table 1).

In males, the most common site was tongue (26.42%) followed by oral cavity (25.69%), hypopharynx (16.32%), larynx (10.49%), tonsil

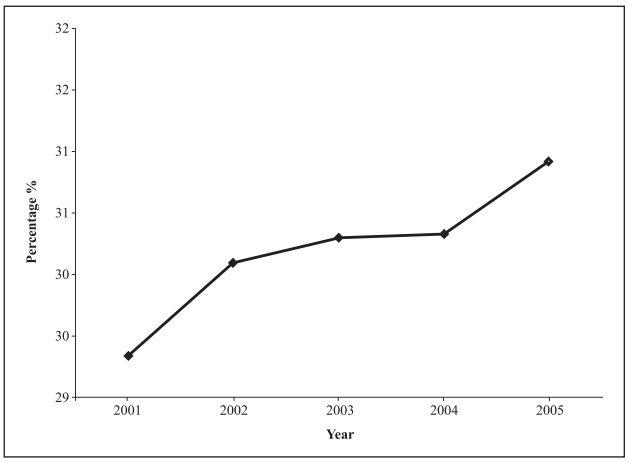

Figure 1: Trend of head and neck cancers

Table 1: Distribution of head and neck cancers by broad age group and gender GCRI 2001-2005

Age group (years)	Male n	Male %	Female n	Female %	Total n	Total %
0-14	51	0.35	16	0.50	67	0.38
15-34	1050	7.18	373	11.65	1423	7.98
35-64	10493	71.76	2280	71.23	12773	71.66
65+	3029	20.71	532	16.62	3561	19.98
Total	14623	100	3201	100	17824	100

p value < 0.000 obtained by Chi-Square Test

(7.07%), pharynx (4.59%), oropharynx (2.37%), nose and sinus (1.87%), nasopharynx (1.57%), lip (1.54%), salivary gland (1.20%) and thyroid gland (0.88%). On the other hand, in females the most common site was oral cavity (29.05%) followed by hypopharynx (20.31%), tongue (18.96%), thyroid gland (8%), nose & sinus (5.37%), pharynx (4.69%), larynx (3.69%), salivary gland (2.59%), tonsil (2.47%), nasopharynx (2.22%), lip (1.87%) and oropharynx (0.78%). Male: Female ratio was 4.57:1. Overall distinctly male preponderance was found in head and neck cancer sites which was statistically highly significant ($p<0.000$) (Table 2).

The most common primary morphology in both males and females was squamous cell carcinoma (92.57% and 86.04% respectively). This was followed by Epithelial Carcinoma (2.78% and 3.87%), Malignant Neoplasms (2.54% and 3.19%) and Adenocarcinomas (0.68% and 3.16%). Other morphology types constituted 1.42% in males and 3.75% in females. Squamous Cell Carcinoma were more likely to diagnosed in both genders than other morphology types ($p<0.0001$) (Table 3).

Discussion

Present study highlights the head and neck cancer which were 30.21% of total cancer registered at GCRI from 2001 to 2005. Similar to the present study, there are several reports that head and neck cancer with respect to total body malignancies varied from 9.8% to 54.48%.[9-15]

In this study, in terms of gender distribution, the sex ratio for head and neck cancers was observed to be 4.57 in males and one for females. This suggested that head and neck cancer was more predominant in males than in females.

Further the commonest site was observed to be tongue in males while oral cavity in females. The highest male:female ratio was found in oropharyngeal cancers (13.84:1). Oral cavity accounted for first prevailing cancer of total cancers (7.94%) and of head and neck cancers (26.29%); having male: female ratio of 4.04: 1, whereas, Bhattacharjee et al,[15] reported it to be the third commonest head and neck cancers.

Cancer of tongue was the second most common site accounted for 7.58% of total cancers and 25.08% of head and neck cancers with male: female ratio of 6.37:1. Hypopharyngeal cancers is the third commonest cancers comprising of 5.15% of all cancers and 17.04% of head and neck cancers and

Table 2: Site wise head and neck cancers by gender GCRI 2001-2005

Site	Gender						Male : Female Ratio	p value
	Male		Female		Total			
	n	%	n	%	n	%		
Lip	225	1.54	60	1.87	285	1.60	3.75 : 1	
Tongue	3864	26.42	607	18.96	4471	25.08	6.37 : 1	
Oral Cavity	3756	25.69	930	29.05	4686	26.29	4.04 : 1	
Salivary Gland	175	1.20	83	2.59	258	1.45	2.11 : 1	
Tonsil	1034	7.07	79	2.47	1113	6.24	13.09 : 1	
Oropharynx	346	2.37	25	0.78	371	2.08	13.84 : 1	< 0.000*
Nasopharynx	229	1.57	71	2.22	300	1.68	3.23 : 1	
Hypopharynx	2387	16.32	650	20.31	3037	17.04	3.67 : 1	
Pharynx	671	4.59	150	4.69	821	4.61	4.47 : 1	
Nose & Sinuses	274	1.87	172	5.37	446	2.50	1.59 : 1	
Larynx	1534	10.49	118	3.69	1652	9.27	13.00 : 1	
Thyroid Gland	128	0.88	256	8.00	384	2.15	0.50 : 1	
Total	14623	100	3201	100	17824	100	4.57 : 1	

* p value obtained by Chi-Square Test

Table 3: Number and percentage of head and neck morphology by gender GCRI 2001-2005

Type of Morphology	Male		Female		Total		p value
	n	%	n	%	n	%	
Squamous cell Carcinoma	13537	92.57	2754	86.04	16291	91.40	< 0.0001*
Epithelial Carcinoma	407	2.78	124	3.87	531	2.98	
Malignant Neoplasms**	372	2.54	102	3.19	474	2.66	
Adenocarcinomas	99	0.68	101	3.16	200	1.12	
Others***	208	1.42	120	3.75	328	1.84	
Total	14623	100	3201	100	17824	100	

* p value obtained by Chi-Square Test.
** Blastoma, Unspecified tumor, Not Otherwise Specified
*** Others includes Mucoepidermoid neoplasms, Ductal and Lobular neoplasms, Myomatous neoplasms, Complex Mixed and Stromal neoplasms, Neuroepitheliomatos neoplasms, Hodgkins and Non Hodgkins lymphoma

male to female ratio was 3.67:1. Other studies reported it to be 2.3% to 7.7% of total body malignancy and 11.7% to 28.3% of head and neck cancers [12-16] and the male: female ratio of 3.6:1 to 5.8:1.[12,14,15] Among histopathological types of head and neck cancers, squamous cell carcinoma was the commonest histological type (91.40%). Bhattacharjee et al[15], reported similar findings (93.29%).

Conclusion

The study data reflects our specific patient population reporting to the regional cancer centre and not the community as a whole. This study concluded that head and neck cancers are the common health problems in males and further studies are required to determine risk factors for common head and neck cancers like oral cavity, tongue, hypopharynx etc. Oral screening is recommended for prevention of head and neck cancers.

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Secondary Glioblastoma Multiforme - Small Cell Type with Distant Metastases and Good Response to Temozolamide - A Case Report

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Summary

Glioblastoma multiforme (GBM) is one of the most aggressive brain neoplasms. Extracranial metastases are rarely described in GBM. We report a case of secondary GBM with cervical lymph node and bone metastases with good disease control by chemotherapy. Our patient is a 30-year-old female with secondary small cell type GBM. Patient was operated for the same. One and half years later patient presented with lymph node and skeletal metastasis, with lymph node histology consistent with GBM metastases. Skeletal metastasis was diagnosed on positron emission tomography (PET) scan done in view of pain in back and left lower limb. Chemotherapy (Temozolamide-150mg/m^2/day for 5days every four weeks) was started after which the patient's clinical course has been stable. The lesion in the brain remained quiescent meanwhile. The interesting facts about our case are development of extra cranial metastasis due to secondary GBM, a rare event, and the fact that the patient continues to enjoy a reasonable quality of life for two years despite developing systemic metastasis as the primary tumor remained quiescent.

Keywords: Secondary glioblastoma multiforme, Lymph node and bone metastasis, Chemo sensitive

Introduction

Glioblastoma multiforme (GBM) is one of the most aggressive neoplasm of the brain. These tumors can develop de novo (primary type) or arise from pre-existing low grade gliomas (secondary type).[1] Glioblastomas tend to spread by local growth and infiltration. The secondary form tends to develop more slowly than the primary type and have a more favourable outcome. Extracranial metastases are rarely described in GBM despite its highly malignant nature. We report a rare case of secondary GBM with cervical lymph node and bone metastases with good disease control by temozolamide.

Case Report

A 30-year-old lady presented with complaints of headache and vomiting for duration of 1 month in August 2007 at the Gujarat Cancer and Research Institute. Magnetic resonance imaging (MRI) brain revealed a 45x39 mm sized lesion which was hypointense on T1 and hyperintense on T2 images in right posterior parietal region. She underwent craniotomy with near total excision of the lesion. Gross examination revealed several gray white hemorrhagic tissue pieces, which on histopathological examination was diagnosed as grade II astrocytoma with low MIB-1 index (8%) (Figure 1). Postoperative MRI revealed no residual disease. Patient was kept on regular follow up. In December 2008, the patient complained of headache and underwent repeat MRI which revealed irregular lesion at the same location with increased mass effect suggestive of recurrence. The patient was advised surgery but was not willing for the same or any other form of treatment. The patient was on follow up and underwent repeat MRI in August 2010. It revealed a 27x27mm sized lesion in the posterior parietal region. Subtotal microsurgical excision was done and histology was consistent with small cell type of GBM having high MIB-1index (40%) (Figure 2). Post operative MRI scan revealed residual lesion in right temporoparietal region with significant perilesional edema. Patient was given radiotherapy (60 gray in 30 fractions) and was kept on regular follow up. In December 2011, patient presented with a gradually increasing, painless, mobile 4x4cm^2 right neck mass. Computerised tomography (CT) scan of thorax showed multiple nodes in right neck, largest measuring 49x41mm^2. Simultaneously, CT scan brain was done which revealed only postoperative gliotic changes.

Surgical excision of the neck node was done. Histomorphological analysis showed small cell proliferation with scanty cytoplasm along with a few gemistocytic cells. Immunohistochemistry (IHC) showed that the cells were glial fibrillary acid protein (GFAP) positive and negative for leucocyte common antigen (LCA), CD20, CD79, CD99 and CD30. MIB-1 index was 60-70% (Figure 3). Hence she was diagnosed as GBM small cell type metastatic to cervical lymph node. At this stage, there was no evidence of viable brain tumor. One month later, the patient underwent PET-CT in view of the pain and

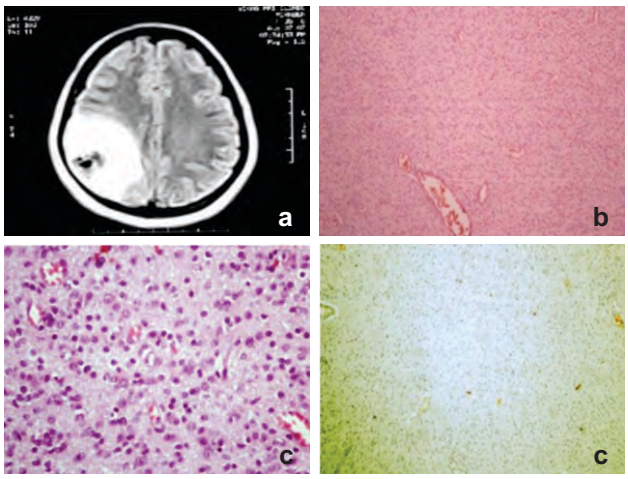

Figure 1: Radiological and pathological features of primary grade II astrocytoma in the year 2007 : T2W MRI image showing right posterior parietal hyperintense lesion with central cystic contents (a). Low power (b; 10x) and high power (c; 40x) view of grade II astrocytoma (H&E) Low MIB- 1 index (d)

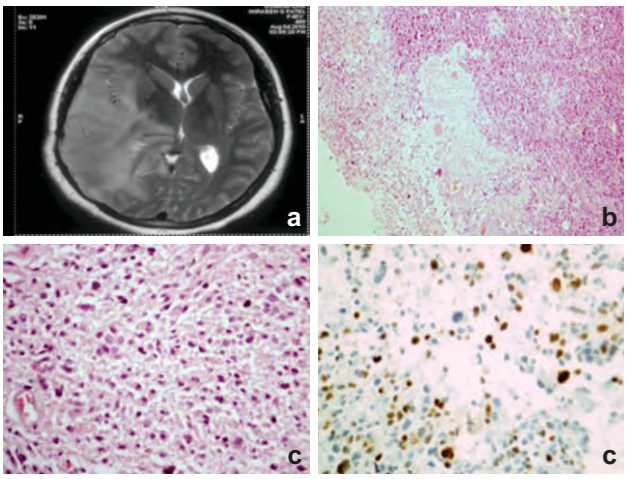

Figure 2: Radiological and pathological features of grade IV astrocytoma in the year 2010 : T2W MRI image showing large ill defined moderately hyperintense lesion involving right temporo parietal lobe with loss of normal grey- white matter differentiation (a). Low power (b; 10x) and high power (c; 40x) view of grade IV astrocytoma with small cell differentiation (H&E). High MIB-1 index (d)

weakness in left lower limb and back, which revealed active neck lesions with multiple bone metastases to dorsolumbar and sacral vertebrae, right scapula, few ribs, bilateral pelvic bones, bilateral proximal femur (Figure 4). Intracerebral tumor site was still without any sign of recurrence. Chemotherapy with temozolamide 150mg/m^2/d for 5 days every four weeks was given. Till now 6 cycles of temozolamide have been given and the course of chemotherapy has been uneventful. The patient has survived for 2 years since the diagnosis of secondary GBM.

Discussion

GBM is a highly malignant primary brain tumor. The occurrence of extracranial metastasis is a rare event with a reported frequency of <2%.[2] The following reasons have been proposed for the rarity of extracranial metastases: Lymphatics are absent in the central nervous system; the intracranial perivascular space doesn't communicate with the extracranial fluid space; connections between subarachnoid space and extra cranial lymphatics are very sparse. Intracerebral veins are thin walled and would probably collapse from compression before the tumor would penetrate. Meningeal tumors grow on the dura mater but remain only on the surface. Dural veins are protected by a dense connective tissue.[3-5] Extracerebral metastases in GBM usually occur in regional lymph nodes (51%) particularly cervical group, lung and pleura (60%) and skeletal (31%), where vertebral bodies are the most common site.[6] Hematogenous and lymphatic spread after infiltration of the skull and extracranial soft tissue represents the most common route, especially in patients who have undergone a surgical intervention.[7] The operative procedure alters the brain anatomy and gives the tumor the access to extracranial soft tissue, blood and lymphatics. Median survival of small cell GBM in a study of 37 patients was 11 months (2-22 months).[8] In a comprehensive analysis of extracranial GBM over 70 years, it was found that the median time from diagnosis of GBM to detection of extracranial metastasis was 8.5 months and from diagnosis of metastasis to death was 1.5 months.[4] In this analysis which spanned nearly 7 decades (1940-2009), there has been progressive lengthening of survival from detection of extracranial metastases to death at a rate of 0.7 months per decade. This increase in both times is probably a result of earlier detection of the tumor, as advances are made in diagnostic technologies. Their data also suggests heterogeneity in survival time depending on which organ is involved; longest for liver and shortest for lung. The reason for this is largely unexplained. Management of intracranial GBM usually involves surgical excision, followed by radiotherapy with or without chemotherapy. Various chemotherapeutic agents have been tried in patients with extracranial metastases. These include temozolamide, carboplatin/docetaxel and adriamycin/cyclophosphamide/etoposide.[9] Our patient developed nodal metastases one and half years after being diagnosed as secondary GBM. The nodal mass was completely excised but she did not receive any chemotherapy. At this time, the patient had no active lesion in the brain. One month later, the patient developed multiple bony metastases with active lesions in neck for which chemotherapy (temozolamide) was started. Local complete remission continued. The improvement in survival with temozolomide has been well documented. One group

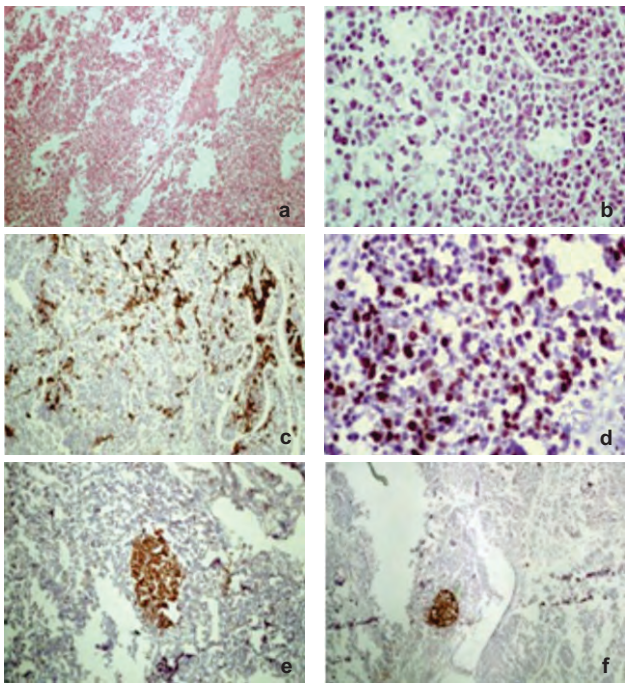

Figure 3: Low power view of lymph node showing metastatic small cell GBM (a). High power view of lymph node showing metastatic small cell GBM (b). GFAP positivity in lymph node (c). High MIB-1 index (60-70%) in lymph node with metastatic GBM (d). LCA negativity in lymph node (e). CD 20 negativity in lymph node (f)

noted median survival of 14.6 months in temozolomide group as against 9.7 months in patients not receiving the drug in the past.[10] One recent study found monotherapy with this drug to be non-inferior to radiotherapy alone in elderly patients with GBM.

