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# Unusual type of myeloid sarcoma of the tongue and liver - A Case report with Review of literature

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**Abstract**

Chloroma, myeloid sarcoma, granulocytic sarcoma (GS) all these words are synonyms to a dreadful form of myeloid leukemia. Acute Myeloid Leukemia (AML) is a hematologic malignancy which sometimes colonizes the extramedullary sites like skin, gingiva, CNS, orbit, liver or rarely tongue give rise to a wide range of presentations.

Here we report a case of 30-year-old male patient who presented with a malignant looking ulcer in the lateral border of tongue and hepatomegaly. On evaluation it was diagnosed as myeloid sarcoma of tongue, liver and eventually unrevealed an underlying AML.

**Keywords:** Acute myeloid leukemia (AML), myeloid sarcoma (MS), granulocytic sarcoma (GS)

## Introduction

Based on the current World Health Organization (WHO) classification, [1] myeloid sarcoma (MS), or granulocytic sarcoma, is a tumoral lesion consists of immature cells of granulocytic series. It is also known as chloroma due to its green colour attributed to the enzyme myeloperoxidase (MPO). It has been identified as an extramedullary presentation of acute leukemia especially in acute myeloid leukaemia. It was shown to be detected simultaneously with the disease or during the course of the disease, and also at relapses after allogeneic stem cell transplantation. Less commonly, it has been observed during the course of myelodysplastic syndrome, chronic myeloid leukaemia and other myeloproliferative diseases Soft tissue changes in the oral cavity such as oral bleeding, mucosal petechiae, gingival enlargement, mucosal ulceration, necrosis, and infection, are known to be associated with leukemia. [2 3]The infiltrations of leukemic cells within the oral cavity is rare. However, some case reports on leukemic cells infiltrating tissues of the oral cavity, including the gingiva were reported.[4]The ulcers may affect any part of the oral mucosa, including the tongue and palate. [5]

The objective of this report is to discuss a case of leukemic infiltration of the oral cavity and liver of a 30-year-old male patient. He had a rare clinical presentation characterized by the development of persistent ulceration on the right lateral border of the tongue and hepatomegaly. We report the clinicopathological and immunohistochemical characteristics of this malignancy.

**Case**

A 30-year-old chronic tobacco chewer presented to oncology OPD with a chronic non-healing ulcer in the right lateral border of the tongue and abdominal discomfort. On examination it was 2*1 cm in size, irregular in out line with infiltrating borders covered by yellowish grey necrotic slough in right lateral border of tongue and hepatomegaly (liver span -18 cm). Patient was admitted for a baseline workup and punch biopsy. (Fig 1).

Figure 1: Right lateral border of the tongue showing a hardened and ulcerated lesion.

He had a hemoglobin of 7.9 g/dl, total leucocyte count was 96,230 cells/ul and platelets were 3, 73,000 cells/ul without any atypical cells in the peripheral blood smear. His base line renal and kidney function was normal. A Punch biopsy was done which showed acanthotic epithelium with focal ulceration and granulation tissue with medium to large atypical cells with eosinophilic cytoplasm, hyperchromatic nucleus and prominent nucleoli infiltrating the muscle bundles. It was reported as granulocytic sarcoma (fig 2).

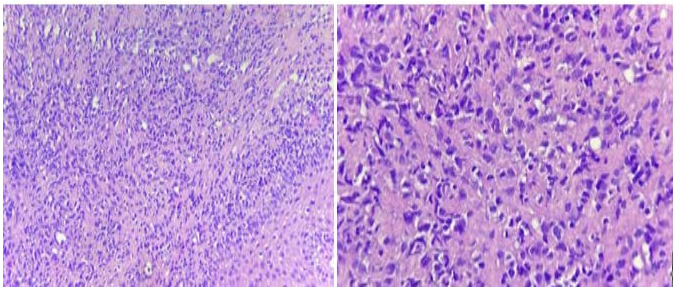


Figure 2: Photomicrographs of the tongue showing stratified squamous epithelium with sub epithelium showing diffuse infiltrate of monocytoid cells. (H&E)

