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Case Report

Acute Myeloid Leukemia Presenting as Granulocytic Sarcoma (Chloroma) of the Tongue: A Case Report

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Abstract

Chloroma or Granulocytic Sarcoma or Myeloid Sarcoma or Myeloblastoma is a tumor composed of immature myeloid precursor cells or blasts. It is an extra medullary manifestation of AML, which is extremely rare but well documented. It can herald, follow or occur with a diagnosis of primary AML. It can also be seen in relapse [1]. The usual sites of involvement are skin, soft tissue and lymph nodes. Intra oral myeloid sarcoma is infrequent and particularly chloroma in the tongue is further uncommon. A thorough review of literature yielded only three reported cases of chloroma of the tongue [2-4]. In this case report, we describe a case of a 36-year-old female who presented with two weeks of dysphagia due to a large tongue lesion accompanied by pancytopenia. The tongue lesion was strongly suspicious of a chloroma. Bone marrow biopsy confirmed a diagnosis of AML and a resolution of the chloroma was observed with induction chemotherapy for AML.

Keywords: Chloroma; Tongue; Myeloid; Sarcoma; Granulocytic

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Introduction

AML or acute myelogenous leukemia is the most common cause of acute leukemia in adults with a reported incidence stable at 3 -5 cases per 100, 000 population [5-7]. It is characterized by a clonal proliferation of myeloid precursors, which results in an accumulation of leukemic blasts or immature forms in the bone marrow, peripheral blood, and occasionally in other tissues. Myeloid sarcoma is an extra medullary presentation of AML. It is a rare entity and stipulates towards treatment resistance and overall poor prognosis. Burns reported the first case in 1811 [8]. Only about two percent of patients with AML will present with a conspicuous extra medullary disease or myeloid sarcoma [7]. Interestingly, the term "chloroma" is derived from the Greek word meaning "green". The high levels of myeloperoxidase in the myeloblasts confer the green color to these tumors. Usual sites of involvement are skin, soft tissue and lymph nodes with intraoral location being a rare and reportable occurrence.

Case Report

A 36-year-old Hispanic female with a past medical history of HELLP syndrome presented to the ED with sore throat and tongue swelling since two weeks. She reported of discomfort while chewing food and dysphagia. She also reported intermittent fever, night sweats, undocumented weight loss and abdominal pain associated with several episodes of nausea and vomiting for the past 5 days. In the ED, the patient was found to be febrile, hypotensive and tachycardic with a temperature of 102 ° fahrenheit, blood pressure of 93/51 mmHg, pulse of 137 beats per minute, and respiration of 19 breaths per minute. Initial laboratory workup revealed pancytopenia (white blood cell count of 3.0 K/mm ^{3}, absolute neutrophil count of 0.5 K/mm ^{3}, hemoglobin of 4.7 G/DL, and platelet count of 20 K/mm ^{3}). The comprehensive metabolic profile and coagulation tests were unremarkable. On examination of the oral mucosa, she was found to have a large firm 2.5 cm x 3 cm fungating mass on superior aspect of the lateral right tongue, covered by a creamy whitish-brown layer (Figure 1). Her pharyngeal wall appeared erythematous and there was significant swelling and erythema of the right tonsil. The rest of the physical examination was unremarkable. A computed tomography (CT) of the neck showed tonsillitis involving the right tonsillar pillar and a 1.7 cm x 1.5 cm peritonsillar phlegmon. She was admitted to the intensive care unit (ICU) for pancytopenia, fever, hypotension, and to rule out a possible underlying sepsis.

In the ICU, the patient was started on vasopressors, supportive care with blood products and broad-spectrum antibiotics. Hepatitis panel, blood and urine cultures, HIV, EBV, and CMV were ordered which eventually came back negative. Hematology and oncology was consulted for the pancytopenia. A possible diagnosis of acute leukemia presenting with a Chloroma on the tongue was suspected.

Review of peripheral smear revealed blasts. Flow cytometry of the peripheral blood showed circulating myeloblasts (9% of total) and abnormal myeloid maturation, suggesting a myeloid neoplasm. The bone marrow biopsy revealed hypercellular marrow with involvement by acute myeloid leukemia with approximately 40% blasts as seen by immunohistochemical stains (Figure 2). Hence, our suspicion that the lesion on the tongue could be a chloroma grew even stronger. Unfortunately, due to persistent severe thrombocytopenia, biopsy of the tongue lesion could not be performed. The patient was immediately started on induction chemotherapy on 7+3 regimen with Cytarabine 100mg/m and Daunorubicin 90mg/m. The patient was tolerating the chemotherapy well and as we had expected, her tongue lesion almost completely resolved. This confirmed our belief that the tongue lesion was a chloroma, a tell tail sign for her underlying acute leukemia.