Conclusion

The interesting facts in our case include the development of extracranial metastasis due to GBM, a rare event, and the fact that the patient continues to enjoy a reasonable quality of life despite developing systemic metastasis as the primary tumor remained quiescent.

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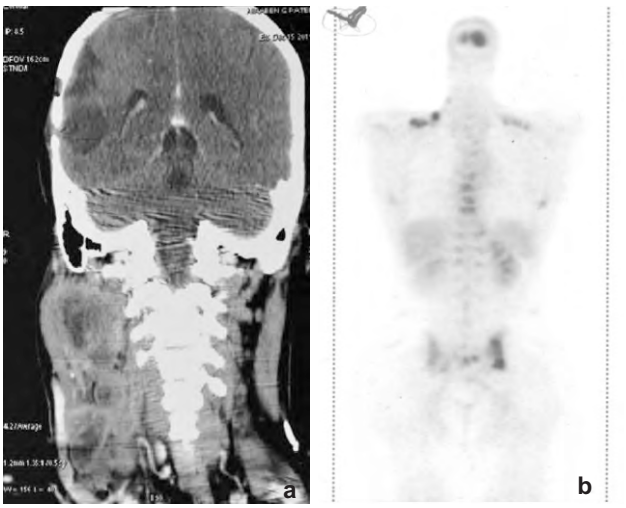

Figure 4: CT brain and neck in December 2011 showing postoperative gliotic change. Multiple enlarged lymph nodes in the right side of neck largest are seen (a). PET CT - hypermetabolic disease involving multiple level cervical nodes and bones (b)

Cytodiagnosis of Fibromatosis Colli

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Summary

Fibromatosis colli (FC) is a peculiar benign fibrous growth of the sternocleidomastoid that usually appears during the first few weeks of life. It is the most common cause of congenital muscular torticollis (wry neck). FC is seen in children born after difficult, prolonged labour, assisted delivery and breech deliveries. Cytology shows spindle shaped mature fibroblastic cells scattered singly along with degene-rated and atrophic muscle fibres, multinucleated giant muscle cells in a clean background. FC has to be differentiated from congenital lesions, inflammatory lesions and neoplastic conditions. In contrast to other forms of fibromatoses, a noninvasive conservative management is usually the line of treatment for FC in most of the cases. Fine needle aspiration cytology (FNAC), as a time saving, rapid and reliable diagnostic procedure has got biggest role to play in reassurance of anxious parents guiding for conservative management and avoiding surgery.

Keywords: FNAC, Fibromatosis colli, Infant

Introduction

Fibromatosis colli (FC) also known as a sternocleidomastoid tumor of infancy or muscular fibromatosis of infants, a self limiting lesion, present as a firm to hard, immobile, fusiform swelling in the lower or middle portion of the sternocleidomastoid muscle and is usually detected 2 weeks of age.[1] The right side is more commonly affected than left and males are affected more than females. More than 50% cases of FC are associated with history of complicated delivery and birth injury.[2] Management of FC in majority of cases is usually conservative and avoids surgical procedure by employing physiotherapy.

Fine Needle Aspiration Cytology (FNAC) is a minimally invasive, cost effective and time saving outdoor procedure and has an important role to play in early diagnosis. The differential diagnosis includes various congenital and inflammatory lesions, neoplastic conditions and other forms of infantile fibromatoses that may occur at that site.[3,4,5,6] The diagnosis of FC based on characteristic clinical presentation and cytological features. We report here a case of a one month old child diagnosed as FC on cytology.

Case Report

One month old child with a well circum-scribed, firm mass at anterior border of sternocleido-mastoid muscle measuring 2x1.5 cm since 15 days diagnosed outside as malignant round cell tumor was referred at the Gujarat Cancer and Research Institute. The swelling was static in size. No evidence of head tilt or rotation was noted. The obstetric history of mother revealed prolonged labour and the baby was delivered by forceps extraction. Post partum period was uneventful. No evidence of other associated congenital abnormalities was noted. Ultrasonography of local part shows 24x12 mm size hypo-echoic lesion within muscular plane anterior to right sternocleido-mastoid muscle, suggestive of benign soft tissue mass.

Review of cytology slides showed mode-rately cellular H & E stained smears with oval to spindle shaped fibroblastic cells scattered singly or in a loose cohesive clusters ("school of fish") (Figure 1). Cells were having plump oval to spindle nuclei with wispy cytoplasm (Figure 2). Many naked stripped nuclei were seen (Figure 3) with large number of muscle giant cells (Figure 4). There was no evidence of inflammation, haemorrhage or necrosis. No atypia or mitotic figures were noted. Based on above cytological findings, a diagnosis of FC was suggested and the patient was managed conservatively.

At present, the child is five and half months old, completely well with disappearance of swelling.

Discussion

Fibromatosis colli is a benign lesion of infancy presenting shortly after birth and generally before the age of one year. The lesion occurs in approximately 0.4% of all newborns and is the most common cause of congenital muscularis torticollis and represents 10-20% of cases.[7]

FC is associated with an increased incidence of musculoskeletal disorders including metatarsus adducts, developmental dysplasia of the hip and talipes equinovarus. Hip dysplasia is an associated feature in approximately 2.4-10% of cases, ranging from subluxation to dislocation.[7,8]

The pathogenesis of FC is poorly understood. The different theories proposed to explain the pathogenetic mechanism include fetal malposition, birth trauma, ischemic necrosis following vascular compression during birth, infection and endogenous factor.[5,9,10] A well recognized association between FC and primiparous birth, breech presentation, forceps deliveries and difficult labour are found.

Clinically, FC has to be differentiated from congenital lesion such as brachial cyst, thyroglossal cyst and inflammatory lesion (tuberculous lympha-denitis) and benign and malignant neoplasms. FNAC is a simple technique that helps in excluding these diseases. Benign neoplastic processes in this region

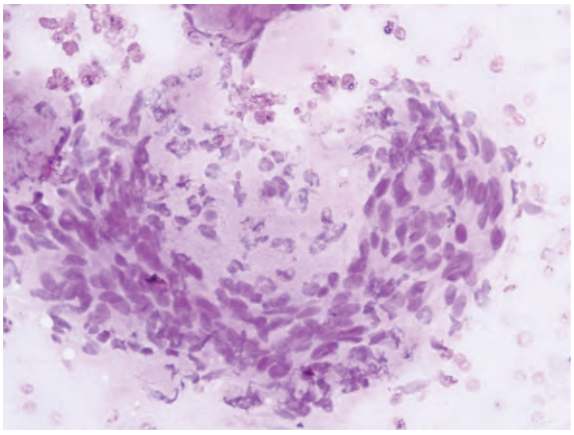

Figure 1: Microphotograph showing "School of fish" arrangement of fibroblast. (H&E x 400)

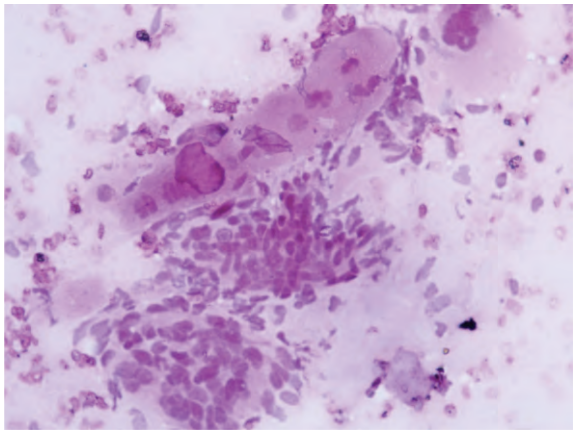

Figure 2: Microphotograph showing clusters and single-lying benign reactive fibroblasts with muscle giant cell. (H&Ex 400)

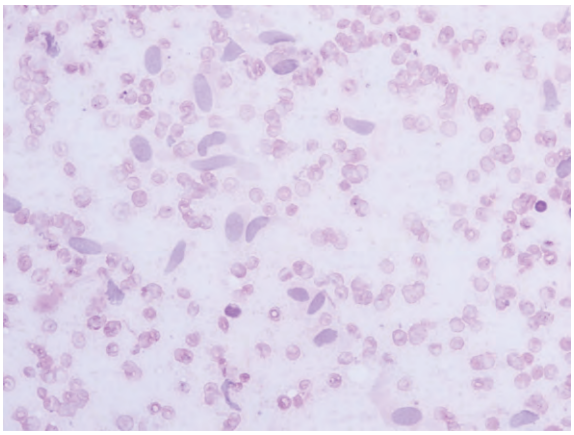

Figure 3: Microphotoghraph showing numerous bare nuclei. (H&E x 400)

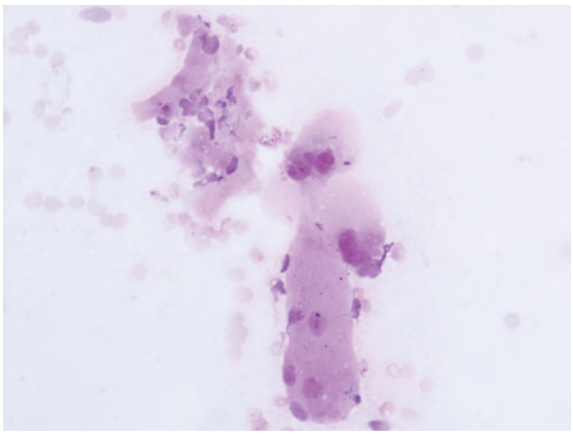

Figure 4: Microphotograph showing multinucleated giant cells. (H&E x 400)

are heamangioma, cystic hygroma and lipoma. Malignant tumors include small round cell tumors such as neuroblatoma, rhabdomyosarcoma and lymphoma. In our case, there were no foamy macrophages or any epithelial cells which ruled out cystic lesions. Absence of necrosis and epitheloid cell granuloma ruled out tuberculous lymphadenitis, absence of inflammatory cells and pleomorphic proliferating fibroblast ruled out nodular fasciitis and presence of benign fibroblast, atrophic muscles and muscle giant cells automatically ruled out round cell tumors. In our case, outside diagnosis was malignant round cell tumor with the possibility of "Rhabdomyo-sarcoma" due to its morphological appearance of round to spindly bare nuclei. Infantile fibromatosis shows infiltrative pattern affecting adjacent muscles.[10] Low grade fibrosarcoma/ infantile fibro sarcoma rarely affects neck region and shows considerable cellularity and atypia.[10,11]

Thus, FNAC is an easy and reliable technique. Surgical diagnostic biopsy may resulting in complication such as cosmetic defect due to contracture band and is reserved only for those cases where malignancy is suspected or cases difficult to diagnose on cytology.[10] FNAC is a time saving cost effective reliable diagnostic procedure and as in this case helps to avoid more invasive procedure. The most accepted treatment for FC before 1 year of age is conservative management consisting of manual stretching. Most series quote a 70-85% success rate with conservative management.[8,12] Surgical treatment is reserved for FC that occurs after 1year of age and for persistent fibrosis in conservatively treated cases.[13]

Conclusion

Although the diagnosis of FC can be suspected clinically and radio logically confirmation can be rendered in a rapid, safe and cost effective way utilizing FNAC as diagnostic method with easy availability in all hospitals and can give an early diagnosis so that conservative management can be started as soon as possible.

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"Failing doesn't stop you. Quitting stops you. Persevere and don't be afraid to fail. You can afford to fail over and over again, because there will always be many, many more opportunities to succeed."

Gerry Schwartz,
Chief Executive, Onex

Plasmablastic Lymphoma: A Diagnostic Dilemma

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Summary

Plasmablastic lymphoma (PBL) has been described as a rapidly progressive and fatal, CD20 negative, CD138 positive diffuse large cell lymphoma with plasmoblastic features. PBL is heterogenous in terms of clinical presentation and morphological features. Morphologically and immunophenotypi cally its close differential diagnosis is plasmablastic myeloma, especially at extramedullary sites. Here, we present two cases with identical morphological and immunophenotypic profile but have different clinical presentation leading to different diagnoses. Case 1 had classical presentation of PBL (HIV positive, oral mucosal involvement), whereas case 2 was HIV negative woman presented with multiple myeloma, who later on developed a lesion in lower alveolus. Both cases showed similar morophological and immunophenotypical features, but they were diagnosed as plasmoblastic lymphoma and plasmoblastic myeloma respectively.

Keywords: Plasmablastic lymphoma, Clinical presentation, Immunohistochemistry

Introduction

Plasmablastic lymphoma (PBL) was originally described in patients with HIV as a subset of diffuse large cell lymphoma (DLBCL), presenting almost exclusively with jaw and oral mucosa involvement.[1,2] Now, it is also recognised in gastrointestinal tract, soft tissue, skin, visceral organs and nodal region.[3,4,5] The clinical spectrum of the disease has been expanding, with a number of single case report or series in HIV-negative patients, in other immunocompromised patients and elderly persons. Morphologically cells resemble large, centroblastic to immunoblastic with a characteristic immunopheno-type. (CD 20-, LCA+/-, CD 138+).[4,6] Here, we discuss two such cases in different clinical settings.

Case 1

A 40-year-old lady presented with a complaint of growth involving right buccal mucosa of one month duration at Gujarat Cancer and Research Institute. On examination, a large polypoidal growth of approximately 5cm size is identified involving right lower gingival and buccal mucosa. Neck node examination revealed an enlarged node at right submandibular region of 3 cm size. Besides being HIV positive, no other significant serological abnormalities were detected. CT scan neck confirmed the mass with localized cortical irregularities of mandible and cervical lymphadenopathy. Clinical diagnosis of carcinoma of buccal mucosa with T2N1 staging was kept. Biopsy was performed.

Case 2

A 75-year-old HIV negative woman was presented at our institute with complaints of back pain. MRI spine revealed multiple lesions involving L4 and D10, D11, D12 vertebras. Vertebral biopsy showed plasma cell dyscrasia. Serum electrophoresis showed presence of M band 2.01 gm/dl. Bone-marrow examination was normal. Patient was given local radiotherapy and systemic chemotherapy. After three months of diagnosis patient developed a soft tissue lesion involving left lower alveolus. Punch biopsy was performed.

Histological features

Haematoxylin and Eosin stained sections of both cases showed ulcerated mucosa. Submucosa showed tumour cells arranged diffusely and focal nesting pattern. Individual cells are large with squared borders, moderate cytoplasm, round nucleus with prominent nucleoli. Frequent mitotic figures along with focal karryorhectic debris were seen (Figure 1). Focal necrosis noted. None of them showed mature looking plasma cells. Morphological differential diagnoses for case 1 was poorly differentiated carcinoma, high grade lymphoma such as PBL, DLBCL and melanoma and for case 2 was extramedullary plasmablastic myeloma and PBL.

Immunohistochemistry

In case 1, primary panel of markers analysed were EMA, AE-1, Vimentin, HMB-45, LCA and CD 20. Tumour cells were negative for EMA and AE-1 which ruled out carcinoma, negativity for HMB-45 and S-100 ruled out melanoma, and CD 20 negativity ruled out DLBCL. LCA was weakly positive. Hence, the second panel of markers analysed were CD79a, CD138, CD30, CD2, S-100, MIB-1. In case 2, except for HMB-45 and S-100 all the markers were analysed. In both cases tumour cells were positive for CD138, CD79a and negative for CD 2, CD 30, and EMA (Figure 2). MIB-1 proliferation index was >90% in case 1 and >70% in case 2.

To summarise, our case 1 had seropositivity for HIV, lesion in buccal mucosa with enlarged neck node, no other external or internal nodal enlargement and normal bone marrow biopsy. Thus, classical clinical presentation with a characteristic tumour immuno-phenotype (CD 20-, LCA+/-, CD 138+), it was diagnosed as PBL. And in case 2 with almost

similar looking morphology and immunophenotypic profile and considering it as a known case of multiple myeloma, the diagnosis was given as plasmablastic transformation of myeloma.

Discussion

PBL accounts for 2.6% of all HIV related non Hodgkin's lymphomas.[5,7] PBL is a distinct B-cell neoplasm that shows diffuse proliferation of large neoplastic cells, most of which resemble B immunoblasts and have immunophenotype of plasma cells. It was originally described as a rare variant of DLBCL involving the oral cavity and occurring in the clinical setting of HIV and latent Epstain-Bar Virus (EBV) infection.[5] But currently, DLBCL with plasmablastic differentiation represents a clinically heterogeneous spectrum with different clinicopathologic characteristics representing a distinct entity.[5,8] Distinguishing these tumours from anaplastic plasmacytoma or myeloma is the most difficult, but most important for clinical management.

Vega et al[9] assessed the immunophenotypic features of PBL and plasmablastic myeloma using a large panel of lymphoid and plasma cell related markers as well as some tumour suppressor gene products and presence of EBV and Human Herpes Virus type 8. They concluded that both these tumours have virtual identical immunophenotypic profile, suggesting a close relationship between these tumours. None of their patients with PBL had monoclonal gammopathy, multiple osteolytic bone lesions or prior history of plasma cell myeloma or plasmacytoma. All cases of PBL were associated with EBV infection. They suggested that to rule out systemic plasma cell myeloma, a skeletal survey and serum protein electrophoresis may be warranted in cases of possible PBL particularly if there are unusual clinicopathologic features (nonmucosal presentation, HIV negativity and/or EBV negativity). We have not done EBV due to limited resources.