IHC was done on the specimen which showed MPO positive, CD 117 occasional positive, CD 15 & CD 34 were negative and a granulocytic sarcoma was favored. (Fig 3)

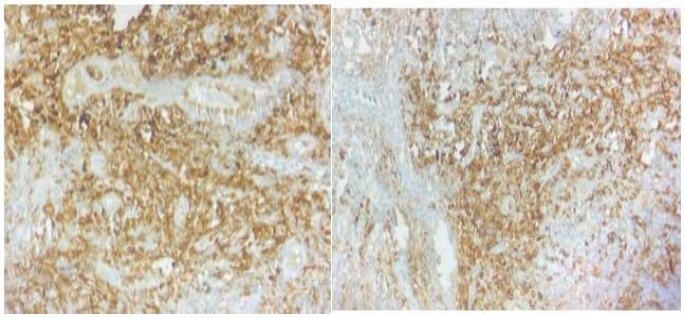
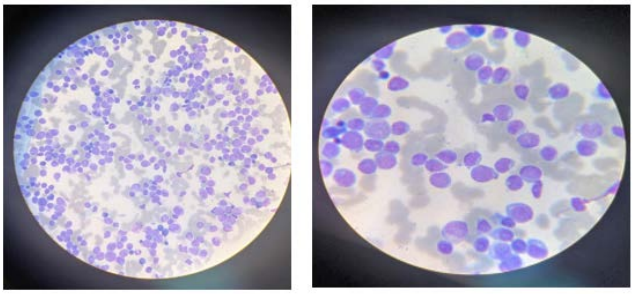


Figure 3: Immunohistochemistry (DAB; 200x). Cytoplasmic Positivity for MPO

A bone marrow aspirate was done on this patient it showed AML M5a variant (fig 4). A flow cytometric analysis was done on the bone marrow specimen and it revealed 85% blasts were gated using CD45 V500c vs. side scatter. The blasts mainly expressed myeloid markers MPO, CD13, CD33, CD14, CD15 and CD117 along with HLADR and CD34 suggestive of AML M5a.Karyotyping was showed normal karyotype. Genetic profile including BCR-ABL, inv16, t(8:21) mutation done by FISH (fluorescence in situ

hybridization) and FLT3 ITD/D835 mutation by PCR-RFLP were negative.



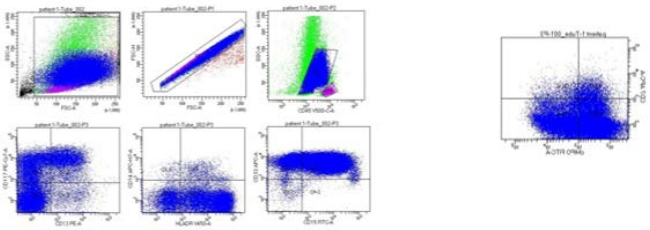


Figure 4: Acute Monoblastic leukemia (AML M5) with flow cytometry showed bivariate dot plots illustrating abnormal blasts (blue) with the expression of myeloid (MPO, CD13 and CD33) and monocytic markers (CD14, CD15, CD117, CD34, and HLA-DR).

CT scan was suggestive of Presence of few hypodense lesions noted in both lobe of liver, largest measures 28x26 mm in segment VII of liver s/o infiltration.

(Fig 5)

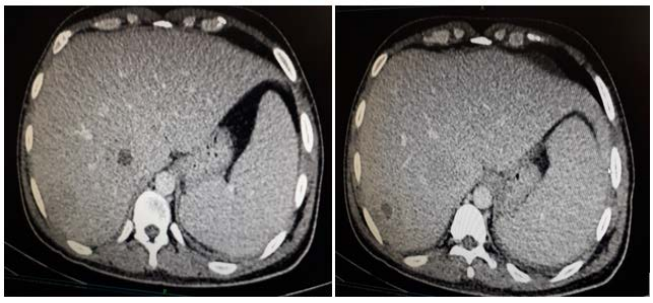


Figure 5: CT scan showing hypodense lesions in liver

Biopsy of liver was performed; Section shows normal liver parenchyma, mixed inflammatory infiltrate along with immature and mature granulocytic precursor's cells. In a known case of Acute Myeloid leukaemia (AML-M5), infiltration by same is suggested Granulocytic sarcoma. (Fig 6)

