

Synchronous Occurrence of Acute Myeloid Leukemia and Carcinoma of Upper Alveolus : A Rare Coexistence

Nagori Varun V, Parikh Sonia K², Anand Asha S³, Panchal Harsha P³, Patel Apurva A³

Resident¹, Associate Professor², Professor³

Department of Medical Oncology

Corresponding Author: doctorsoniaparikh@gmail.com

Summary

Synchronous occurrence of two malignancies of different histologies is a rare clinical scenario. Synchronous diagnosis of hematological and solid malignancy poses a challenge in treatment planning. Here, we report a case of 37 year old female patient with upper alveolar growth and pancytopenia. Bone marrow examination for pancytopenia suggested acute myeloid leukemia (AML M4). The upper alveolar growth was clinically suspected to be chloroma after marrow diagnosis of AML; however the histopathological diagnosis from the same was squamous cell carcinoma.

Keywords : Synchronous malignancies, acute myeloid leukemia, carcinoma upper alveolus

Introduction

Multiple primary cancers are not unusual phenomena in current oncology practice. These can be commonly metachronous (separated by duration of more than 6 months between diagnosis of two malignancies) or less commonly synchronous (within 6 months of diagnosis of first primary).¹ There are many cancer predisposition syndromes in which sequential occurrence of different types of primary malignancies have been reported.¹ However occurrence of synchronous malignancies of different histological origin is very rare. Immunosuppression is a well recognised cause of second malignancies, especially squamous cell carcinoma (SCC) of skin and other regions in patients with hematological malignancies undergoing chemotherapy. However SCC has been reported late in the course of the disease or many years after completion of treatment. Here in we report, a case of acute myeloid leukemia (AML) and carcinoma of the upper alveolus diagnosed at the same time in a patient as synchronous malignancies which is a rare scenario. The synchronous occurrence of the respective malignancies has not been reported in literature before.

Case Report

A 37-year old female patient presented to us with 2 months history of swelling over buccal mucosa in left upper alveolar region which was gradually increasing in size with proliferative growth over mucosa and intermittent mild bleeding from the same. Patient had consulted dental surgeon at local clinic and was treated with oral antibiotics and anti-inflammatory agents with no response. She was referred to us with complete blood counts suggestive of pancytopenia with haemoglobin (Hb) 10.8g/dl, total leucocyte count (TLC) of 1510/cmm, differential counts of 64% lymphocytes

and 32% neutrophils with no abnormal cells on peripheral smear and platelet count (PC) of 84000/cmm. There was no positive family history of cancer. There was no history of blood or blood component transfusion. On physical examination she had mild pallor, normal vital parameters with no lymphadenopathy or hepatosplenomegaly, the systemic examination was normal. On oral examination she had a ulceroproliferative growth over left upper alveolar buccal mucosa with irregular margins bleeding on pressure application (Figure 1). She was investigated with bone marrow aspiration and trephine bone biopsy on outpatient basis initially which was suspicious for acute leukemia with 15% blasts population. So she was advised admission and work up for suspected acute leukemia. The investigations showed Hb 9.0g/dl, TLC 3700/cmm, PC 52000/cmm, manual differential counts showed 40% blast cells with normal renal and liver function tests. A repeat bone marrow examination was suggestive of acute myeloid leukemia (AML-M4) with 31% blast population (Figure2). Immunophenotyping of bone marrow aspiration showed positive expression for CD13, CD33, CD117, CD15, CD 11b, CD 11c, along with CD34 and HLA-DR consistent with AML. The conventional cytogenetic examination showed complex karyotype with multiple chromosomal rearrangements suggestive of poor risk group AML. The upper alveolar buccal mucosal lesion was clinically suspected as possible leukemic infiltration (chloroma) in view of AML-M4 being known to be associated with tissue infiltration including gums. However, with high index of suspicion the lesion was biopsied, the histopathology report of which showed 'moderately differentiated squamous cell carcinoma' (Figure3). The CECT scan of Paranasal sinuses and neck showed a locally eroding soft tissue density lesion of size 99x28x16 mm involving mucosa of upper alveolar buccal mucosa. The lesion was extending into left upper buccal space and left upper gingivobuccal sulcus, consistent with malignant neoplastic lesion (Figure4). The final diagnosis was AML M4 with SCC of left upper alveolus. With two synchronous different histological malignancies, the consideration of treatment was discussed and prioritized in terms of urgency, pace of disease and patient's medical condition and performance status. With falling haemoglobin and platelet counts, patient was started on induction treatment for AML with standard 7+3 protocol of daunorubicin (60mg/m² for 3 days) and cytarabine