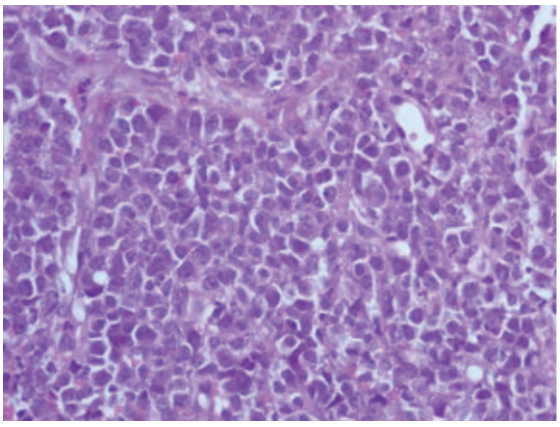

Figure 1: Microphotograph showing sheets of large tumor cells with squared borders, prominent nucleoli and mitotic figures. (H & E, X400)

On the other hand, Teruya-Feldstein et al[4] in their study of CD20-negative large cell lymphoma with plasmablastic features in HIV positive and negative patients, found that nine of twelve cases of PBL had stage IV disease. Bone marrow biopsies were negative in six of seven patients despite extensive bone metastases by CT and PET scans. Six of twelve patients (50%) had minimal IgM spikes. Cyclin D1 and CD56 were positive in myelomas and extramedullary plasmacytomas but negative in PBL.[8] The proliferation fraction highlighted by MIB-1 is much higher in PBL (ranging from 75% to 100%) compared to plasmablastic myeloma (upto 60%) and myelomas (5%).

Our both cases showed similar immunophenotypic profile as suggested by above mentioned studies. Case 1 was HIV positive and case 2 was HIV negative but had multiple bone lesions and M-band. So, case 1 was treated as PBL and was given systemic therapy while case 2 was treated as plasmablastic myeloma and treated as myeloma protocol. Though, our case 2 showed more than 70% MIB-1 index, which differs from most studies.[1,4,10] The basis for this discordance is unclear.

Conclusion

Most of plasmablastic lymphomas are extranodal location, mostly occur in clinical setting of HIV and latent EBV infection but can occur in other immunocompromised hosts and HIV negative individual. Pathologist must be aware of this entity and its different morphological subtype and immunophenotype as its close differentials carries major therapeutic implication. Distinction between extramedullary plasmablastic myeloma and plasmablastic lymphoma remains critical as treatment for the two diseases is significantly different.

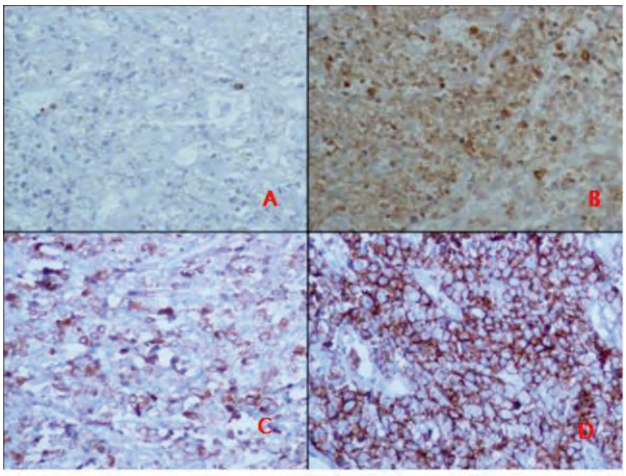

Figure 2: Immunophenotypic profile of tumor cells(IHCX400) (A)Negative for CD 20, (B) Weak cytoplasmic positive for LCA, (C) Membranous positive for CD 79a, (D) Strong membranous positive for CD 138

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"The test of success is not what you do when you are on top. Success is how high you bounce when you hit bottom."

George Patton,
U.S. General, World War II

Granular Cell Tumor Masquerading as Neuroendocrine Tumor on Cytology-A Case Report

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Summary

Granular cell tumor (GCT) is an uncommon benign neoplasm of uncertain histogenesis. Here, we present a case of 40-year-old woman who presented with swelling in nape of neck. Clinical and radiological diagnosis was of enlarged lymph node at level V. Fine needle aspiration cytology was performed and was reported as possibility of neuroendocrine tumor or paraganglioma. Hence, biopsy was advised which revealed a granular cell tumor. Therefore, the slides of cytosmears were rereviewed, and it was observed that the granular cells were misinterpreted as cells of neuroendocrine origin because of their fine granular nuclear chromatin, intranuclear inclusions and few cell clusters traversed by endothelial cells. Since granular cell tumor can occur almost anywhere, a careful examination of cytosmears and knowledge of its distinct cytomorphological features would be supportive.

Keywords: Granular cell tumor, Aspiration biopsy, Neuroendocrine tumor

Introduction

Granular cell tumor (GCT) is an uncommon soft tissue neoplasm that may be asymptomatic or may present as a slow growing nodule. They have a wide anatomic distribution, with roughly one half of the lesions found in head and neck. Common sites of involvement are tongue, breast, upper respiratory tract and soft tissue of upper extremities. Lesions have also been reported in orbit, larynx, parotid, oesophagus, gastrointestinal tract, urinary bladder, etc.[1] Here, we report a case of granular cell tumor in the neck misdiagnosed as neuroendocrine tumor on cytology.

Case report

A 40-year-old female was referred to our centre with swelling in the nape of neck since 3 months and weight loss. On local examination a single, mobile swelling of 2 cm size was palpable at left level V region. Local thyroid examination was within normal limits and hence she was further investigated for lymphadenopathy. No abnormality was detected on systemic examination. Routine blood investigations were within normal limits. Ultrasonography of neck showed a 24x15 mm sized well defined hypo echoic lesion in intermuscular plane of nape of neck on left side suggesting possibility of metastatic deposit. Patient had already undergone fine needle aspiration cytology (FNAC) at another centre and was referred to our institute with a cytological diagnosis of metastatic Hurthle cell carcinoma. Repeat FNAC was performed at our centre with a 22G needle and smears were wet fixed in methanol and stained with Papanicolaou (Pap) stain.

Smears were moderately cellular and showed plenty of polygonal cells arranged in loose clusters and dispersed singly amidst a background of skeletal muscle fibers. Few cell clusters showed intersecting thin walled capillaries (Figure 1). Individual cells had a low N:C ratio with abundant dense pink granular cytoplasm, round slightly eccentric bland nuclei with fine chromatin and small but conspicuous nucleoli. Cells showed mild anisonucleosis and intranuclear inclusions (Figure 2). Due to fragility of the cytoplasm, many naked nuclei were present in the background of abundant granular material. Mitoses or necrosis was absent. No lymphoid cells were seen. Correlating with clinical history and radiological features, we suggested possibilities of neuroendocrine tumor or paraganglioma. Biopsy was advised.

An incision biopsy was performed. Histopathological examination showed polygonal neoplastic tumor cells with abundant granular cytoplasm arranged in lobules. Mild nuclear pleomorphism was evident. However no mitoses or necrosis was seen. Immunohistochemically cells were positive for S100. A final diagnosis of granular cell tumor was given.

Discussion

GCTs are rare benign neoplasms usually occurring in third to fourth decade. They are of uncertain histogenesis, although current theory, based on immunohistochemical and electron microscopic findings, favors a Schwann cell derivation. The neural marker S100 has been shown to be almost invariably expressed in granular cell tumors.[2] Electron microscopy of granular cell tumors shows abundant lysosomes.[3]

GCT has distinct cytomorphological features as suggested by others[4-10] as also seen in our case. Considering the above cytological findings and with clinico radiological correlation, the likely possibilities considered are that of a neuroendocrine tumor, paraganglioma, metastatic Hurthle cell tumor and GCT. These differential diagnoses have also been suggested by Smith et al.[7] Possibilities of neuroendocrine tumor or paraganglioma were favored in this case due to monomorphic cell population, uniform fine chromatin, abundant granular cytoplasm, intranuclear inclusions and most

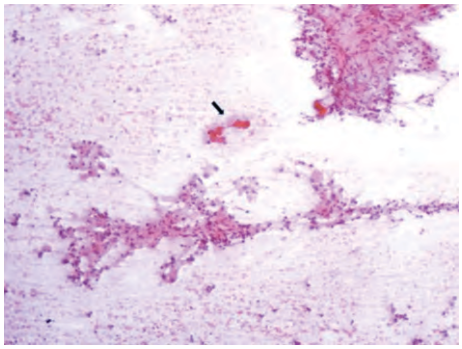

Figure 1: Photomicrograph shows clusters of tumor cells traversed by endothelial cells and skeletal muscle fibers (arrow) (Pap x 100)

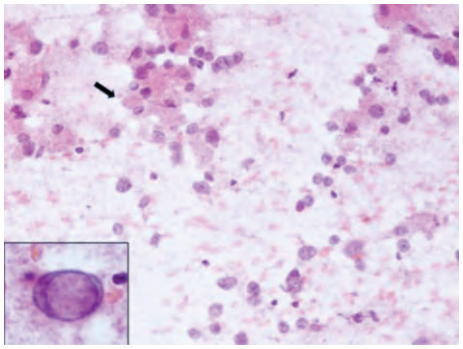

Figure 2: Photomicrograph shows single cells with abundant granular cytoplasm (arrow) and many bare nuclei (Pap x 400). Inset shows intranuclear inclusion (Pap x 1000)

importantly, traversing of few cell clusters by endothelial cells. Tumor cells can be misinterpreted as Hurthle cells because of abundant granular cytoplasm. However, the lack of follicular pattern, cellular atypia, colloid material and normal appearing thyroid on USG, ruled out Hurthle cell tumor. Due to fragility of the cytoplasm of granular cells, background shows abundant granular material which can be misinterpreted by neophytes as necrotic material suggestive of metastatic carcinoma. Absence of significant nuclear atypia or mitotic figures rules it out.

Cytology smears and literature were reviewed after histopathological diagnosis.GCT does occur in intramuscular plane.[11]Closer inspection of nuclei showed that nuclei were more finely granular than the characteristic stippled nuclei of neuroendocrine tumor. Intranuclear inclusion in granular cell tumors have been reported by Liu et al.[5,6] Sirgi et al have described endothelial cells intersecting cell clusters in GCT as also seen in our case.[12]

We misdiagnosed this case because of several reasons. Foremost being the site of occurrence (intermuscular plane of nape of neck), clinical and radiological opinion of enlarged lymph node and finally misinterpretation of cytosmears because we rarely encounter such type of lesion.

Conclusion

We present this case to create awareness among the cytologists regarding the difficulties encountered in the cytodiagnosis of granular cell tumor. Pathologist may occasionally encounter GCTs at unusual sites and awareness of this entity prevents misdiagnosis.

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Parathyroid Carcinoma- A Case Report

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Summary

Parathyroid carcinoma is a rare endocrine neoplasm. Although most patients present with hyperparathyroidism, it is difficult to distinguish preoperatively parathyroid carcinoma from its benign counterpart (parathyroid adenoma), due to their nonspecific clinical features, biochemical profile and imaging findings. Usually it is associated with more severe clinical manifestations and biochemical profile than parathyroid adenoma. Surgery with en bloc tumor resection is the only curative treatment. We report a case of 34 year old female who presented with pathological fracture of left femur with severe hypercalcemia and primary hyperparathyroidism. Imaging studies were not conclusive as to whether it was parathyroid adenoma or carcinoma. Right inferior parathyroidectomy was performed. Postoperative serum calcium and parathyroid hormone (PTH) returned to normal. Final histopathology examination revealed parathyroid carcinoma.

Keywords: Parathyroid carcinoma, Hypercalcemia, Hyperparathyroidism

Introduction

Parathyroid carcinoma is a rare malignancy, with an incidence of 0.5 to 5% of all cases of primary hyperparathyroidism.[1-3] Parathyroid cancer is often seen in cases of primary hyperparathyroidism, but in rare instances it has been reported to occur in secondary hyperparathyroidism and may very rarely be nonfunctioning. Ninety five percent of parathyroid carcinomas are functioning i.e. secrete parathyroid hormone.[45] If a patient has severe symptoms and metabolic complications associated with primary hyperparathyroidism, along with a palpable and large parathyroid tumor, serum calcium level greater than 14 mg/dL and parathyroid hormone levels 5 to 10 times greater than the upper normal limit, then the diagnosis of a parathyroid cancer should be suspected.[6] Parathyroid cancer has an equal gender distribution and the age at diagnosis ranges from 23 to 90 years with median age at diagnosis is 55 years.[7] Certain risk factors have been identified in association with parathyroid carcinoma like chronic hypercalcemia of renal failure, irradiation to head and neck, familial cancer syndromes like hyperparathyroid-jaw tumor syndrome (HPT-JT), multiple endocrine neoplasia (MEN) type 1 and multiple endocrine neoplasia (MEN) type 2A.[8] There is no American Joint Committee on Cancer staging system for parathyroid cancer because of its rarity.

Case Report

We describe a 34-year-old female who presented to an orthopedic surgeon with complaint of sudden fracture of left leg. Patient was referred to our institute (GCRI) with a diagnosis of Brown tumor and pathologic fracture of left femur. Patient had complaints of joint pains and backache for 8 years and muscle weakness, tingling and numbness in lower extremities for about a year. She wasn't aware of any neck mass and or any hoarseness of voice. Her medical history was not significant. There was no past history of irradiation to the neck, urinary complaints, peptic ulcer or pancreatitis. Family history was unremarkable.

Routine blood tests revealed severe hypercalcemia (14.36 mg/dL serum calcium), elevated intact parathyroid hormone (PTH) (1458 pg/ml), low serum inorganic phosphorus (1.93 mg/dL), elevated serum alkaline phosphatase (259.0 IU/L) and blood urea nitrogen (59.03 mg/dL). She was anemic with her hemoglobin of 9.4 gm%.

On clinical examination a palpable 2x2 cm, firm, nontender swelling was noted in the right neck lateral to right thyroid gland without any cervical lymphadenopathy. Heart, lung, and abdominal examinations were unremarkable.

X ray left femur showed a lytic lesion with pathological fracture and multiple bony fragments of mid diaphysis of left femur (Figure 1). Mild diffuse osteopenia was noted in right femur. Expansile lytic lesions were also noted in bilateral few ribs on chest imaging and nephrocalcinosis was noted in both kidneys on renal imaging studies. Ultrasound examination of neck showed a 26x25x38 mm solid lesion with internal cystic components in posterior and inferior to right lobe of thyroid with extension into pretracheal region. A computerized tomography (CT) scan of the neck and upper mediastinum revealed 29x35x46 mm heterogeneously enhancing soft tissue density lesion with non enhancing cystic/necrotic areas posteroinferior to right lobe of thyroid gland between right common carotid artery and trachea. Lesion was abutting right lateral wall of trachea, right thyroid gland and prevertebral muscles with preserved fat planes (Figure 2). On ultrasound/CT scan, no lymph nodes were visualized.

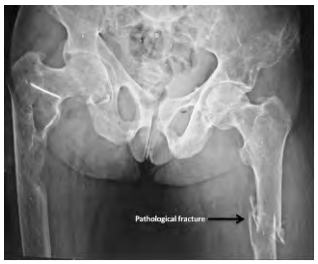
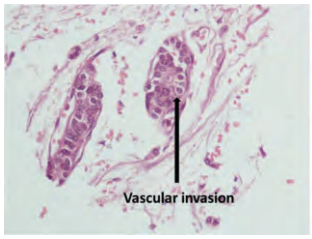


Figure 1: Pathological fracture of mid diaphysis of left femur

Figure 2: Axial CT image of right inferior parathyroid mass with enhancing cystic/necrotic areas



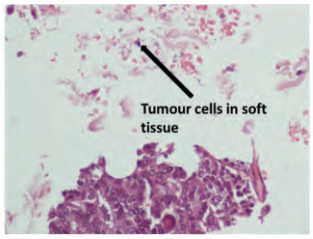


Figure 4: Histopathologic picture of parathyroid carcinoma showing vascular and soft tissue invasion

She was treated preoperatively with aggressive rehydration and loop diuretics. Right inferior parathyroidectomy was performed with removal of intact encapsulated tumor. Since there was no local invasion to surrounding soft tissues or strap muscles and no adherence to the thyroid lobe, it could be easily separated (Figure 3). Regional lymph nodes were not enlarged. In the absence of gross local invasion and regional metastasis, removal of surrounding structures and neck dissection was not indicated. Right recurrent laryngeal nerve was identified and preserved. On first postoperative day, both serum calcium (8.59 mg/dL) and PTH level (6 pg/ml) decreased and were within normal limits. Histopathology report was a parathyroid carcinoma of 2.3 cm, well encapsulated with vascular, capsular, and soft tissue invasion (Figure 4).