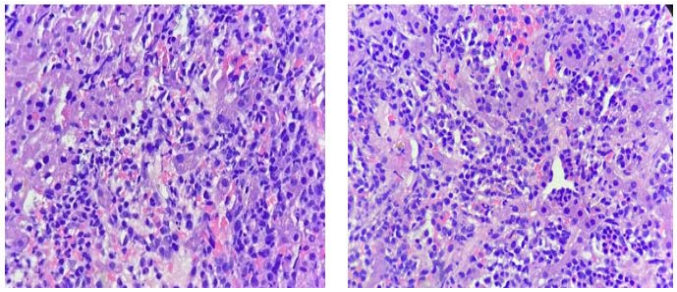


Figure 6: Liver biopsy shows infiltrate of monocytoid cells in to the parenchyma with destruction of normal architecture.

Patient was treated with HIDAC (High dose cytarabine) 2 GM/M2 for 2 days in view of poor performance status and patient developed fever on day3 so started on broad spectrum antibiotic and chemotherapy was stopped. Patient had persistent leukemic activity on day 20 of HIDAC chemotherapy. Patient was received standard induction chemotherapy 7+3 consists of 7 days of standard-dose cytarabine (100mg/m2), and 3 days of daunorubicin (60mg/m2). Clinical response in form of disappearance of tongue ulcer on day 18 of induction chemotherapy. Patient achieved complete remission in bone marrow after induction chemotherapy and received four cycles of high-dose cytarabine (3 g/m$^2$, bid, Days 1,3,5) consolidation chemotherapy.

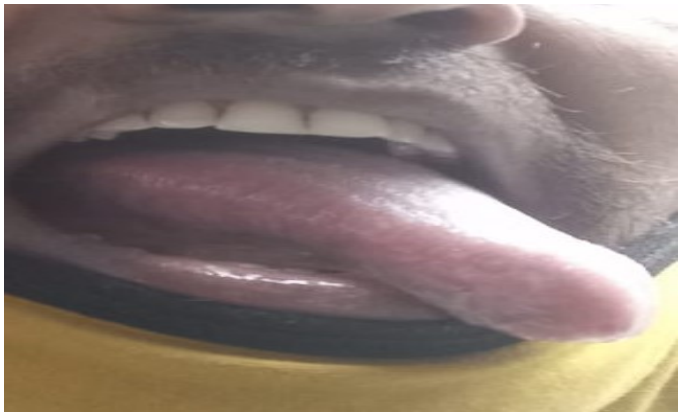


Figure 7: Clinical appearance of the tongue after the first cycle of chemotherapy

**Discussion**

Leukemia is a worldwide public health problem. The microscopic and molecular diagnostic criteria, currently proposed by WHO [1] for its classification, require the molecular markers. The rate of new cases of acute myeloid leukemia was 4.3 per 100,000 men and women per year. The death rate was 2.8 per 100,000 men and women per year. Estimated New Cases 2021 are 20,240 and Estimated Deaths 2021 are 11,400. Acute myeloid leukemia represents 1.1% of all new cancer cases in the U.S. 2

Myeloid sarcoma is a rare extramedullary tumor formed with immature myeloid cells. The clinical course of granulocytic sarcoma can be varied and may be associated with three clinical situations: (i) AML, (ii) chronic myeloproliferative disorders, or (iii) Myelodysplastic syndrome.[9]Isolated myeloid sarcomas are unusual and typically progress to form AML. [1] The clinical features reported on the oral cavity are diverse. The most common presentation of the tumor is a nodule with variables pigmentations, possible ulceration, and bleeding. It can affect the oral cavity on the tonsils, lips; gingiva, palate and tongue.[5]Among the different acute leukemia, the myelocytic and monocytic variants most frequently cause severe oral changes. [4]

The oral manifestation of myeloid sarcoma is rare. To the best of our knowledge, few cases have been reported in the literature, of which some cases had isolated oral myeloid sarcomas with bone marrow involvement. [8]