Figure 1 : Upper alveolar growth at presentation

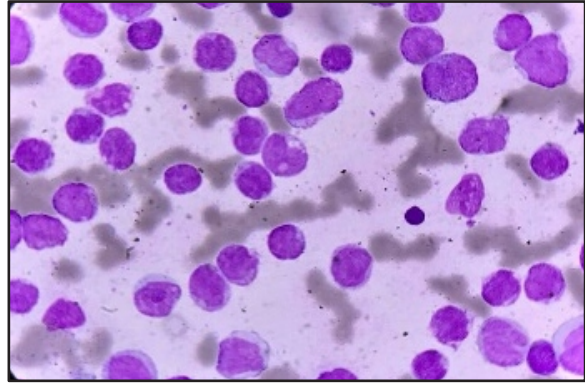


Figure 2: BM aspiration at diagnosis (AML M4)

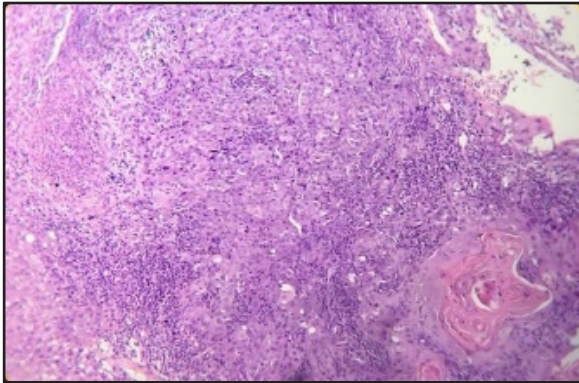


Figure 3: Upper alveolar growth biopsy
(Squamous cell carcinoma showing keratin formation)

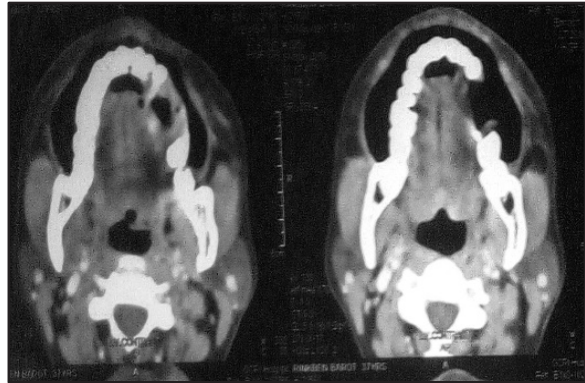


Figure 4: CECT picture of upper alveolar growth at diagnosis

(200mg/m² infusion for 7 days). Post chemotherapy course was complicated with neutropenic sepsis and pneumonia managed with broad spectrum IV antibiotics, blood component transfusion support. Post induction bone marrow was under morphological remission but with persistent thrombocytopenia (CRp). Surprisingly the upper alveolar lesion also decreased in size significantly. Patient was asked to follow up weekly with CBC monitoring for starting consolidation therapy, however she could not be given consolidation therapy in face of persistent thrombocytopenia, a repeat bone marrow aspiration done after 2 weeks for worsening thrombocytopenia and deteriorating performance status showed relapsed leukemic activity with 40% blast cells. In view of being a poor risk AML category with complex karyotype further plan of treatment was re-induction chemotherapy followed by high dose chemotherapy and hematopoietic stem cell transplant, however due to financial constraints and non-availability of HLA matched donor she did not remain a candidate for transplant and hence was started on palliative oral metronomic therapy with 6 MP + etoposide + prednisolone and supportive care with transfusions. The upper alveolar lesion was not planned for any local treatment in view of rapidly deteriorating performance status of the patient with very low blood counts, patient was not fit for any interventional procedure. With aggressive nature of disease, the patient expired within 2 months on supportive care.