Discussion

A diagnosis of hyperparathyroidism attributable to parathyroid carcinoma may be difficult to arrive both at pre- and intraoperatively.[7] The typical clinical picture is characterized by severe hypercalcemia with up to 80% of patients having renal involvement (nephrocalcinosis, nephrolithiasis, and impaired renal function), and in up to 90% patients with bone involvement (osteitis fibrosa cystica, subperiosteal resorption, "salt and pepper" skull, diffuse osteopenia).[11] Other symptoms include renal colic, muscle weakness, fatigue, depression, nausea, polydipsia and polyuria, bone pain, and fractures. Recurrent severe pancreatitis, peptic ulcer disease, and anemia can also occur, Up to 76% of patients with parathyroid carcinoma have a palpable neck mass.[11]

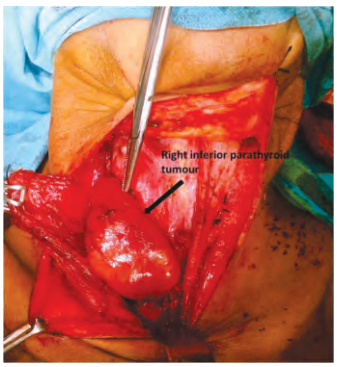


Figure 3: Right inferior parathyroidectomy with intact encapsulated tumor removal

Our patient also had hyperparathyroidism, hypercalcemia, pathological bone fracture and a palpable neck mass but none of these features is pathognomonic of malignancy. Fine needle aspiration cytology (FNAC) or needle biopsy is not advisable due to needle track seeding of the tumor.[12] The presence of lymph node metastases, distant metastases, and obvious local invasion are sine qua non of parathyroid carcinoma.[13] Subtle pathologic findings such as mitoses, nuclear pleomorphism, rosette formation, trabecular pattern with thick fibrous bands with interstitial fibrous septa, capsular and vascular as well as soft tissue invasion may point to the diagnosis of parathyroid carcinoma.[14] Several markers have been studied also to distinguish parathyroid carcinoma from parathyroid adenoma. DNA aneuploidy is observed in 60% cases of parathyroid carcinoma and associated with worst prognosis, Immunohistochemistry analysis for increased Ki-67, galectin 3 expressions and absence of parafibromin expression are the promising markers of parathyroid carcinoma.[17]

Surgery is the only curative treatment for parathyroid carcinoma and consists of complete resection of the primary lesion at the time of initial operation.[1,5] Shaha and his colleague[13] suggested if the tumor is large or invading surrounding structures such as the thyroid gland, trachea, or esophagus, it would be appropriate to suspect parathyroid carcinoma and perform an radical local procedure including removal of thyroid gland and it would be prudent to do lymph node sampling of central compartment and lower jugular chain at the time of surgery. Parathyroid cancer is generally not radiosensitive. Some case reports suggested that postoperative radiotherapy decreases the risk of recurrence but it does not affect the survival. Similarly, chemotherapy has not shown any role even in metastatic disease and on the survival.

The 10 year survival ranges from 13% to 78% in patients with parathyroid cancer. Loco regional recurrence is common even after en bloc surgical resection. Nearly 25% to 80% of patients with parathyroid cancer develop local recurrence.

Biochemical monitoring for parathyroid hormone and calcium levels is a very sensitive and accurate method to detect persistent or recurrent disease. Distant metastasis to the lung, bone, and liver occur late and is best detected with wholebody Sestamibi scan and computed tomography or magnetic resonance imaging scan.

Majority of the patients with parathyroid cancer succumb to uncontrollable hypercalcemia, and not due to direct tumor effect. Management of patients with unresectable disease, recurrent disease or diffuse metastatic disease should be focused on controlling calcium levels by loop diuretics, and various hypocalcemic drugs like bisphosphonates, calcitonin and plicamycin. Recently, a calcimimetic agent, cinacalcet has been shown successful results to control hypercalcemia.

Conclusion

It is difficult to recognize parathyroid carcinoma preoperatively in case of primary hyperparathyroidism. Clinical suspicion of parathyroid carcinoma can be made on the basis of signs and symptoms of palpable neck swelling, severe hypercalcemia, and increased level of PTH and metabolic complications of primary hyperparathyroidism (bone and renal disease) as seen in our case. Major emphasis should be placed upon en bloc resection of such tumor. Cervical nodal dissection and surrounding soft tissue resection is indicated if the tumor is invading them. Final diagnosis of parathyroid carcinoma was confirmed by capsular and vascular invasion on histopathology examination in our case. We recommend genetic and immunohistological analyses for further confirmation of diagnosis.

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Leiomyosarcoma of the Tongue - A Case Report

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Summary

Soft tissue sarcomas arising in the head and neck are rare among adults. They account for approximately 10% of all soft tissue sarcomas and approximately 1% of head and neck tumors. Leiomyosarcomas are among the unusual soft tissue sarcomas in the head and neck which account about 0.2% of the cases in the reported series. We are presenting a case of 30-year-old man with leiomyosarcoma of the lateral aspect and base of oral tongue, who was operated outside in private hospital followed by postoperative radiation therapy at Gujarat Cancer Research Institute, Ahmedabad. Initially he presented with ulcer over left lateral aspect of tongue since two months and fine needle aspiration cytology was reported as squamous malignant cells. Preoperative computed tomography (CT) scan revealed 46x25x53 mm well defined lesion in oral cavity on left side of tongue extending up to floor of mouth with few enlarged nodes seen at level II on left side of neck, largest node measuring approximately 17x12 mm. Patient underwent wide excision of the lesion on left lateral side and base of tongue along with left modified neck dissection type II. Gross examination of operated specimen (tumor size) was 5x4.5x2.5 cm; while microscopically tumor showed malignant spindle cell neoplasm and neoplastic cells expressed vimentin and smooth muscle actin. Patient was treated with radiation therapy with linear accelerator (6 megavoltage photons) with two lateral opposed portals using orfit for immobilisation for total dose of 60 Gy (200 cGy/# , five days a week x 30 days). During treatment patient had developed grade II mucositis, grade I dermatitis and grade II dysphagia, which were manageable. There was no evidence of disease at the end of 4 months of follow up. Appropriate treatment options, and accurate estimation of survival outcome, however, will not be conclusive until sufficient cases have been reviewed.

Keywords: Leiomyosarcoma, Oral tongue, Dysphagia

Introduction

Soft tissue sarcomas arising in the head and neck are rare among adults. They account for approximately 10% of all soft tissue sarcomas and approximately 1% of all head and neck tumors. Leiomyosarcomas are among the unusual soft tissue sarcomas in the head and neck which account about 0.2% of the cases in the reported series. To the authors knowledge only 25 cases of primary leiomyosarcomas of the tongue have been reported in the English literature.[1] We are presenting a case of 30 year old man with leiomyosarcoma of the lateral aspect and base of the oral tongue, who was operated outside in private hospital, referred for postoperative radiation therapy at Gujarat Cancer and Research Institute, Ahmedabad.

Case Report

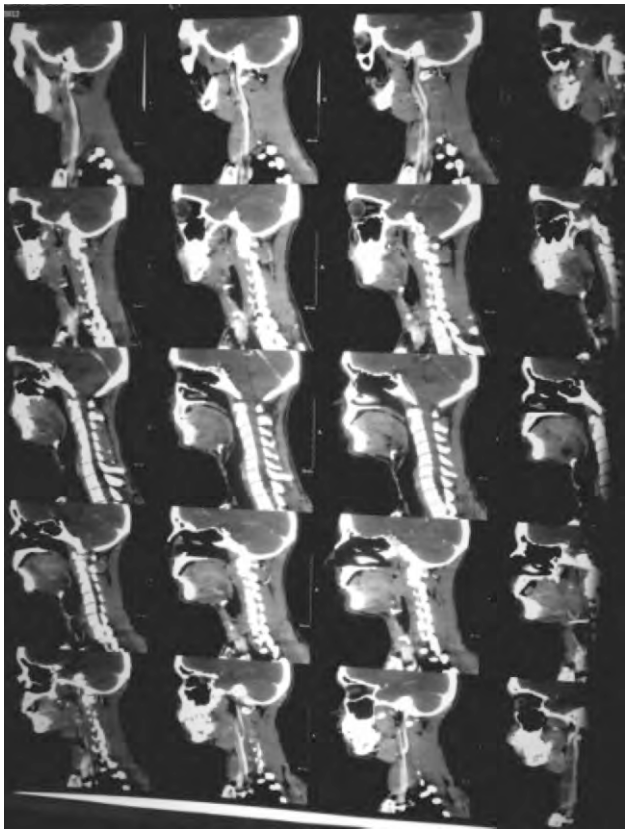
A 30 year old male initially treated at private hospital for ulcer of 3x2 cm in size on left lateral aspect of the tongue since two months. Outside report of fine needle aspiration cytology showed squamous malignant cells. Patient's preoperative multislice-computed tomography (MSCT) scan report was (Figure 1 and 2) 46x25x53 mm well defined lesion in oral cavity on left side of tongue extending up to the floor of mouth with few enlarged nodes seen at the level II on left side of neck, largest node measuring approximately 17x12 mm. Wide excision of left oral tongue and base via mandibulotomy, reconstruction of mandible with left pectoralis major myocutaneous (PMMC) flap, temporary tracheostomy and left modified radical neck dissection type II under general anaesthesia was done at a private hospital. On histopathological examination, gross tumor size was 5x4.5x2.5 cm; microscopically tumor showed malignant spindle cell neoplasm with nuclear pleomorphism, atypical mitosis count (5-6/10 high power field) along with foci of necrosis; tumor involved underlying muscle bundles; all mucosal margins were free but closest margin was 0.2 cm away; lymphovascular permeation was absent and all submitted 14 lymph nodes were free of metastatic tumor and showed reactive changes.

Thereafter, the patient was referred to GCRI for adjuvant radiotherapy (RT) treatment. At the time of presentation, patient had no postoperative complaints and clinically no palpable lymphadenopathy. Chest X-ray and other blood investigations were normal. Review of slides at our institute, showed interlacing fascicles of spindle cells (Figure 3a,b). A marked cellular pleomorphism was observed, represented by cells with irregular shape and eosinophilic cytoplasm; nuclei were large, hyperchromatic and cigar shaped. Further, immunohistochemical examination showed neoplastic cells which expressed vimentin (Figure 4a) and smooth muscle actin (Figure 4b) which confirmed the diagnosis of leiomyosarcoma.

Patient was treated with radiation therapy with linear accelerator using 6 megavoltage photons with two parallel lateral opposed portals using orfit for immobilisation, for total dose of 60 Gy (200 cGy/# , five days a week x 30 days). During treatment patient had developed grade II mucositis, grade I dermatitis, grade II dysphagia, which were manageable. Patient was disease free at the end of 4 months of followup.

Discussion

Squamous cell carcinomas are the most



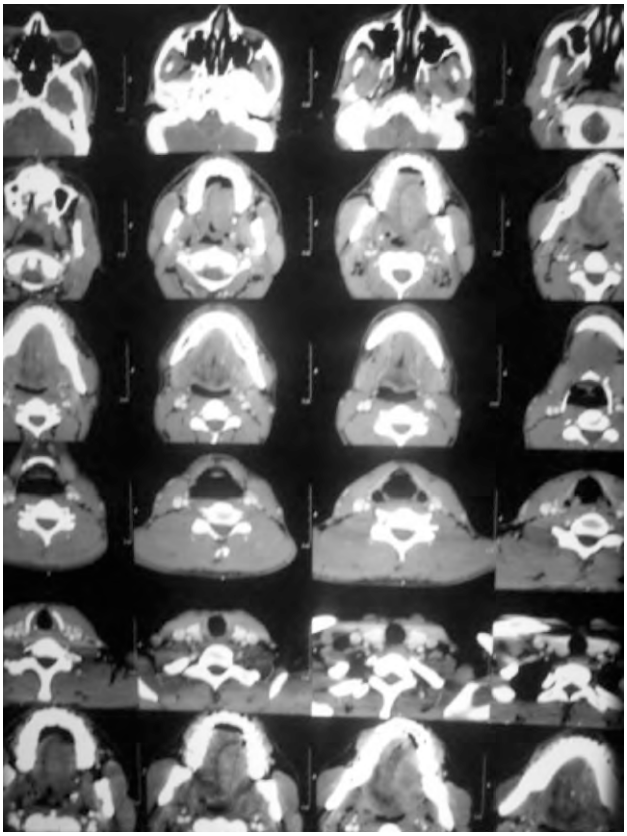


Figure 1 and 2 : MSCT scan of neck showing 46x25x53 mm well defined lesion in oral cavity on left side of tongue extending up to the floor of mouth with few enlarged nodes seen at the level II on same side of neck

common type of cancer found in head and neck tumors including that of tongue. The leiomyosarcomas are very rare tumors of tongue due to the relative absence of smooth muscle in the tongue. They are thought to be arising from smooth muscle associated with blood vessels, myoepithelial cells or the circumvallate papillae in case of tongue. The etiology remains unclear; however Epstein-Barr virus, trauma, ionizing radiation and oestrogenic stimulation have been reported. Soft tissue sarcomas of the head and neck in adults are rare, more common in males than females; however, there is a 1.7:1 male predominance in leiomyosarcomas arising in the tongue. There is a peak incidence in the 6th decade of life, although some tumors have been diagnosed also in infants.[2]

Mostly head and neck soft tissue sarcomas are high grade. A wide spectrum of histologic subtypes is observed, but there is preponderance of angiosarcoma in this site. Leiomyosarcoma may arise in any location, but more than half are located in retroperitoneal or intraabdominal sites, while head and neck account for about 0.2% of the cases in the reported series. Leiomyosarcoma of the oral cavity is a very rare tumor that is associated with aggressive clinical behaviour and low survival. The behaviour of this disease is site-related. Leiomyosarcoma of the tongue is a very rare tumor. To our knowledge only 25 cases of primary leiomyosarcomas of the tongue have been reported.[1]

Most of these tumors present as a painless mass. The median interval between onset and diagnosis is 5.5 months.[3] As for all head and neck cancer, full radiological evaluation of oral leiomyosarcoma is essential for both staging and preoperative planning. CT scan and magnetic resonance imaging (MRI) are used for the local and regional evaluation. The likelihood of regional lymph node metastases is low as in the reports; the incidence of positive regional nodes was about 2-5%.[3] The likelihood of distant metastases is related to histologic grade and tumor size; the risk is highest for large, high-grade lesions. The most common site for distant metastases is the lung. Thus, patients should undergo a chest CT scan before treatment. Metastases to other sites are unlikely, particularly in the absence of pulmonary metastases, so that additional diagnostic studies, such as a brain MRI or a bone scan, are not necessary in the absence of symptoms.

If surgery is feasible than it should be the primary mode of treatment in tongue leiomyosarcomas, which can be followed by postoperative adjuvant radiotherapy in cases where indicated; for patients with low-grade tumors who have close (<1 cm) or positive margins, as well as those with high-grade tumors. Our patient also underwent primary

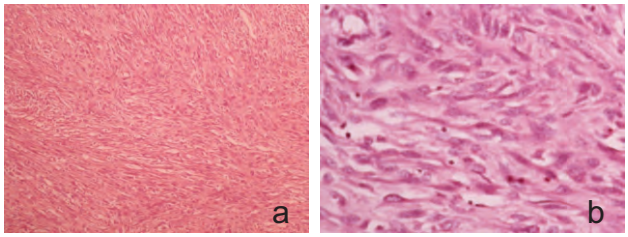


Figure 3 a,b: Leiomyosarcoma of tongue showing interlacing fascicles of spindle cells (H&E, 20x)

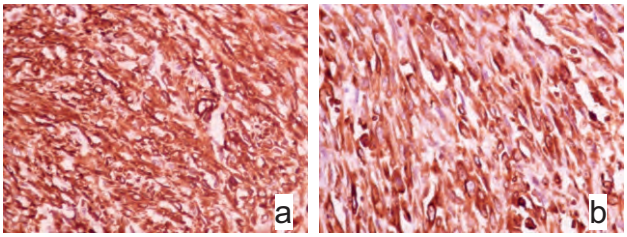


Figure 4: Leiomyosarcoma of tongue;IHC, 20x: Vimentin positivity (a), Actin positivity (b)

surgery followed by postoperative adjuvant radiotherapy since it was a high grade tumor with close margins. If surgery is not feasible, the tumor is treated with definitive RT with a high dose. It is difficult to assess the efficacy of RT alone, because it is usually used for large unresectable tumors that have a low chance of cure after any treatment modality. However, it is likely that surgery and RT are more efficacious than RT alone for resectable tumors. The value of adjuvant chemotherapy is unclear. Few data directly pertain to the efficacy of adjuvant chemotherapy for head and neck soft tissue sarcomas; therefore, it is necessary to extrapolate data from soft tissue sarcomas arising in more common locations.[3] However, subset analysis of patients with extremity soft tissue sarcomas revealed a significant improvement in overall survival for patients who received adjuvant chemotherapy (NCCN Guidelines Version 1.2012 with category 2A evidence).