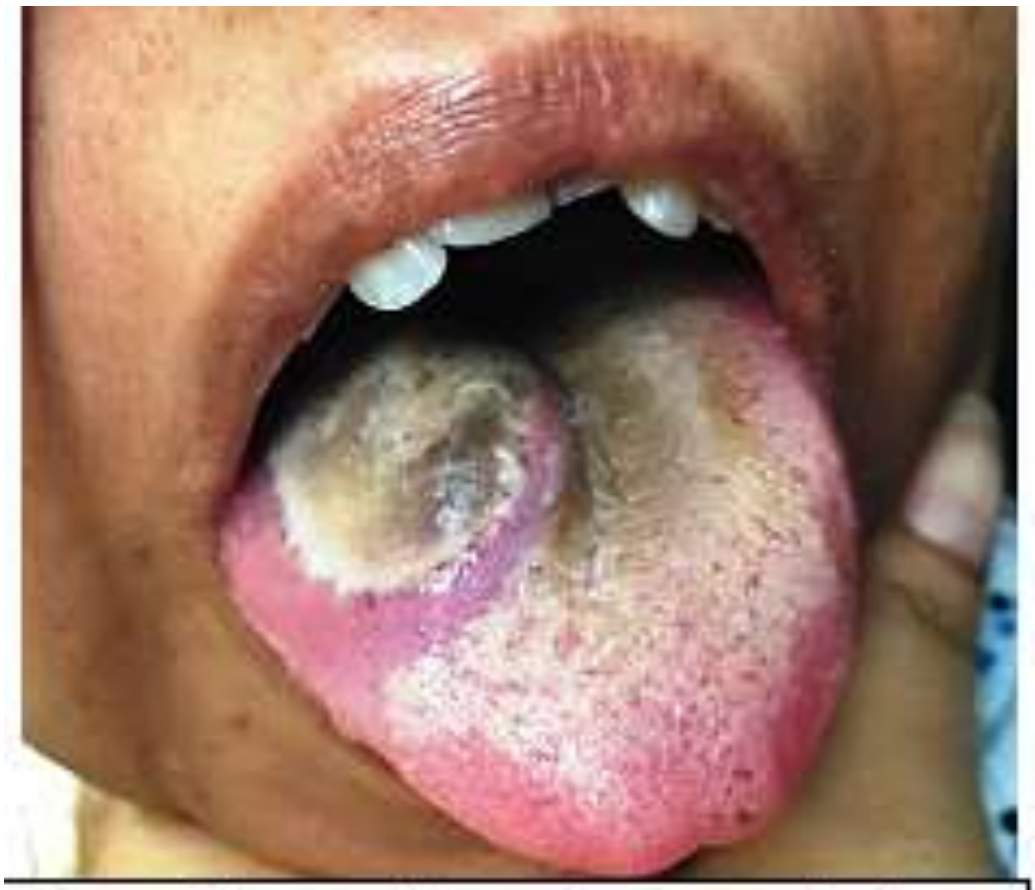

Figure 1: Image of the oral mucosa showing a large firm 2.5cm by 3cm fungating mass on the superior aspect of the lateral right tongue. This mass was identified to be a chloroma.

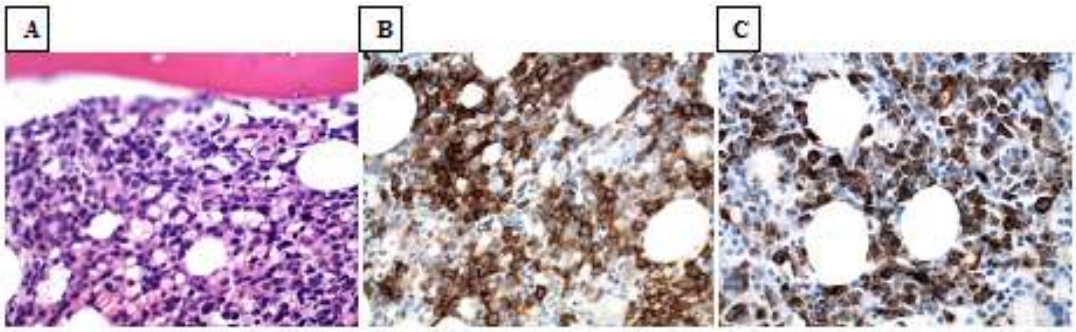

Figure 2: A) H&E stain of bone marrow core biopsy showing myeloid hyperplasia with marked left shifted myelopoiesis. Many mononuclear blasts like cells can be noted throughout the interstitium. B) Immunohistochemistry showing that CD117+ myeloblasts are increased and account for approximately 40% of the total cellularity suggesting involvement of bone marrow by acute myeloid leukemia. C) Immunohistochemistry highlighting the CD34+ myeloblasts.

However, on day 11th of the hospital admission, the patient had an acute mental status change and was found to have a right cerebellar hemorrhage on CT scan of the head, most likely secondary to persistent severe thrombocytopenia. Patient's condition started progressively deteriorating and within hours of the prior event, she was noted to have fixed and dilated pupils. A repeat CT of head showed new hydrocephalus, herniation, and increased amount of hemorrhage. The patient was pronounced dead after a cerebral perfusion study of the brain confirmed brain death.