According to Stafford et al., [9] oral lesions are more frequently seen in patients with acute leukemia. Oral manifestations are three times less frequent in chronic leukemia compared to acute leukemia. [3] They may be either the result of direct infiltration by leukemic cells (primary), or could be secondary to underlying thrombocytopenia, neutropenia, or impaired granulocyte function. Gingival infiltration, as the initial presentation of AML, is seen in 5% of the cases. Dreizen et al. [10] showed that the incidence of gingival infiltrates was higher in patients with acute monocytic leukemia (66.7%), followed by those with acute myelomonocytic leukemia (18.5%) and acute myeloblastic leukemia (3.7%).

As seen in our case, in the majority of the patients, myeloid sarcoma occurs in association with AML. However, Byrd et al. [11] showed that the granulocytic sarcoma could be initially misdiagnosed in 46% of leukemia patients. Our case highlights a rare clinical presentation of myeloid sarcoma in the oral cavity in the context of AML, characterized by the development of persistent ulceration on the lateral border of the tongue, in addition to the hepatomegaly.

The cytogenetic analysis is one of the most important prognostic determinants in AML. [12] Based on the cytogenetics and molecular findings, patients are stratified as having favourable, intermediate, and unfavourable risk. [13]

Our case revealed no mutations in FLT3 and NPM1 genes, patient stratified as intermediate risk.

Recently, Visani et al. [14] stated that the combination of genetic, epigenetic, and transcriptional data would represent the molecular basis for treatment decisions with the highest predictive potential. These agents include FLT3 inhibitors, farnesyl-transferase inhibitors, histone deacetylase inhibitors, and DNA methyltransferase inhibitors

Although the infiltration of malignant cells into the oral tissues is not an uncommon feature in leukemic patients, especially in patients with acute leukemia, infiltration of the tongue is rare. On the other hand, while myeloid

sarcomas can occur in any part of the body, the involvement of the oral cavity is uncommon, with only 37 cases reported according to the Yap et al. [15] report.

Another recent case-report by Ignacio-Cconchoy et al. [16] also described oral myeloid infiltration in the tongue as the first manifestation of an oncohematologic disease.

Lillington et al., the patient was diagnosed to have a GS with a normal marrow. However, the cells in marrow as well as the GS had the same molecular and cytogenetic abnormality highlighting presence of occult myeloid disease despite a normal marrow. This indicates that isolated GS and GS could be in the same disease spectrum.[17]The most common differential diagnosis for a GS is a lymphoma followed by malignant melanoma, undifferentiated cancer, and extramedullary hematopoiesis.[18]

Modalities of treatment are radiotherapy, surgery or chemotherapy. Although there is no important role for surgery for symptomatic MS patients, excision or debulking may be considered before starting chemotherapy [19]. While there is no consensus on the treatment of MS, it is almost always treated with AML induction regimens. In the literature, since there is a high rate for progression to acute leukaemia especially in patients who are treated with localized methods (88-100%), systemic treatment is recommended to all patients with isolated MS. The main role of surgery becomes clear when reaching a diagnosis is difficult and an excisional biopsy is needed. Radiotherapy should be considered in isolated MS, inadequate response to chemotherapeutic regimen, in recurrence following bone marrow transplantation, and when rapid symptom relief is needed. Using a regimen of 24 Gy in 12 fractions can be offered to most MS patients[20]

**Conclusion**

MS is considered to be a subgroup of AML where myeloid blasts form a tumor mass occurring at a site other than the bone marrow.

The diagnosis of myeloid sarcomas in the oral cavity and liver can be very challenging, especially without a history of hematological disorders or gingival leukemic involvement, due to nonspecific clinical features. These patients offer insights to the pathophysiologic, diagnostic, and therapeutic challenges associated with this rare disorder. A sound knowledge of the disease for a clinician and an expert pathologist is an utmost necessity for early suspicion, diagnosis, and treatment of MS.

**References**

1. Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of hematopoietic and lymphoid tissues: 2. Gene bra: WHO; 2017.