Due to the rarity of this tumor, there is a limited number of leiomyosarcoma of the tongue reported in the literature. Kazemian et al[3] reported a 32-year-old man with leiomyosarcoma of the lateral aspect of the oral tongue with neck metastasis where glossectomy and radical modified neck dissection was done. Six months after chemoradiotherapy, he developed a single metastasis in his right femur and unfortunately he died in few weeks due to lung metastasis. A 48-year old woman with leiomyosarcoma of the tongue was reported by Wollenberg et al.[4] The tumor was surgically removed. The prognosis was not mentioned in the report. Crossman et al[5] described a case of a 46-year-old woman who presented with a lesion rapidly increasing in size on the lateral aspect of her tongue, which was excised and completed-5-year follow-up. Kwang II Kim et al[6] reported a case of leiomyosarcoma of the tongue in a 48-year-old woman who was considered initially as having a benign tumor. Calos et al[7] reported a case of primary leiomyosarcoma of the lateral border of the tongue treated with local excision having 4 years of disease free survival. A case report of this disease was published by Mayall et al in a 60-year-old man.[8] Partial glossectomy was done without further treatment and he was disease free at the end of one year of follow up. Aydin et al also reported a case of the leiomyosarcoma of the base of tongue who was treated with radiation therapy and was disease free at the end of 1.5 years.[9] On the other hand a case study by Muzio et al[10] on leiomyosarcoma of the oral tongue in a 67-year-old man who had a wide local excision and had no recurrence after five years. Another review of literature was done by Montgomery et al[11] in which cases diagnosed with leiomyosarcoma of the head and neck was retrieved from the archives of three institutions. They concluded that head and neck leiomyosarcomas are rare and aggressive neoplasms with a high propensity for metastasis, and adjuvant therapy has limited effect. Other authors have also reported cases in literature.[12-15]

The present case report is of a 30-year-old man with leiomyosarcoma of the lateral aspect and base of oral tongue, who was operated outside in private hospital followed by postoperative radiation therapy and there is no evidence of disease at the end of 4 months of follow up.

Leiomyosarcomas of head and neck are very few and are more uncommon in the oral cavity, so the standard treatment for this disease has not been established. Surgery, radiation therapy and chemotherapy were the options that have been used in various reported cases.[3] It is logical that surgery should be the primary treatment of this lesion like soft tissue sarcoma of other sites, and in some of the reports satisfactory results has been seen with this approach.[3,7,8] But unfortunately there were fewer experiences with adjuvant therapy. Adjuvant RT likely improves the probability of cure in patients with high-grade tumors and those with close or positive margins. RT alone may cure a small subset of patients with advanced unresectable lesions. Although the efficacy of adjuvant chemotherapy is ill defined, it should be considered for patients with high grade lesions.

Conclusion

This case has been reported for its rarity. Appropriate treatment options, and accurate estimation of survival outcome, however, will not be conclusive until sufficient cases have been reported. With the rarity of this tumor, such knowledge may require more practices.

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"When I'm trying to plan, I think very broad. But when I'm trying to accomplish something, I'm very focused."

Deborah McGuinness,
Senior Research Scientist, Stanford

Primary Orbital Lymphoma: A Case Report

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Summary

A 50 year male presented with swelling of the right eye for 6 months with cervical lymphadenopathy. Biopsy revealed B cell Non Hodgkin's Lymphoma large cell type. The patient is being treated with chemotherapy. The literature is reviewed.

Keywords: Primary, Orbital lymphoma, Non hodgkin's lymphoma, CHOP

Introduction

Lymphomas can disseminate to a wide variety of sites. The orbit is an uncommon site for primary presentation of lymphoma. Non-Hodgkin's lymphoma (NHL) can have extra nodal presentation in 25% of cases unlike Hodgkin's lymphoma which rarely involves extra nodal sites.[1] Orbital lymphomas constitute 2% of all lymphomas.[2] Majority are of non-Hodgkin's type and are seen mostly in adults during the fifth to the seventh decades of life. Chemotherapy and radiotherapy is the mainstay of treatment. Here is a case report of a 50 year old male patient, presenting as right eye swelling that turned out to be a case of primary orbital lymphoma.

Case Report

A 50 year old male patient presented at the Gujarat Cancer and Research Centre (GCRI) with gradually progressive painless swelling of the right eye for 6 months with loss of vision for 3 months. Examination revealed an exophytic growth involving the whole right eye and the upper and lower eyelids (Figure 1 and 2). General examination revealed enlarged right cervical level I b nodes. Rest of the physical examination was unremarkable. Magnetic resonance imaging (MRI) of para nasal sinuses (PNS) and brain was done which revealed an 89x66x52 mm lesion in retrobulbar (Figure 3) space of right orbit involving both intraconal and extraconal compartments along with medial, lateral, inferior recti and displacing optic nerve superiorly with loss of fat plane. Lesion was also eroding medial, lateral and inferior orbital walls extending into ethmoid and maxillary sinuses (Figure 4). It was abutting dura of left temporal lobe, however without any intracranial extension. Externally it involved skin and muscles of right cheek. Ultrasonography of neck revealed multiple right level Ib nodes largest measuring 26x30mm and bilateral level II nodes largest measuring 14x4mm on left side. No lymphadenopathy was noted elsewhere. Ultrasound guided biopsy of the retrobulbar mass revealed malignant round cell tumor with likelihood of NHL. Immunohistochemistry (IHC) showed diffuse large B cell NHL (LCA, CD20 and CD79A positive). Cerebral spinal fluid cytology was negative. The patient was diagnosed to have primary NHL of orbital region stage IIE.

The patient has received 2 cycles of chemotherapy till date with cyclophosphamide, adriamycin, vincristine and prednisolone (CHOP) with intrathecal methotrexate. There is objective improvement in form of visibly reduced size of the tumor and reduction of symptoms. Further plan of management is to continue with 4 more cycles of chemotherapy followed by radiotherapy depending on the response.

Discussion

Malignant orbital lymphoma is usually a low-grade malignancy characterized by a proliferation of monoclonal B cells (non-Hodgkin's), which arise in lymph nodes or in an extra nodal site such as the orbit.[3,4] In 75% of cases the process is unilateral with a predilection for the superior and anterior orbits, and in 25% it is bilateral; 40% of cases are associated with systemic disease at time of diagnosis. The patient usually presents with painless, slowly progressive proptosis, downward displacement of the globe, a palpable non tender orbital mass, with or without extraocular motility problems and ptosis. On Computed Tomography (CT) scan, lymphomas appear homogeneous in texture, isodense to muscle, and show mild contrast enhancement. A diffuse or well defined orbital mass with molding to the globe, optic nerve, and orbital bones strongly suggests the diagnosis of orbital lymphoma; molding usually is associated with indolent histology, whereas bone destruction is associated with aggressive histology. MRI usually shows intermediate signal intensity on T1- and T2-weighted images and moderate signal intensity with gadolinium enhancement.[5] Similarly in our study, T1 weighted post contrast fat sat MRI sagittal section revealed a moderately enhancing mass invading facial muscles and ethmoid and maxillary sinuses.

A distinction between "primary" and "secondary" orbital lymphoma is arbitrary. Primary lymphomas are considered to be limited to the orbit or stage I disease. In secondary orbital lymphomas, the

Figure 1,2: Right orbital mass involving both eyelids

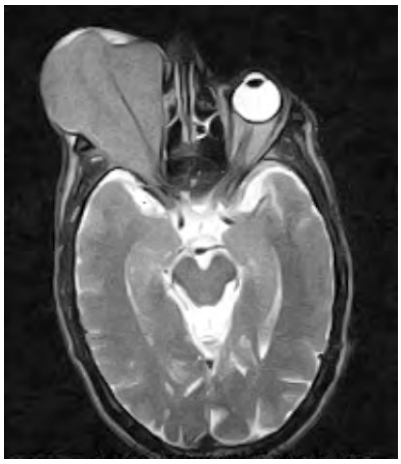

Figure 3: T2 weighted axial image showing sagittal section showing moderately enhancing mass

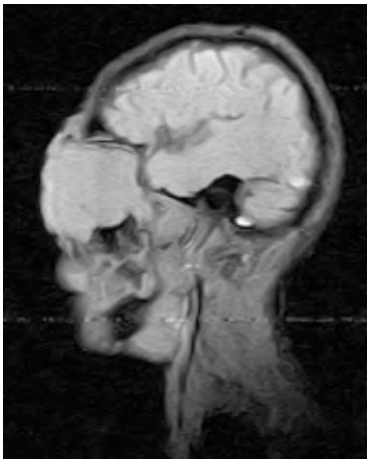

Figure 4: T1 weighted post contrast fat sat retrobulbar lobulated mass invading facial muscles and ethmoid sinuses

orbit is considered as a secondary extra nodal site of involvement. In these cases, the systemic disease exists or is diagnosed at the same time as the discovery of orbital lymphoma.[6] Ours was a case of primary orbital lymphoma.

Current laboratory workup for lymphoma includes IHC, flow cytometry, cytogenetics and molecular studies. The present case was of diffuse large B cell NHL with LCA, CD20 and CD79A positivity on IHC. Nearly 85% to 90% of orbital lymphomas are categorized as diffuse, low-grade proliferations of small, monoclonal B-cell lymphocytes. The remaining 10% to 15% have follicular or diffuse large B cell characteristics. Lesions displaying high mitotic activity are most likely to be associated with extraorbital, systemic disease; follicular lesions with germinal centers are likely to be indicative of localized disease.[7]

The Revised European-American Classification of Lymphoid Neoplasms (REAL) was the most widely used diagnostic classification system based on morphology, immunophenotype, genotype and clinical features of the lymphoma (Table 1). In this classification, lymphomas were grouped as indolent, aggressive and highly aggressive types.[8] It was succeeded by the WHO classification of lymphoid neoplasms in 2008 that further refined the definitions of well recognized diseases, identified new entities and variants, and incorporated new emerging concepts in the understanding of lymphoid neoplasms.[9] The Ann Arbor Staging System is usually used to assign a stage for lymphomas (Table 2).[10]

A thorough staging workup with a complete history and physical examination, including gastrointestinal endoscopy, orbital and systemic imaging, barium studies of the gastrointestinal tract, and morphologic studies is necessary for patients with orbital lymphoma in order to recognize systemic disease.[11] PET has replaced bone and gallium scans for detecting small foci of lymphoma throughout the body because of its high sensitivity.[12]

Therapeutic approach should be tailored based on the histological classification and staging of the disease. Lymphomas are radiosensitive; although External Beam Radiation Therapy (EBRT) at a 30-Gy dose may be successful in controlling local orbital disease in a majority of patients with low-grade indolent lymphoma, intermediate-grade lymphomas are more appropriately treated with higher doses of up to 40 Gy. Distant relapse has been observed in approximately 25% of patients with low-grade lymphoma and 50% of those with higher grade lymphomas.[13] In patients with more aggressive orbital lymphoma for which widespread systemic involvement is likely, combining systemic chemotherapy with local radiation treatment is a better approach.[14] We would like to go for this approach as it has a better response rate.

Conclusion

In conclusion, a diagnosis of lymphoma should be borne in mind in the differential diagnosis of an orbital tumor that can facilitate timely diagnosis and appropriate management of this highly curable malignancy.

Table 1: Revised European-American classification of lymphoid neoplasms[8]

Indolent lymphomas
Follicular lymphoma
B-CLL/small lymphocytic lymphoma
Lymphoplasmacytic lymphoma
Marginal zone lymphoma (nodal and/or extranodal)
T/NK large cell granular lymphocyte leukemia
T-CLL
Aggressive lymphomas
Mantle cell lymphoma
Diffuse large B-cell lymphoma
Peripheral T-cell lymphoma (unspecified)
Peripheral T-cell lymphoma (angioimmunoblastic, angiocentric)
T/NK cell, hepatosplenic, intestinal T-cell lymphoma
Anaplastic large cell lymphoma
Highly aggressive lymphomas
Precursor T- or B-cell lymphoblastic leukemia/ lymphoma Burkitt and Burkitt-like lymphoma
Adult T-cell leukemia/lymphoma

Table 2: Ann Arbor staging system for lymphoma with Cotswolds modifications[10]

Stage	**description**
I	Single lymph node region or lymphoid structure (e.g. spleen, thymus or Waldeyer ring)
II	Two or more lymph node regions on the same side of the diaphragm OR localized involvement of an extranodal lymphoid structure AND of one or more lymph node regions on same side of diaphragm
III	Lymph nodes on both sides of diaphragm ± extranodal sites
IV	Two or more extranodal sites or liver or bone marrow
	(All cases are subclassified to indicate the absence (A) or presence (B) of the systemic symptoms of significant unexplained fever, night sweats, or unexplained weight loss exceeding 10 percent of body weight during the six months prior to diagnosis. "E" refers to extranodal contiguous extension and "X" is used if bulky disease is present.)

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Retropharyngeal Lipoma- A Case Report

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Summary

Lipoma of retropharyngeal region is a rare, slow growing tumor. It does not cause symptoms until it reaches a large size. It is a rare entity, few reports appear in literature. Treatment is surgical excision. We present a case of 70 year old female having lipoma in retropharyngeal space causing airway obstruction and dysphagia. The radiological findings and surgical management are discussed.
Keywords: Lipoma, Retropharyngeal, Dysphagia

Introduction

Lipomas are the most common benign tumors of mesenchymal origin. Only 13% of these tumors arise in head and neck.[1] Retropharyngeal space involvement is not common. Mostly lipomas arise in posterior region of neck and are encapsulated. Surgical approach for excision is based on location of tumor.

Case Report

A 70 year old female who had undergone emergency tracheostomy for respiratory distress was referred to Gujarat Cancer and Research Institute for further management. Since last 15 years, she had history of large swelling in left side of neck. She had dysphagia with aspiration. Ryle's tube was inserted for feeding. Patient was having no comorbid illness. Examination revealed approximately 5x6 cm smooth ill defined mass in left side of neck (level II and III). Mass was soft to firm and non-tender. There were no palpable lymph nodes in the neck. Intraoral examination and routine investigations were both within normal limit. Direct laryngoscopic examination revealed a smooth bulge in the posterior pharyngeal wall with normal overlying mucosa. Computerized tomographic scan (CT) neck done outside revealed a large well defined, non-enhancing, fat attenuating lesion in the retropharyngeal space, more towards left side. Magnetic resonance imaging (MRI) done in our institute was suggestive of 45x45x75 mm altered signal intensity lesion in neck extending into prevertebral space at level of C3 to C7 (Figure 1 and 2). The lesion was compressing posterior pharyngeal wall and oesophagus.

Excision of tumor was planned through trans-cervical approach. Skin crease transverse neck incision kept. There was soft tissue bulging in neck arising from retropharyngeal space (Figure 3). A large lobulated lipomatous mass was removed en bloc. There was an associated traction diverticulum in the left pyriform fossa, which was removed and primary closure of mucosa was performed. Post operatively, the patient was kept on Ryle's tube feeding. On 4th post operative day tracheostomy tube was blocked. Ryle's tube was removed on 7th post operative day. Patient was discharged on 8th postoperative day with oral feeding and recovery was uneventful. Histopathological examination of excised specimen was reported as pleomorphic lipoma.

Discussion

Most retropharyngeal space neoplasms are of salivary gland origin, few are neurogenic tumors. Lipomas of retropharyngeal space are rare. In literature, till date, only 30 cases of retropharyngeal lipoma have been reported.[2] This benign tumor often causes unspecific clinical symptoms. Due to slow growth and relatively inaccessible site, these tumors are detected when large[3] and symptomatic.

In the present study, since 15 years the patient had swelling in the neck. According to location of tumor, the likely symptoms may be hoarseness of voice, respiratory distress, dysphagia and obstructive sleep apnoea. Presence of pain in long standing mass with neurological deficit points towards malignant transformation. Lipomas are of mesenchymal origin. They are composed of mature adipose cells separated by a thin capsule of connective tissue. Longstanding lipomas may convert into liposarcomas. CT and MRI are useful investigations to differentiate between benign and malignant retropharyngeal lipomas. Histopathological examination is gold standard.[4] CT scan shows a low attenuation related to fat lesion ranging (50-150) Hounsfield[5] with 75-90% accuracy. Lipomas typically do not show contrast enhancement hence CT scan cannot definitively distinguish lipoma from liposarcoma therefore liposarcoma should be kept as a differential diagnosis.[6] MRI is considered as imaging modality of choice for characterization of lipomatous lesion. Although the malignant potential of retropharyngeal lipoma is low; these tumors need to be surgically excised if they produce life threatening symptoms therefore, surgery remains the treatment of choice.[7] There are various surgical approaches depending upon location of tumor. MRI allows the surgeon to select the most appropriate approach.[8] Ultimate goal is complete tumor removal with minimal injury to adjacent vital structures.

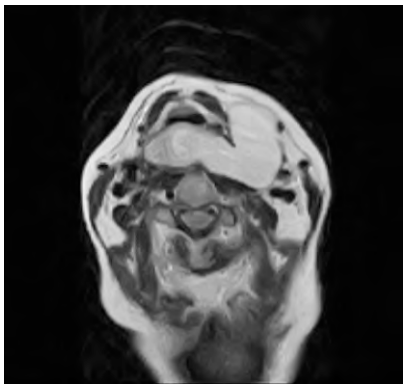

Figure 1: Axial MRI image of retropharyngeal lipoma

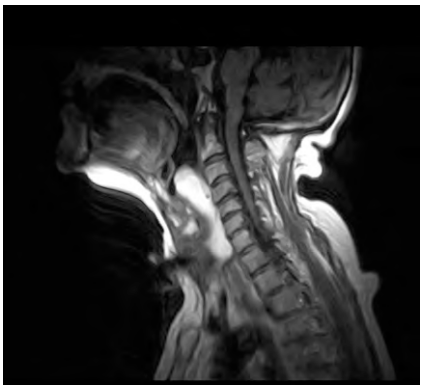

Figure 2: Sagittal reconstructed image of retropharyngeal lipoma

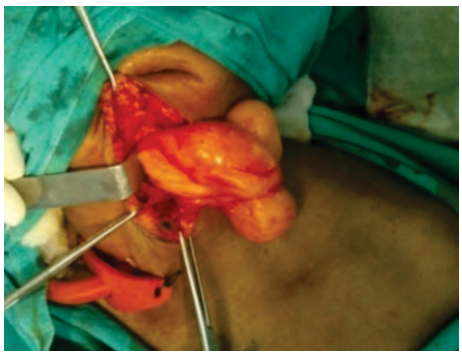

Figure 3: Intraoperative image of retropharyngeal lipoma

Conclusion

Lipoma of retropharyngeal space is a rare entity. Usually they present with obstructive sleep apnea or rarely with stridor. Diagnosis is usually made on CT scan or MRI. In all symptomatic patients, surgical excision is warranted as it results in remission of symptoms.