Discussion

Chloroma or granulocytic sarcoma is a well known but rare entity and chloroma of the tongue is further uncommon. In the oral cavity, chloroma can affect the hard and soft palates, tongue, maxillary and mandibular gingival, buccal mucosa, lips and tonsils. Gingival chloroma so far has been reported to be the most commonly affected. After a comprehensive review of literature, we found forty-five cases of chloroma reported in the oral cavity [9-11]. Out of which only three cases were reported as chloroma of the tongue, making this, more rare of an occurrence [2-4]. Hence, our case is the fourth reported case of chloroma associated with AML, presenting as a tongue lesion. Other documented unusual sites of myeloid sarcoma occurrence include CNS, nasal mucosa, breast, genitourinary tract, chest wall, pleura, retro peritoneum, gastrointestinal tract and testis [12].

Although, most frequently seen with AML, myeloid sarcoma can also be seen in association with a primary diagnosis of MDS (Myelodysplastic syndrome) and CML (Chronic myeloid leukemia) with blast crisis [13]. On rare occasions, they can occur in isolation, without concomitant acute leukemia; however, they almost always precede the development of acute leukemia within months or years [14].

There is limited data about the pathogenesis of myeloid sarcoma. Myeloid sarcoma is believed to arise in the bone marrow and spread to the periosteum via the Haversian canals and from there, they can spread to different sites in the body [15]. Faaji et al. in 2010 reported that different chemokine/chemokine receptor interactions underlie the localization and resultant tumor genesis of the AML blasts in the skin [16]. As per two separate studies by Stefanidakis et al. and Wang et al., it was shown that there is higher expression of various matrix metallo-proteinase (MMP) in some leukemic cell line and their resultant interaction with the surrounding contribute to invasiveness and extra medullary blast accumulation .

Chloroma is often misdiagnosed as either a lymphoma or undifferentiated carcinoma due to the similar morphological patterns [19]. Immunohistochemistry and immunophenotyping is the key to definitive diagnosis. According to WHO 2008 classification, the diagnosis of chloroma should include cytochemical staining for myeloperoxidase (MPO), lymphocyte common antigen, and CD117 [19]. Flow cytometry may also be used to make a diagnosis. In tumors with myeloid differentiation, CD13, CD33, CD117, and MPO are the most common markers and in tumors with monoblastic differentiation, CD14, CD163, and CD11c are most commonly found markers during flow cytometry analysis [19].

Due to lack of sufficient randomized prospective trials, there is no consensus on the management of myeloid sarcoma [1]. In general, treatment usually is geared towards the individual patient since several important factors such as patient's age, associated medical co-morbidities, clinical symptoms, tumor type and stage, and the extent of the disease involvement must be taken into consideration [19]. In general, these patients are considered is having high risk AML, with overall poor prognosis. The conventional AML chemotherapy protocol, with the addition of radiotherapy, and/or surgical excision is often employed and universally accepted choice of treatment.

Ideally, systemic chemotherapy is recommended for both isolated chloroma and chloroma with concomitant AML, since studies suggest higher rate of progression to AML in isolated chloroma with

localized chemotherapy [19]. However, on occasions where it is not associated with acute leukemia, local therapy with radiation alone has been employed with success, as described in the case report of tongue chloroma in a non leukemic patient by Asna N. et al[2]. Although treatment with systemic chemotherapy results in a favorable survival outcome, the overall prognosis is still poor with a 53% mortality rate and a mean life expectancy of less than 12 months in patients with AML diagnosed with chloroma [19, 20].

Mohamedbhai, S. et al., in 2008 described a case of acute promyelocytic leukemia (t15; 17) presenting with tongue chloroma who went into complete remission with treatment with ATRA. Interestingly, during treatment course, copious exudates were noticed and the tongue lesion that was assumed to be due to local differentiation of the promyelocytes. There has been only one case that has been reported which is a tongue chloroma in association with MDS, which was initially misdiagnosed as carcinoma of the tongue.

In the case of our patient, we decided to treat her underlying AML with 7+3 induction chemotherapy in view of her age and good baseline performance status. Interestingly, the tongue lesion significantly shrunk with ongoing systemic treatment barring the need for local therapy.

Hence, after comprehensive literature review and to the best of our knowledge, we conclude that a finding like ours is a very rare occurring entity and reportable. When a patient presents with a solitary lesion of the tongue, it becomes very challenging to diagnose the patient with chloroma due to a long list of differential diagnosis. Therefore, myeloid sarcoma, as a part of the differential diagnosis along with a high index of suspicion is quintessential to avoid delaying of diagnosis and jeopardizing patient survival.

Conclusion

In conclusion, chloroma in the oral cavity is rare but well documented and should always be considered in the differential diagnosis of intraoral lesions.The gross and histologic findings can mimic an infectious or inflammatory process or another type of malignant neoplasm.It also needs to be realized that a chloroma can precede the presentation of a leukemic process by months to several years and hence awareness and knowledge of this entity can aid in early diagnosis in patients with or without active acute leukemia. It is also an indicator of poor prognosis and can assist in making decisions regarding the future treatment options like bone marrow transplant. The chloroma described in our case is unique with respect to its rare location and highlights the importance of high degree of suspicion, especially in the appropriate setting, which could lead to early diagnosis and appropriate management.

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