Discussion

Synchronous diagnoses of AML and carcinoma of upper alveolus have not been reported till date. There have been sporadic case reports of synchronous occurrence of AML with various malignancies like Gastrointestinal stromal tumors (GIST)², renal cell carcinoma (RCC)³, gastric carcinoma⁴, adenocarcinoma of large bowel⁵ have been reported. The Warren and Gates criteria for diagnosis of multiple primary malignancies are as follows.⁶

1. Each of the tumors must be malignant, each confirmed by histology
2. Each must be geographically separate and distinct. The lesions should be separated by normal mucosa
3. Probability of one being the metastasis of the other must be excluded.

Billroth first reported multiple primary tumors of different histology, in different organs, at different time interval in same individual in 1860.⁷ Perilongo et al reported a case of a child manifesting five different tumour types simultaneously.⁸ These multiple primary cancers are known to occur with greater frequency in certain familial cancer predisposition syndromes like Li-Fraumeni syndrome.⁹ However our patient had no familial history of malignancy in first or second degree relatives. Synchronous malignancies are thought to arise in certain populations following exposure to carcinogens, such as tobacco smoke, accounting for as

much as 17% of myeloid leukemias.¹³ In our patient there was no history of any tobacco use or exposure, neither there was any history of radiation exposure. An early mutation occurring during embryonal development may predispose the individual for double malignancies involving the different tissue types.¹⁰ This supports the stem cell theory of cancer origin that stem cells of cancer maintain the capacity to differentiate, migrate and develop into a new malignant tumour with completely new traits.¹ Some people with second malignancy have a known genetic susceptibility, such as point mutation of the p53 tumour suppressor gene and allele loss of Rb gene, neurofibromatosis and immunodeficiency.¹² The tumour genetic abnormality observed in our patient was a complex karyotype. Further mutational analysis could not be performed due to limited resources. Whole genome analysis of such cases may help in detecting the underlying mutation which may otherwise be missed by conventional cytogenetics. Of interest are rare 'Syndromes of Telomere shortening' like Dyskeratosis congenita which has been reported to involve skin manifestations along with multi systemic involvement of bone marrow failure diseases and leukemia with squamous cell carcinomas and interstitial lung diseases.¹³ However there was no obvious skin lesions or stigmata of previous lesions in this patient. This represents a particularly unusual and difficult oncologic scenario involving two significant hematological and solid tumor malignancies for which prioritizing the chronology and focus of treatment must be considered. The therapeutic dilemma raised by such cases is the simultaneous management of two cancers which may have quite different treatment strategies. Some suggest that treatment should be directed towards the malignancy that is more advanced and aggressive at presentation.¹⁴ However ideal treatment option would be to use combination of treatment modalities likely to be effective against both. We could not find the literature on the management of patients with synchronous squamous cell carcinoma of upper alveolus and AML. In general, outcome in these cases with synchronous malignancies is likely to be poor and new novel treatment options need to evolve. This also illustrates the need for active involvement of multidisciplinary team for effective treatment strategies.

The synchronous presentation of AML and squamous cell carcinoma of upper alveolus is somewhat surprising. Although rare, we conclude that any questionable lesion should be assessed with biopsy in a case of leukemia. Early diagnosis by regular and thorough physical examination provides the best chance of successful outcome.

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