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"Success seems to be connected with action. Successful people keep moving. They make mistakes, but they don't quit."

Conrad Hilton
Founder, Hilton Hotels

Esthesioneuroblastoma- A Case Report and Review of Literature

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Summary
We report here a rare case of 28 years old lady presented with nasal cavity mass, epistaxis, headache, found to have locally advanced Esthesioneuroblastoma, treated with craniofacial resection which recurred rapidly within 45 days after surgery. She has recently completed concurrent chemoradiation uneventfully. Literature is also reviewed.
Keywords: Esthesioneuroblastoma, Olfactory neuroblastoma, Chemoradiation

Introduction

Esthesion is a French term for sensation or perception. Esthesioneuroblastoma (ENB) was first described in 1924 by Berger and Luc in the French medical literature under the name esthesioneuro epitheliome olfactif.[1] Various terminologies have been ascribed to this tumor, but the only two terms used in recent publications are esthesioneuroblastoma and olfactory neuroblastoma. It is a rare neuroectodermal tumor that originates from the olfactory sensory epithelium. A 1997 literature search identified 1,457 cases in the published literature since its discovery in 1924.[2] This tumor constitutes 3% of all intranasal neoplasms and can be seen in all ages, with a peak in the second and sixth decades of life and with equal distribution between the sexes.[2,3] Because ENB are so uncommon, few data exist with respect to optimum management strategies, multiple opinions exist regarding its origin, diagnosis, and management. Unfortunately early diagnosis is still uncommon and no significant changes to the proportions of Kadish classes at first diagnosis have been noted in recent decades.[2] A greater awareness of the tumor and earlier diagnosis is needed for better outcome.

Case report

A 28 year old female presented with three month history of progressive nasal obstruction, headache and intermittent epistaxis. On examination there was ill-defined mass seen in right nostril. There was no abnormality detected on rest of head and neck examination. Neurological examination was normal. Computed tomography (CT) of paranasal sinuses suggested 31x16mm sized heterogeneously enhancing soft tissue density lesion involving right ethmoid sinuses, right sphenoid sinus and right nasal cavity (Figure 1).The lesion extended into right pterygopalatine fossa, superiorly the lesion eroded cribriform plate (Figure 2) with extension into olfactory region of frontal lobe. The intracranial extension was confirmed on magnetic resonance imaging (MRI). On laboratory studies, complete haemogram, kidney function tests, liver function tests were normal. Lactate dehydrogenase (LDH) was slightly raised to 540 U/L (normal range 266-500 U/L).

A biopsy was performed from right nostril mass. Histopathological examination showed diffuse proliferation of round shaped cells in nests and sheets. Review of morphology showed poorly differentiated tumor. On immunohistochemistry (IHC), cells were immunoreactive for neuron specific enolase (NSE) and immunonegative for leukocyte common antigen (LCA) and cluster of differentiation-99 (CD99). On clinicopathological correlation diagnosis of high grade Esthesioneuroblastoma was done. As patient had intracranial extension, Kadish stage C was ascertained. Surgeon opined lesion to be operable and surgery was planned. Craniofacial resection and removal of tumor with bifrontal craniotomy and lateral rhinotomy approach was done. Final histopathology of operated specimen which was received in multiple pieces came to be same as biopsy report i.e. Esthesioneuroblastoma. Post operative recovery was good except one episode of generalized tonic clonic convulsions which was managed conservatively with anti edema measures and antiepileptic augmentation. Patient was referred for adjuvant radiation. Before proceeding to radiation (on post operative day 45) MRI paranasal sinus and brain performed which suggested recurrence of lesion with more local extension and dural involvement (Figure 3). Concurrent chemoradiation with weekly cisplatin in dose of 40 mg/m^2 was started as per NCCN2012 guidelines[4] for head neck cancer and she has recently completed concurrent chemoradiation with good tolerance except for grade II mucositis and is relatively asymptomatic at present.

Discussion

Esthesioneuroblastoma (ENB) is a small blue round cell tumor. It is thought to be of neural crest origin and arising from olfactory mucosa. Very few case reports have been published in India.[5-7] Most of the patients in India are locally advanced, Kadish stage C, at the time of presentation.[6]

Presentation: Symptoms at the time of presentation include: nasal congestion, anosmia, epistaxis, and pain. There is no specific age, sex, or racial predilection. There are no known etiological factors.[7] Because of the nonspecific nature of these symptoms and can be attributed to chronic sinusitis, diagnosis can be delayed for prolonged period of time, hence patients often present with locally advanced disease. ENB is characterized by a tendency toward

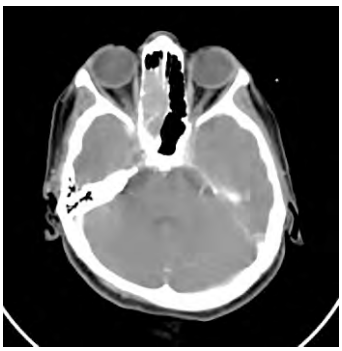

Figure 1: CT image showing 31x16 mm sized heterogeneously enhancing soft tissue density lesion involving right ethmoid sinus, right sphenoid sinus and right nasal cavity

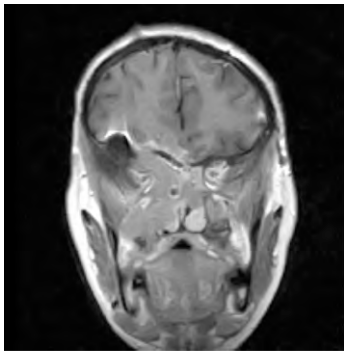

Figure 3: MR image showing local recurrence with more extensive lesion

invasion of local structures including the paranasal sinuses, orbits, anterior cranial fossa dura, cavernous sinus, and frontal lobe. Less than 5% of patients present with nodal metastases; disseminated disease is usually restricted to patients with recurrence. Metastasis to lung, bone, liver, pancreas, skin, mediastinum and brain has been described.[7] Our patient presented with similar symptoms with extensive local invasion into adjacent structures and intracranial extension. There was no nodal disease and distant metastasis.

Staging and grading: Historically, patients have been staged using the Kadish staging system (A-limited to the nasal cavity, B-involving the paranasal sinuses and C-extending beyond the nasal cavity and paranasal sinuses). Morita et al modified the Kadish staging system by re-classifying patients with lymph node or distant metastases as stage D.[8] Imaging features are usually non specific. MR imaging is superior to CT scan to assess intracranial extension whereas CT scan can assess bony details and calcification. MR and CT scan are complementary to evaluate local disease and both should be performed for accurate staging and surgical planning.[9,10] In metastatic work up, bone scan and CT scan thorax and abdomen pelvis should be done. PET-CT is sensitive to detect widespread disease. Although patients with nodal disease have significant decrease in survival, overall stage at diagnosis does not consistently predict survival. Tumors are graded using the Hyams classification (grade I-well-differentiated tumors through IV-poorly differentiated tumors. Poorly differentiated tumors must be carefully reviewed to rule out other pathologic entities such as sinonasal undifferentiated carcinomas, which have a distinct and more rapidly progressive course. Unlike stage, histological grade appears to be prognostic for survival. Our patient was having Kadish stage C. The tumor was poorly differentiated and sinonasal undifferentiated carcinoma and lymphoma was ruled out by reviewing tumor morphology and performing IHC on tumor sample.

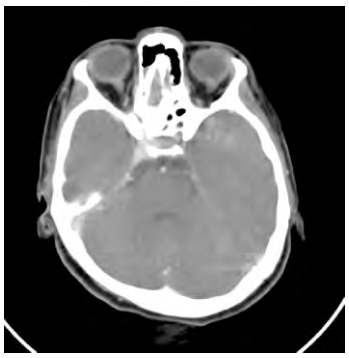

Figure 2: CT image showing lesion causing erosion of cribriform plate with extension into olfactory region of frontal lobe

Differential diagnosis: Histologically ENB resembles to embryonal rhabdomyosarcoma, lymphoma and Ewing sarcoma/PNET. Usually it can be distinguished by close attention to morphological, immunohistochemical, and anatomical detail. Specifically its neurofibrillary stroma, immunophenotype (immunopositive for NSE and synaptophysin and immunonegative for LCA and desmin) and confinement to olfactory epithelium are defining features.[5] In addition, presence of characteristic S-100 reactive dendritic cells around lobules of tumor cells in ENB[5] is a finding not shared by other small round blue cell tumors and contrast with the diffuse strong staining seen in melanoma. This patient has tumor with malignant round cells on morphology with poor differentiation with cells immunopositive for NSE, synaptophysin, chromogranin and negative for CD 99, LCA and vimentin confirming the diagnosis of neuroblastoma. Therefore, S-100 was not included in the present study.

Treatment: Treatment is based on stage at diagnosis. Combination surgery and RT seemed to be the optimal approach to treatment, with single-modality treatment being reserved only for a patient with a small tumor located well below the cribriform plate.[11] Locally advanced resectable tumors are usually treated with resection followed by radiation of dose 50-60 gray. After resection, if adverse features like positive margin or intracranial extension present then radiation to be combined with chemotherapy in form cisplatin in the dose of 100mg/m^2 every 3 week.[4] If no adverse features then post operative radiation only without chemotherapy can be given.[12] Patients with unresectable or marginally resectable disease

may be treated with combined chemotherapy and radiation therapy with curative intent. The role of chemotherapy is not defined, but is generally for most advanced cases and used in the neoadjuvant setting and/or postoperatively with irradiation.[13] In literature, regimen described for neoadjuvant setting are cisplatin, etoposide (PE), vincristine, doxorubicin, cyclophosphamide (VAC), VAC alternating PE, V+C, Cisplatin, 5-FU(P+F).[14] In our case, as the lesion was resectable, craniofacial resection was done followed by postoperative chemoradiation.

Prognosis: Prognosis depends on the stage and grade of the disease. Negative prognostic factors are age (more than 50 years at presentation), female gender, tumor recurrence, and metastasis.[15] Compared with other sinonasal malignancies, the prognosis of ENB is much better, with a disease-free survival at 5 years of more than 80.0%[16] A study of 311 patients based on Surveillance, Epidemiology and End Results (SEER) database showed that disease-specific survival at 10 years correlated with modified Kadish staging (83%, 49%, 39%, and 13% for stages A, B, C, and D, respectively).[17]

Recurrence: The median time to first recurrence is generally less than 2 years; however late recurrences are common. The most common site of recurrence is local followed by nodal recurrence. Recurrence can develop in spite of aggressive therapy soon after treatment[5]. Our patient had recurrence early on post operative day 45. Researchers at the Mayo clinic reported that 42% of local recurrences developed within five years post operatively.[8] In a review of 40 patients, Eden et al.[18] reported a recurrence rate of 55%; two-thirds of these patients had loco regional disease, and 39% of them developed recurrences within five years of combined modality (surgery + radiation) treatment.

Conclusion

Poorly differentiated esthesioneuroblastoma, have high early local recurrence rate. Despite aggressive therapy, recurrence can develop soon after treatment as it occurred in our case. It should be kept in mind that this disease has variable biology from indolent growth to a very aggressive disease with high chance of extensive local recurrence anticipated to have poor prognosis.

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Summaries of Presentations at Conferences by International Bodies

01. Obstructed Uropathy in Cancer Cervix

Nayak Mehul K
Department of Gynecological Oncology

Summary

Over 70% patients with cancer cervix present in advanced stage of disease and in many of them it is difficult to offer definitive treatment as they present with some urological complication like obstructed uropathy. In this study we evaluated patients with obstructed uropathy with uremia for urinary diversion to facilitate further definitive treatment for cancer cervix. In this study, 24 patients with cancer cervix whether treated or un treated, who had obstructed uropathy were evaluated for type of complication, their management and effect on the primary disease. 11 patients underwent urinary diversion in form of percutaneous nephrostomy and they were followed up after tumor specific treatment. Urinary diversion procedure in obstructed uropathy in form of percutaneous nephrostomy in case of advanced cancer cervix was effective to save function until tumor specific treatment could be offered in form of radiotherapy or chemotherapy, which helps in prolongation of life in such patients for at least few months.

World Congress on Dilemmas in Ob/Gy (GO CON), Nagpur, India, November 30 to December 2, 2012 (Oral)

02. Huge Aggressive Angiomyxoma of Vulva in Pregnancy: A Case Report

Nayak Mehul K
Department of Gynecological Oncology

Summary

Aggressive Angiomyxoma (AA) of pelvis and perineum was identified as a distinct clinico-pathologic entity in 1983 with less than 250 cases reported since then. AA is a myxomatous tumor involving the blood vessels with a marked tendency for local recurrence, but usually does not metastasize. The tumour usually arises in women of the reproductive age group with peak incidence in fourth decade. We here describe a case of a huge (40 x 30 x35 cm) angiomyxoma in the left labium majus in a 43 year-old woman. The tumour had been neglected for 10 years due to poverty, initial insidious growth of tumour and the fear of being diagnosed as a case of carcinoma. She sought help when it grew drastically during and after her pregnancy. In world literature fewer than 250 cases of these rare tumours have been reported but perhaps none of this size. Aggressive angiomyxoma is a very rare, locally infiltrative neoplasm. Thus, after surgery, close follow-up is needed because of a high risk of local recurrence.

World Congress on Dilemmas in Ob/Gy (GO CON), Nagpur, India, November 30 to December 2, 2012 (Poster)

"You only ever grow as a human being if you're outside your comfort zone."

Percy Cerutty
Renowned Running Coach

Summaries of Published Articles

01. Effect of Oral Clonidine Hydrochloride as a Premedication on Haemodynamic Responses and Isoflurane Requirements in Head and Neck Cancer Surgery

Makwana Damini S, Shah Bhavna, Patel Bipin M
Department Of Anesthesiology

Summary

The purpose of this study was to evaluate effect of oral clonidine hydrochloride, an alpha-2 adrenergic agonist, in a dose of 3 mcg /kg as a premedication in the patients of head and neck cancers planned for commando surgery. Fifty, adult patients of ASA grade I & II were included in this study and divided in two groups of 25 each. Group-1 patients were premedicated 90 - 120 minutes before with tablet clonidine hydrochloride along with tablet diazepam 5 mg orally, while in group -2 only oral diazepam was given. We observed sedation score, stress response to intubation and haemodynamic changes intrao-peratively and postoperatively. We also studied requirement of isoflurane during operation. We observed that clonidine hydrochloride produce a significant reduction in anxiety. Increase in pulse and blood pressure response to intubation was attenuated by clonidine ($P<0.05$). Patients were haemo-dynamically stable throughout operation. In clonidine group isoflurane requirement was reduced up to 50% (0.84 ± 0.39 vs 1.63 ± 0.73%). We concluded that clonidine hydrochloride produce a significant reduction in anxiety. Clonidine hydrochloride was effective to prevent stress response to intubation. It also reduced volatile anaesthetics requirement with less changes in haemodynamics throughout operation.

Asian Archives of Anaesthesiology and Resucitation: 2011; 72: (A-J)

02. Modification of Mcgregor Fan Flap for Reconstruction of Full Thickness Defect of Lower Lip and Vermilion

Saraiya Hemant A
Department of Surgical Oncology

Summary

The lips are the primary aesthetic and functionally dominating feature of the lower one-third of the face. Due to their specialized structure, lip reconstruction poses special challenges. Apart from primary lip carcinomas, oral cavity carcinomas often involve the lips which require excision and some sort of reconstructive procedures. Restoration of oral competence and adequate aperture while maintaining sensation, mobility, and cosmesis is often elusive. Reconstruction of vermilion is a key element in any lip reconstruction. McGregor fan flap was chosen for post oncosurgical lateral lower lip defects. This flap was further modified for better vermilion reconstruction. 55 flaps were carried out between the year 2003 and 2009 for the lower lip defects which were of more than 40%. There were no complications like hematoma, necrosis, and infection in any of the flaps post operatively. Mean time for recovery of sphincteric function was 3.5 months. Mouth opening was adequate and there was no microstomia in any of the cases. The cosmetic results were good in all cases, with pleasing vermilion. Long-term functional and aesthetic results were satisfactory. The McGregor flap with our modification remains the flap of choice for moderate to large full thickness defects of lower lip and vermilion. Consistently good results in such a large series are testimony of this procedure.