2. Statistics adapted from the American Cancer Society's (ACS) publication, Cancer Facts & Figures 2021.

3. Gomez RS, Duarte ECB, Guimaraes ALS, et al. B-leukemic infiltrate in palate. Oral Oncol Extra. 2004; 40(3):54–57.

4. Hasan S., Khan N. I., Reddy L. B. Leukemic gingival enlargement: report of a rare case with review of literature. Int J Appl Basic Med Res. 2015 Jan-Apr; 5(1): 65–67.

5. Dinesh Kumar T, Suresh V, Ramya R, Rajkumar K. Primary intraoral granulocytic sarcoma: a rare case presenting as generalized gingival enlargement. J Oral Maxillofac Pathol. 2016;20(3):523–526.

6. Zimmermann C, Meurer MI, Grando LJ, Gonzaga Del Moral JÂ, da Silva Rath IB, Schaefer Tavares S. Dental treatment in patients with leukemia. J Oncol. 2015; 2015:571739.

7. Jordan RCK, Glenn L, Treseler PA. Granulocytic sarcoma: case report with an unusual presentation and review of the literature. J Oral Maxillofac Surg. 2002;60(10):1206–1211.

8. Kirnbauer B, Wölfler A, Sill H, Beham A, Prettenhofer U, Jakse N. Myeloid sarcoma in the oral cavity. Int J Stomatol Occlusion Med. 2013;6(2):65–69.

9. Stafford R, Sonis S, Lockhart P, Sonis A. Oral pathoses as diagnostic indicators in leukemia. Oral Surg Oral Med Oral Pathol. 1980;50(2):134–139.

10. Dreizen S, McCredie KB, Keating MJ, Luna MA. Malignant gingival and skin 'infiltrates' in adult leukemia. Oral Surg Oral Med Oral Pathol. 1983;55(6):572–579.

11. Byrd JC, Edenfield WJ, Shields DJ, Dawson NA. Extramedullary myeloid cell tumors in acute nonlymphocytic leukemia: a clinical review. J Clin Oncol. 1995; 13(7):1800–1816.

12. Grim wade D, Walker H, Oliver F, et al. The importance of diagnostic cytogenetics on outcome in AML: analysis of 1,612 patients entered into the MRC AML 10 trial. The Medical Research Council Adult and Children's Leukaemia Working Parties. Blood. 1998; 92(7):2322–2333.

13. Schoch C, Kern W, Schnittger S, Hide man W, Haferlach T. Karyotype is an independent prognostic parameter in therapy-related acute myeloid leukemia (t-AML): an analysis of 93 patients with t-AML in comparison to 1091 patients with de novo AML. Leukemia. 2004;18(1):120–125.

14. Visani G, Loscocco F, Isidori A, Piccaluga PP. Genetic profiling in acute myeloid leukemia: a path to predicting treatment outcome. Expert Rev Hematol. 2018;11(6):455–461.

15. Yap M, Hewson I, McLean C, Ciciulla J. Oral myeloid sarcoma: two case reports. Aust Dent J. 2014;59(4):511–515.

16. Ignacio-Cconchoy FL, Benites-Zapata VA, Yanac-Avila RL, Vela-Velàsquez CT. Myeloid sarcoma of the tongue as a first manifestation of acute promyelocytic leukemia: a case report. Rep Pract Oncol Radiother. 2020;25(2):174–177.

17. Lillington DM, Jaju RJ, Shankar AG, Neat M, Kearney L, Young BD, et al. Cytogenetic and molecular evidence of marrow involvement in extramedullary acute myeloid leukaemia. Br J Hematol 2000; 110:547-51.

18. Paydas S, Zorludemir S, Ergin M. Granulocytic sarcoma: 32 cases and review of the literature. Leuk Lymphoma 2006; 47:2527-41.

19. Bakst RL, Tallman MS, Douer D, Yahalom J. How I treat extramedullary acute myeloid leukemia. Blood. 2011 Oct;118(14):3785–93.

20. Almond LM, Charalampakis M, Ford SJ, Gourevitch D, Desai A. Myeloid Sarcoma: Presentation, Diagnosis, and Treatment. Clin Lymphoma Myeloma Leuk. 2017 May; 17(5):263–7.