Journal of Plastic and Reconstructive Surgery: 2011; 64: 1390-1392

03. Avoidance of Major Lower Limb Amputation with the Use of Reverse Sural Artery Fasciocutaneous Flap in Post Oncosurgical Defects of Ankle and Heel

Saraiya Hemant A, Shah Mukesh N
Department of Surgical Oncology

Summary

The surgical management of patients with malignant tumors of bone is challenging. Reconstruction of post oncosurgical defects on the ankle, malleoli and heel remains a demanding task for plastic surgeons. These defects tend to be large and demand a durable soft tissue cover. Inappropriate treatment of these defects can lead to chronic inflammation, infection, and amputation. The goal of limb-salvage surgery is to achieve a complete resection with an adequate margin and to preserve a useful functioning limb without increasing the risk to the patient. The reverse sural fasciocutaneous flaps were used to cover the post oncosurgical defects of lower leg, ankle and heel. We performed 11 reverse sural fasciocutaneous flaps in last 14 months for malignant disease of foot and leg. Only one flap developed partial necrosis. Mean follow up of 11 months showed stable flap in all patients. None of our patients showed any sign of local recurrence or required amputation at a later date. The distally based sural artery flap provides large piece of skin with minimal donor site morbidity. Elevation of the flap is easy and quick. The vascular supply is constant and reliable. There is no need to sacrifice any major artery or major sensory nerve. The distally based sural fasciocutaneous flap has been found to be an

important skin flap that can be used for coverage of soft tissue defects in heel and foot to save patients from unwanted amputations.

Gujarat Medical Journal: 2012; 7: 91

04. Use of Retroauricular Temporal Flap for Large Post Oncosurgical Glabellar and Forehead Defects

Saraiya Hemant A
Department of Surgical Oncology

Summary

Reconstruction of large defect in glabellar and forehead areas poses a perplexing problem for a reconstructive surgeon. Although coverage of small defect can be straight forward, few options are available for the coverage of large area. Two patients were operated for recurrent basal cell carcinoma and dermatofibrosarcoma respectively. Excision left very large defect which was reconstructed by retroauricular temporal flap. Both flaps survived completely. Flap cutting and final insetting was done on 21st day. The postoperative result was very satisfactory. Retroauricular temporal (Washio) flap is a robust and reliable flap. It satisfactorily caters the need of the recipient area. The scars are oncologically and aesthetically acceptable. We believe that this technique is a simple and effective solution to a difficult problem.

Int J Head and Neck Surg. 2011;2:83-86

05. Granulosa Cell Tumours: A Study of 37 Cases

Nirmala C, Dave Kalpana S, Chauhan Anjana S, Bhansali Ronak P, Arora Ruchi P
Department of Gynecological Oncology

Summary

Data of 37 women with granulosa cell tumour were collected and their clino-pathological features, surgical procedures, postoperative treatment and their relation to survival were studied and reviewed retrospectively. 45.9% with stage Ia, 27% with stage Ic, 16.2% with stage III and 10.8% unstaged. Overall survival was 93% at 5 years. Disease free survival at 5 years was 63%. Advanced tumour stage and residual disease were associated with poor prognosis. Mitotic rate and tumour grade were not of prognostic significance. Stage of disease and residual disease are valuable prognostic factors.

The Journal of Obstetrics and Gynecology of India: 2012; 62: 322-326

Summaries of Presentations at Clinical Meetings

01. American Society of Clinical Oncology Identifies Five Key Opportunities to Improve Care and Reduce Costs: The Top Five List for Oncology

Jain Sachin
Department of Medical Oncology

Summary

Advancements in the prevention, diagnosis, and treatment of cancer have contributed to improved survival, better quality of life, and declining death rates. With these successes level of cost is also increasing, that is now causing serious financial burdens to patients, families, and society at large. The basis for the rising cost of care is complex and is due, in part, to unnecessary use of health care resources. The Congressional Budget Office estimates that up to 30% of care delivered in the United States goes toward unnecessary tests, procedures, physician visits, hospital stays, and other services that do not improve a patient's health. Cancer is a terrifying diagnosis that elicits appropriate anxiety in anyone hearing the words “you have cancer.” Patients and family members understandably want “everything done,” despite not having sophisticated awareness of the evidence base that should be guiding the physician. Concerns about litigation regularly factor into physician's decision making, especially in situations in which the outcome might be limited survival. The economics of health care delivery are also misaligned with respect to the shared goal of using appropriate testing or intervention for the appropriate clinical circumstance - no more and no less.The American Society of Clinical Oncology (ASCO) has identified the rising cost of cancer care as an opportunity to sharpen the focus on the need to ensure high quality care while reducing unnecessary expense for our patients, their families, and society at large. After careful consideration by experienced oncologists, ASCO highlights five practices that are in common use despite the absence of evidence supporting their clinical value. Methods:Each participating organization in the American Board of Internal Medicine Foundation's Choosing Wisely® initiative was charged with identifying five tests or procedures commonly used in their field whose necessity is not supported by high-level evidence. Each society was free to determine how to create its own list, provided that it used a clear methodology and adhered to the following set of shared guidelines: 1) Each item should be within the specialty's purview and control. 2) The tests and/or interventions should be used frequently and/or carry a significant cost. 3) Each recommendation should be supported by generally

accepted evidence. 4) The selection process should be thoroughly documented and publicly available on request.

- Initially, a subcommittee of Task Force members suggested a number of practices they believed were overused or misused.
- Once an initial Top Five list was drafted, it was presented to the ASCO Clinical Practice Committee, a group composed of community based oncologists and the presidents of the 48 state/regional oncology societies in the United States.
- A plurality of more than 200 clinical oncologists reviewed and supported the Top Five list.
- Ultimately, it was presented to, discussed by, and approved by the Executive Committee of the ASCO Board of Directors.

02. Rational Use of Blood and Alternatives to Standard Blood Transfusion Therapy

Kusumgar Rima
Blood Bank, Department of Pathology

Summary

Blood is a scarce resource hence should be used rationally. Due to lack of awareness for voluntary blood donation there is always large demand and supply gap. Clinician should think about proper indications and improvement to be needed and than only ask for blood transfusion. Blood should be componentized and give only what is needed. Blood Transfusion is dangerous also as we cannot rule out window period chances in any blood donor even after using novel blood testing techniques. Avoidance of blood transfusion by prevention and early diagnosis of anemia use of simple alternatives to transfusion, such as intravenous replacement fluids, good anesthetic and surgical management is the first step to rational use of blood. Clinician should think of other alternatives to blood transfusion like pharmacological agents, autologous predonation, meticulous technique, isovolemic haemodilution, intraoperative blood retrieval and reinfusion.

03. Salivary Genomics and Proteomics Biomarkers in Oral Cancer

Bhairavi Vajaria
Biochemistry Research Division, Cancer Biology

Summary

Oral cancer has emerged as an alarming public health problem with increasing incidence and mortality rates all over the world. Therefore, the implementation of newer screening and early detection approaches are of utmost importance which could reduce the morbidity and mortality associated with this disease. Unlike other deep cancers, oral cancer is located in oral cavity. Hence, the direct contact between saliva and oral cancer lesion makes the measurement of tumor markers in saliva an attractive alternative to serum and tissue testing. The DNA, RNA and protein molecules derived from the living cancer cells can be conveniently obtained from saliva. Thus, salivary biomarkers, a non-invasive alternative to serum and tissue based biomarkers may be an effective modality for early diagnosis, prognostication and monitoring post therapy status. In the current post-genomic era, various technologies provide opportunities for high-throughput approaches to genomics and proteomics; which have been used to evaluate altered expressions of gene and protein targets in saliva of oral cancer patients. Therefore, main aim of our lab is to study genomics and proteomics biomarkers from saliva of oral cancer patients. We mainly focus on biomarkers related to genetic susceptibility, cancer progression and invasion and metastasis. We observed increased frequency of GSTT1 null genotype in oral cancer patients. Higher percentages of CYP1A1 homozygous variant were found in oral cancer patients than in controls. Increased salivary TSA/TP ratio and α-L-fucosidase activity suggests increased glycosylation in saliva of oral cancer patients. The salivary IL-8 mRNA and protein expression measured by Electrochemical-biosensor were found to be significantly elevated in oral cancer patients. The expression of salivary MMP-2 and MMP-9 were significantly elevated in oral cancer patients compared to controls. Thus, the emerging field of salivary biomarkers has great potentials to prove its clinical significance to combat oral cancer.

04. Hypofractionated Radiotherapy in Advanced Oesophageal Carcinoma

Patel Shah Sonal
Departmnent of Radiotherapy

Summary

Oesophageal malignancy is an aggressive disease accounting for 5% of all gastrointestinal cancers. Two year survival ranges from 5-10%, with median survival of not more than 9 months. Majority of patients present in advanced or metastatic stage (60-70%). Dysphagia is most disturbing and distressing symptom in majority of patients, therefore rapid and prolonged relief from dysphagia becomes the primary goal of treatment. In patients not fit for surgery, concurrent chemoradiotherapy has shown benefit in terms of survival and disease control as compared to radiotherapy alone but majority of patients are too ill to undergo concurrent therapy. Therefore hypofractionated radiotherapy in these patients is used as monotherapy for palliation. In this study we evaluated 310 patients of non metastatic oesophageal cancers from June 2011-12 and about

70% patients were treated with hypofractionated palliative radiotherapy (long oesophageal involvement >5cm, KPS <60, wt <40 kg, grade 3-4 dysphagia). RT regime was 30Gy/10#, 5 days/weeks for 2 weeks with or without boost. Around 60% patients achieved significant dysphagia relief 3 weeks post RT and around 37% patients were symptom free at the end of 1 yr with the median follow up of 6 months. So we have concluded that shorter regime of EBRT is not inferior in the palliation of dysphagia and hypofractionated RT provides durable control of symptoms while minimizing treatment related discomfort and toxicity.

05. Cancer Related Fatigue and Exercise

Patel Tejas
Department of Physiotherapy

Summary

Cancer related fatigue can occur as a result of a patient undergoing aggressive chemotherapy or radiation therapy which depletes the bone marrow of much needed red blood cells. This fatigue was thought to be a sequel of the malignancy itself, or secondary to treatment-related anemia. There are also psychosocial factors contributing to fatigue that includes anxiety, depression or insomnia. Until recently, patients receiving chemotherapy were advised plenty of rest and avoid activities that were physically challenging. In spite of rest, cancer patient's fatigue still remained at the cost of disruptive to the activities of their daily living, and this had a more negative impact on their life. Change in fatigue was mainly associated with change in physical parameters (e.g. muscle force, exercise capacity). Exercise program should be more of aerobic form with a goal of 70% of maximum heart rate. It should be progressive dosage in varied and individualized form (twice a week; 40 min, for 12 to 16 weeks). On the basis of certain clinical research and studies it is proved that aerobic form of exercise reduces the fatigue and its associated problems. It helps in following ways: stimulates the bone marrow to make new red blood cells, increase in protein synthesis and so it helps in muscle fiber regeneration, improves in connective tissue integrity, decreases pain, improves carbohydrate, fat and protein metabolism, improved energy production and utilization, improves removal of cellular metabolites and toxins, improves cardiovascular efficiency, improves confidence, body image, decreases stress, improves sleep. It also helps in regulation of immune function. It is advisable to start exercise before or early into treatment. An experienced physical therapist, exercise psychologist, or rehabilitation consultant should help guide individualized, comfort-based exercise programs to stabilized fatigue. In conclusion, to be healthy does not mean to be free of disease; it means that one can function, do what they want to do, and become what one would like to become.

06. New Government Scheme to Support Needy Patients

Goswami Jignesh
Departmnent of Surgical Oncology

Summary

A large number of households are pushed into poverty as a result of high costs of household spending on health care. The Below Poverty Line (BPL) population is especially vulnerable to the catastrophic health risks. To address this key vulnerability faced by the BPL population in the Gujarat, the State Government has launched a medical care scheme called **Mukhyamantri Amrutum (MA) Yojana.** The objective of the scheme is to improve access of BPL families to quality medical and surgical care for the treatment of identified diseases involving hospitalization, surgeries and therapies through an empanelled network of health care providers. The surgeries covered are: cardiovascular surgeries, neurosurgery, burns, poly trauma, **cancer** (malignant), renal (kidney), and neo-natal (newborn) diseases. 'MA' yojana provides quality medical and surgical care for the catastrophic illnesses involving hospitalization, surgeries and therapies through an empanelled network of hospitals to the BPL families. The **scheme** benefits Below Poverty Line (BPL) families of all the 26 districts of Gujarat which is expected to be approximately 39 lakh BPL families (as per Rural Development and Urban Development Department). All predefined medical procedures are part of the disease/treatment packages. An enrolled BPL beneficiary may go to any of Network Hospital with a QR Coded Plastic Card and come out without making any payment to the Hospital for the procedures covered under MA. The total sum assured for the BPL family is of Rs.2,00,000/- per family per annum on family floater basis. A unit of five members (Head of family, spouse, and three dependents) of BPL family is covered under MA. Services will be rendered by both identified private/public/trust hospitals. QR coded (Quick Response Code) Plastic cards will be issued to the eligible families under the scheme. The transactions for the treatment of inpatients shall be cashless. Rs. 300/- per hospitalization with a ceiling of maximum Rs.3,000/- per year will be reimbursed as transportation cost to the beneficiary. To implement the scheme State Government has established a "State Nodal Cell (SNC)" at the State, which will administers the Mukhyamantri Amrutum (MA) Yojana.

For the claim processing, deployment of Arogya Mitras, District Coordinators, IEC activities,

empanelment of hospitals etc. is been done by the Implementation Support Agency (ISA).

07. Can Ovarian Preservation be Considered in Young Patients with Endometrial Cancer?

Basra Minu
Departmnent of Gynecological Oncology

Summary

Endometrial cancer mostly presents in perimenopausal age. However, in 5% cases, it is seen in <40 years age. At present, the standard of care is to remove both ovaries in endometrial cancer patients, even in young women for several well documented reasons. However, surgical castration has its own, sometimes, serious sequelae. Considering these factors, we decided to perform an audit of our operated cases of endometrial cancer to detect the actual frequency of ovarian involvement. 165 patients of endometrial cancer operated at GCRI between 2007 to 2011 were retrospectively analyzed. A total of 165 endometrial cancer patients were operated in GCRI during the study period, 16 (10.2%) patients had ovarian metastasis, while one patient had synchronous ovarian malignancy. No ovarian metastasis was found in patients <40 years age. When poor prognostic factors were analyzed, ovarian metastasis was seen in 37.5% serous papillary type, 15.1% with deep myometrial invasion and 20% with lymph node involvement. There is significant risk of ovarian involvement in endometrial cancer patients. Hence, if the current recommendation is to be modified, large, prospective, multi-centric trials are required.

08. Role of Level IIB Nodal Dissection in Clinically N0 Neck in Oral Cancer

Nandy Dipayan
Departmnent of Surgical Oncology

Summary

Metastatic nodal disease is the most important prognostic factor for oral cancers. The pattern of nodal spread in oral cancers is largely predictable and treatment of neck can be tailored with this knowledge. Level IIB lymph node dissection is known to be associated with tractional SAN injury resulting in shoulder dysfunction. The purpose of this study is to analyse the extent of level IIB involvement in patients with oral cavity SCC who underwent primary surgery with functional neck dissection. A prospective study of 105 patients of oral SCC admitted to Surgical Unit I, Dept of Surgical Oncology, GCRI during the period of January 2011 to May 2012 was conducted. During neck dissection, level IIB lymphnodes were dissected, labeled and processed separately from the remainder of functional neck dissection specimen. We studied the incidence of histopathological metastasis to level IIB nodes in cN0 patients. Of 105 cases of cN0 neck, 80% were pN0. Out of remaining 20% pN+, 66% showed evidence of level IB nodal involvement. Only 1 patient showed evidence of level IIB node involvement (<1%). This was associated with simultaneous involvement of level IIA. There was no evidence of isolated level IIB lymph node involvement in cN0 disease. Isolated level IIB nodal involvement is rare in patients of oral SCC with cN0 neck. It is almost always associated with simultaneous level IIA involvement. To improve the functional outcome of spinal accessory nerve, level IIB lymph node dissection may be avoided. This study requires further clinical trials for functional assessment of spinal accessory nerve after preservation of level IIB lymph nodes in cN0 neck.

09. Overexpression of Epithelial Growth Factor Receptor (EGFR) Predicts Better Response to Neo-Adjuvant Chemotherapy in Patients with Triple-Negative Breast Cancer

Brahmbhatt Birva
Division of Immunohistochemistry and Flowcytometry, Cancer Biology

Summary

Triple negative breast cancer (TNBC) occurs in approximately 10% to 25% of all patients with breast cancer and is associated with poor prognosis. Neo-adjuvant chemotherapy has been reported to produce a higher pathologic complete response (pCR) rate in TNBC. If pCR is achieved, patients with TNBC had a similar survival with non-TNBC patients. The aim of our study was to investigate the protein expression of epithelial growth factor receptor (EGFR) and response to neo-adjuvant chemotherapy and clinical outcome in patients with TNBC compared with non-TNBC. A total of 198 locally advanced breast cancer patients who received neo-adjuvant chemotherapy were studied. Immunohistochemistry (IHC) was carried out to detect the protein expression of EGFR in tumor samples. Clinical and pathological parameters, pCR rate and survival data were compared between 40 TNBCs and 158 non- TNBCs In 198 cases who received neo-adjuvant chemotherapy, significant differences exist in surgical therapy (p=0.005) and pCR rate (p=0.012) between patients with TNBCs and non-TNBCs. Overexpression of EGFR was significantly associated with pCR rate in patients with TNBCs (P < 0.001). Survival analysis revealed that patients with TNBCs had worse DFS and OS than those with non-TNBCs (p=0.001, p<0.001 respectively). Furthermore, for patients with non-TNBCs, those who acheived pCR had better DFS and OS than those who acheived RD (both P < 0.001). Our results suggested that patients with TNBCs had

increased pCR rates compared with non-TNBC. Overexpression of EGFR predicted better response to neo-adjuvant chemotherapy in patients with TNBCs.

10. Management of Spinal Metastasis

Patel Tejas
Departmnent of Neuro-Oncology

Summary

Spinal column is a common location for metastatic deposits and it's a sinister Manifestation of systemic cancer. Controversy continues concerning the relative merits of radiation, surgery, chemotheraphy or a combination of these treatment options for patients with symptomatic spinal metastases. Clarification of the indications of surgery and evolution of various operative approaches and techniques have resulted in the refinement of surgical strategies for spinal metastases. Despite of these advancement of techniques for the management of patients with spinal metastases, the treatment remains largly palliative and directed towards improvement of quality of life of these patients. Here we have discussed the treatment protocols being followed in our department for management of spinal metastases.

11. Surgical Outcomes - Post-Neoadjuvant Chemotherapy in Stage IV Oral Cancer

Batra Tarun
Departmnent of Surgical Oncology

Summary

To know the effect of neoadjuvant chemotherapy on surgical outcomes (R1 resections, post operative complications, recurrence and follow up) in Stage IV borderline operable cancers of oral cavity. Patients in group A (n=45) were those who were referred for neoadjuvant chemotherapy (NACT) with an intention to operate at a later date. These were compared with 45 patients of group B who were operated upfront. All 90 patients had stage IV squamous cell carcinoma of oral cavity. Details of patients were studied retrospectively from hospital records of surgical, medical, radiotherapy and pathology departments. All patients referred for NACT were wet lesions with perilesional edema and diffuse margins of lesions where the demarcation from normal tissue was not clear. Treatment response was assessed clinically and radiologically. Any reduction in tumor size on CT scan, MRI or clinically was considered response to chemotherapy.Various chemotherapy regimens were given in different patients - TPF (Taxol- Docetaxel or Paclitaxel, Cisplatin, 5 Fluoro uracil), PMF (Cisplatin, Mitomycin C, 5 Fluoro uracil), Cisplatin + Methotrexate and Cisplatin with 5 Fluoro uracil. Inoperability was defined as involvement of the upper infratemporal fossa where R0 resection was difficult. Patients were followed up monthly after completion of treatment for one year and three monthly thereafter. Survival was calculated from the day of surgery to the death of the patient or last patient contact. The time of recurrence was also calculated from the day of surgery. Statistical methods used in the study were simple frequencies and proportion. Test of significance was Z test. $Z \geq 2$ was considered significant. Kaplan Meir survival analysis was used through SPSS software for disease free survival **Results:** Total 39 patients were operated in group A as remaining six progressed to inoperability while on chemotherapy. There were 3 R1 resections in group A and 9 R1 resections in group B (Z=1.67). Eleven and three postoperative complications in group A and B respectively (Z=2.67). There were nine and 16 recurrences so far in group A & B respectively (Z=1.27). DFS at 01 year was 90% and 55% respectively (p=0.017). Conclusion: Though the study shows a trend in favor of NACT when R1 resections, recurrences and survival at one year are considered but this was at the cost of those six patients who progressed on NACT and could have been operated initially. Such patients were present in each and every subset of chemotherapy used.

"The first qualification for success in my view is a strong work ethic".

Henry Ford II,
President of Ford

Presentations at Clinical Meetings

(July 2012 to December 2012)

Sr.	Date	Speaker/Department	Title
1	14.07.12	Jain Sachin Medical Oncology, Unit III	American Society of Clinical Oncology Identifies Five Key Opportunities to Improve Care and Reduce Costs: The Top Five List for Oncology
2	28.07.12	Kusumgar Rima Blood Bank, Pathology	Rationale Use of Blood and Alternatives to Standard Blood Transfusion Therapy
3	11.08.12	Vajaria Bhairavi Biochemistry Research Division	Salivary Genomics and Proteomics Biomarkers in Oral Cancer
4	11.08.12	Yadav Vijay Surgical Oncology, Unit III	Cancer and Nutrition
5	08.09.12	Sonal Patel Shah Radiotherapy	Hypofractionated Radiotherapy In Advanced Oesophageal Carcinoma
6	22.09.12	Patel Tejas Physiotherapy	Cancer Related Fatigue and Exercise
7	22.09.12	Goswami Jignesh Surgical Oncology, Unit IV	New Government Scheme to Support Needy Patient
8	13.10.12	Basra Minu Gynecological Oncology, Unit II	Can Ovarian Preservation be Considered in Young Patients with Endometrial Cancer?
9	27.10.12	Parekh Urvi Endocrinology	Thyroid Nodule – A Clinician's Approach
10	10.11.12	Nandy Dipayan Surgical Oncology, Unit I	Role of Level IIb Nodal Dissection in Clinically N0 Neck in Oral Cancer
11	10.11.12	Brahmbhatt Birva Immunohistochemistry and Flowcytometry, Cancer Biology	Overexpression of Epithelial Growth Factor Receptor (EGFR) Predicts Better Response to Neoadjuvant Chemotherapy in Patients with Triple-Negative Breast Cancer
12	08.12.12	Patel Tejas Neuro Oncology	Management of Spinal Metastasis
13	22.12.12	Batra Tarun Surgical Oncology, Unit III	Surgical Outcomes - Post-Neoadjuvant Chemotherapy in Stage IV Oral Cancer

Journal Club / Guest Lecture / Review Lecture Presentations

(July 2012 to December 2012)

Sr. No.	Date	Presenter / Department	Topic	Authors	Citation
1.	11.08.12	Sen Sanjoy Surgical Oncology, Unit IV	Axillary Reverse Mapping Technique For Breast Cancer Patients – A Summary Of Different Journal Publications Of Last Five Years	Review	
2.	13.10.12	Thakar Krutarth Surgical Oncology, Unit VI	Prevalence and prognosis of synchronous colorectal cancer: A Dutch population-based study	Mulder SA, Kranse R, Damhuis RA et al	Cancer Epidemiology 2011; 35: 442-447
3.	10.11.12	Brahmbhatt Birva Immuno histochemistry and Flowcytometry Division	Overexpression of epithelial growth factor receptor (EGFR) predicts better response to neo-adjuvant chemotherapy in patients with triple-negative breast cancer	Yiqing Tang, Li Zhu, Yafen Li et al	Journal of Translational Medicine 2012; 10 (Suppl 1): S4
4.	24.11.12	Rajan Deepa Gynecological Oncology Unit III	Adolescent Young Adults In Onco-Gynaecology		NCCN guidelines2012
5.	08.12.12	Dave Jigna Molecular Endocrinology Division, Cancer Biology	Exploring Biomarkers In Head & Neck Cancer	Trivedi TI, Tankshali RA, Goswami JV, Shukla SN, Shah PM, Shah NG	Neoplasma 2011; 58: 3 doi:10.4149/neo_2011_03_217

Case Presentations for Morbidity, Mortality at Clinical Meetings

(July 2012- December 2012)

Sr No	Date	Presenter/ Department	Case Discussion
1	28.07.12	Ganatra Yatrik Anesthesiology	Mortality and Morbidity Data Presentation of Surgical and Medical Units
2	28.07.12	Kumar Tarun Surgical Oncology, Unit lll	A Case of Ca Central Arch with Acute Cardiopulmonary Arrest - Mortality
3	22.09.12	Ganatra Yatrik Anesthesiology	Mortality and Morbidity Data Presentation of Surgical and Medical Units
4	22.09.12	Sharma Mohit Surgical Oncology, Unit l	A Case of Operated Transhiataloesophagectomy, Mortality after Discharge from Ward
5	27.10,12	Barakhane Ruchi Anesthesiology	Mortality and Morbidity Data Presentation of Surgical and Medical Units
6	27.10.12	Wategaonkar Ravi Kumar Medical Oncology, Unit I	Bilateral Pneumonia in Case of ALL - Mortality
7	24.11.12	Prajapati Devendra Anesthesiology	Mortality and Morbidity Data Presentation of Surgical and Medical Units
8	24.11.12	Sharma Mohit Surgical Oncology, Unit l	A Case of Intra-operative Colonoscopy for Bleeding PR - Mortality
9	22.12.12	Ganatra Yatrik Anesthesiology	Mortality and Morbidity Data Presentation of Surgical and Medical Units
10	22.12.12	Ganatra Yatrik Anesthesiology	A Case of Post-operative Renal Failure and Septicemia - Mortality

About the Journal and Instructions to Author

Gujarat Cancer Society Research Journal is a biannually (April and October), ISSN 2320-1150, peer-reviewed journal published by the Gujarat Cancer Society. The journal's full text is available online at http://www.cancerindia.org

The Editorial Process

A manuscript will be reviewed for possible publication with the understanding that it is being submitted to Gujarat Cancer Society Research Journal at that point in time and has not been published anywhere, simultaneously submitted, or already accepted for publication elsewhere. The journal expects that authors would authorize one of them to correspond with the journal for all matters related to the manuscript. On submission, editors review all submitted manuscripts initially for suitability for formal review. Manuscripts with insufficient originality, serious scientific or technical flaws, or lack of a significant message are rejected before proceeding for formal peer-review. Manuscripts that are unlikely to be of interest to the Gujarat Cancer Society Research Journal readers are also liable to be rejected at this stage itself.

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Manuscripts accepted for publication are copy edited for grammar, punctuation, print style, and format. Page proofs are sent to the corresponding author. The corresponding author is expected to return the corrected proofs within two days. It may not be possible to incorporate corrections received after that period.

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3. Submit one copy printed on A4 size papers.
4. Please mail the articles/abstracts on gcsjournal2012 @gmail.com**,** alternatively CD (soft copy) can also be sent to room no.301.
5. Manuscripts reporting clinical studies should, where appropriate, contain a statement that they have been carried out with ethical committee approval.
6. Manuscript should have signature of the first author and unit head.

The following documents are required for each submission:

- Title Page
- Summary and Keywords
- Text (Introduction, Aims and Objectives, Materials and Methods, Results and Analysis, Discussion with Conclusions)
- Tables (separate page, Number Arabic numerals (e.g. 1,2,3) as it comes in results)
- Figures and Illustration (separate page, JPEG format, Number Arabic numerals (e.g. 1, 2,3) as in results, if photographs of persons are used, the subjects or patients must not be identifiable).
- Legends to Figures and Illustration: Present the legends for illustrations separate page using double-spacing, with Arabic numerals corresponding to the Illustrations.
- References (separate page, Number references consecutively in the order in which they are first mentioned in the text. Identify references in the text in numerals in superscript and parenthesis).
- Acknowledgement

Units and abbreviations

Avoid abbreviations in the title and abstract. All unusual abbreviations should be fully explained at their first occurrence in the text. All measurements should be expressed in SI units. ***Drug names*** Generic drug names should be used.

Abbreviations of units should conform to those shown below:

Decilitre	dl	Kilogram	kg
Milligram	mg	hours	h
Micrometer	mm	Minutes	min
Molar	mol/L	Mililitre	ml
Percent	%		

Title Page

The title page should include

1. Type of manuscript (article/case report)
2. The title of the article, which should be concise, but informative; (Title case, not ALL CAPITALS, not underlined)
3. The name by which each contributor is known (Last name, First name and initials of middle name), with institutional affiliation;
4. The name of the department(s) and institution(s) to which the work should be attributed;
5. The name, address, phone numbers and e-mail address of the contributor responsible
6. The total number of pages and total number of photographs
7. Source(s) of support in the form of grants, equipment, etc
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Language and grammar

- Uniformly American English
- Abbreviations spelt out in full for the first time
- Numerals from 1 to 10 spelt out
- Numerals at the beginning of the sentence spelt out

Summary and Keywords: Summary no more than **250 (150 for Case Report)** words. Should have following headings: **Introduction** (state the purposes of the study or investigation), **Materials and Methods** (selection of study subjects/patients, observational and analytical methods), **Results** (give specific data and their statistical significance, where ever possible), and **Conclusion** (succinct emphasis of new and important aspects of the study or observations). Do not use symbols in the summary; rather, spell out what they stand for in full. Three to eight keywords must be included below the summary.

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Results: Present your results in a logical sequence in the text, Tables, and Illustrations. Do not repeat in the text all the data in the Tables or Illustrations. Emphasize or summaries only important observations. Specify the statistical methods used to analyze the data. Restrict Tables and Illustrations to those needed to explain the argument of the paper and to assess its support. Where possible, use Graphs as an alternative to Tables with many entries. Do not duplicate data in Graphs and Tables.

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Illustrations (Figures) and Legends for Illustrations: All Illustrations must be submitted in JPEG finished format form that is ready for reproduction. Figures should be numbered consecutively in Arabic numerals (e.g. Fig. 1, 2, 3) according to the order in which they have been first cited in the text. If photographs of persons are used, the subjects or patients must not be identifiable.
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Acknowledgements: State contributions that need to be acknowledged.

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Standard Journal
You CH, Lee KY, Chey RY, et al. Electrogastrographic study of patients with unexplained nausea, bloating, and vomiting. Gastroenterology 1980; 79:311-314
Online journal article
Miyamoto O, Auer RN. Hypoxia, hyperoxia, ischemia and brain necrosis. Neurology [serial online] 2000; 54:362-71. Available at: www.neurology.org. Accessed February 23, 2000.
Chapter in a book
Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: Saunders, 1974: 457-472
Online book or website
Garrow A, Weinhouse GL. Anoxic brain injury: assessment and prognosis. In: UpToDate Cardiovascular Medicine [online]. Available at: www.UpToDateInc.com/ card. Accessed February 22, 2000.
In press
Lillywhite HB, Donald JA. Pulmonary blood flow regulation in an aquatic snake. Science. In press.

Referees
Generally, submitted manuscripts are sent to one experienced referee from our panel. The contributor's may submit names of two qualified reviewers who have had experience in the subject of the submitted manuscript, but not associated with the same institution(s) as contributors nor have published manuscripts with the contributors.

Blood Bank Activities at Gujarat Cancer and Research Institute

The blood bank at Gujarat Cancer and Research Institute occupies 289 m^2 area which is separated into various rooms as per requirement of Food and Cosmetic Act, 1940, which is the regulatory authority of blood bank. Blood bank collects blood from voluntary (30%) and replacement (70%) donors only after judicial screening in the hospital and outside by arranging the outdoor blood donation camps. Donors are bled aseptically as per FDA and WHO guidelines.

Blood bank separates blood in various components like packed red cells (PCV), Platelets concentrate (PC) and Fresh Frozen Plasma (FFP). Ninety percent of the PCV are leucoreduced type which prevent blood transfusion reactions (BTR) in our multipally transfused immunocompromized patients. Eighty percent removal of WBC from blood bags prevents various BTR like febrile non hemolytic transfusion reaction, by using automatic component separation machines like optipress II and T-Ace II plus. Blood bank also prepares pediatric units in close system to prevent contamination of blood product by using sterile connecting device. Blood bank has 3 blood bag refrigerators with storage capacity of around 800 units of PCV. Three deep freezers of -40°C to store fresh frozen plasma, two -80° C deep freezers to store stem cells and rapid freezing of plasma, three platelet agitators with incubator to store platelet concentrate with proper agitation to maintain their viability.

Blood bank performs all the blood groups of donors and patients by tube method and cross match (CM) by column agglutination by using gel card. All the blood bags are tested for transfusion transmissible infections (HIV, HBsAg, HCV, RPR, MP) by using fully automated ELISA machine to prevent all clerical and subjective errors.

Specialised Work

Apheresis is a specialized type of procedure to collect or remove desired blood or plasma components from donor or patient, respectively. Blood bank performs around 750 such procedures to collect platelets, 50 procedures to collect stem cells from peripheral blood and few therapeutic procedures to remove leukocytes from critical patients.

Blood bank also has irradiation facility (first to start in Gujarat) since 1999 to prevent graft versus host disease (one of the adverse transfusion reactions) mainly in transplant patients.

Academic Activities

- Training program for resident doctors for M.D. degree.
- Training program for the existing technicians/ junior Laboratory technicians.
- Training program of MLT students.
- MD (Transfusion Medicine) students from the B.J.Medical College, as well as doctors and technicians from all over Gujarat come for training of component separation and aphaeresis procedures.
- Organization of CME and workshops on blood transfusion services
- Organize felicitation program for camp organizers

Hospital Transfusion Committee

Appointed recently and as actively looking after,

- Transfusion policy and procedures
- Arrange training of staff
- Review adverse transfusion events
- Review rationalism in blood transfusion
- Corrective action if needed
- Promote voluntary blood donation

Blood bank celebrates world blood donors' day every year during the month of June. On that day GCRI staff members and their relatives donate blood for our patients.

Average workload per year:

Details of work done	No
Blood Banking	
Blood Tapping	14304
Replacement Donors	8729
Voluntary Donors	4734
Outdoor Camps	81
Transfusions	
Whole Blood	-
Packed Red Cell (PCV)	13057
Platelet Concentrate (PC)	11380
Fresh Frozen Plasma (FFP)	4905
Single Donor Platelet	743
Autologus and Allogenic Bone Marrow Collection	43
Therapeutic Leucacytapheresis	2

Future Perspective

- Blood bank is planning to Automation in grouping and cross matching with antibody screening and indentification
- Chemiluminicense Assay for TTI testing
- ELISA for Malarial parasite and Syphilis testing
- License for cryoprecipitate
- Increase voluntary blood donation
- All donor screening by hemocue
- MD course in transfusion medicine
- Research for stem cell viability
- MSBOS data of GCRI NABH Accreditation in blood bank

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Blood bag irradiator

Voluntary blood collection van for outdoor camps

Apheresis equipment

Automatic component separator equipments to prepare various blood component

Blood donation area