

Leukemic gingival enlargement: A case report and review of literature

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Abstract

The oral cavity manifests signs of various systemic diseases. This entails thorough examination of the oral mucosa, gingiva, teeth, tongue and other oral tissues. Occasionally, oral signs can be an expression of systemic conditions such as endocrine imbalance, nutritional deficiencies and blood disorders. Leukemia is a malignancy of white blood cells, which may result in significant morbidity and mortality. Oral changes maybe the first and only presenting features in leukemia patients, making it imperative for the dentist to diagnose the disease accurately.

Keywords: Acute monocytic leukemia, acute myeloid leukemia, gingival enlargement, immunophenotyping

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Received: 23.09.2017, **Accepted:** 21.12.2017

INTRODUCTION

Leukemia is a malignancy characterized by proliferation of abnormal white blood cells within the bone marrow. There is a failure of maturation of precursor cells (blasts) with the result that the blasts accumulate in the marrow and suppress normal hematopoietic stem cells leading to deficiency of mature leukocytes, erythrocytes and platelets. As a result, immunodeficiency, anemia and thrombocytopenia develop.^[1] Leukemic cells may also infiltrate into the body tissues, such as skin, spleen, gingiva, lymph nodes and central nervous system.^[2]

The etiology of leukemia is poorly defined. However, chemical injuries, chromosomal abnormalities, radiation exposure and viral infections are implicated.^[3] With a worldwide incidence of 3.7 per 100,000 persons and age-dependent mortality of 2.7 to almost 18 per 100,000

persons, leukemia accounts for about 4% of all deaths from malignancies.^[4]

According to evolution, leukemia is classified into chronic, subacute and acute. Acute leukemia is abrupt in onset and aggressive. Leukemia can be further classified as lymphocytic or myelocytic, depending on the lineage of leukocytes involved. The rate of progression varies considerably in different types of leukemia, but death is the usual outcome in untreated disease as a result of compromised production of mature blood cells [Table 1].^[2,5]

Typical oral manifestations of acute leukemia include gingival swelling, oral ulceration, spontaneous gingival bleeding, petechiae, mucosal pallor, herpetic infections and candidiasis.^[6] AML is a clonal proliferation of immature myeloid cells. It presents with marrow failure and cytopenia. Symptoms include fever, fatigue, pallor, mucosal bleeding, petechiae and local infections.^[7]

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How to cite this article: Chowdhri K, Tandon S, Lamba AK, Faraz F. Leukemic gingival enlargement: A case report and review of literature. *J Oral Maxillofac Pathol* 2018;22:S77-81.

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DOI:

10.4103/jomfp.JOMFP_205_17

CASE REPORT

A 40-year-old male patient with low socioeconomic status reported in June 2017 to the Department of Periodontology, Maulana Azad Institute of Dental Sciences, New Delhi. The patient's chief complaints were the swollen gums and difficulty in chewing for the past 2 months. The patient had experienced difficulty in swallowing food, nausea, dizziness and weight loss in the past few months.

On physical examination, marked pallor of the palpebral conjunctiva and the ventral surface (palm) of hands was observed. Lymphadenopathy and induration of the deep cervical lymph nodes were observed.

On oral examination, pallor of the buccal mucosa and gingiva was observed. The gingival enlargement involved the buccal, labial, palatal and lingual aspect of marginal and attached gingiva of the maxillary and mandibular arches. Gingiva was swollen, shiny, pale pink in color. In the posterior region, the enlargement extended to the occlusal surface of the teeth. The enlargement was firm in consistency with lobulated appearance. There was minimal bleeding on probing. Pseudopockets were present. The oral hygiene was fair. The orthopantomogram revealed generalized horizontal bone loss. While significant loss of attachment must be present for 6–8 months before radiographic evidence of bone loss appears, the acute presentation of symptoms along with rapidly progressing gingival overgrowth substantiated an underlying systemic cause [Figures 1 and 2]

The complete blood count of the patient revealed leukocytosis, thrombocytopenia and anemia. Peripheral blood smear showed marked leukocytosis with 7%–8% blasts and 60% monocytoid population comprising of promonocytes and atypical monocytes morphologically. A 1 cm × 0.8 cm gingival specimen was obtained from the buccal gingiva of lower left quadrant and sent for histopathologic examination. The patient was advised brushing twice daily by use of soft bristle toothbrush and 0.2% chlorhexidine rinses thrice daily.^[8,9] Oral prophylaxis was performed, and the patient was referred to an oncology center for further treatment, where a flow cytometric immunophenotyping of the patient's blood confirmed acute monocytic leukemia (M5b) [Figures 3 and 4, Table 2].

RESULTS OF IMMUNOPHENOTYPING AND IMMUNOHISTOCHEMISTRY

The flow cytometric immunophenotyping analysis of peripheral blood found CD11b, CD64 and CD33 to be strongly expressed by the monocytoid cells. CD14

was assayed and found positive in only 20% of the monocytoid population. CD117 was dimly expressed by the blast cells. The expression of CD34 was negative. On immunohistochemistry, the gingival specimen showed focal positivity for CD117 whereas CD34 was found to be negative. Therefore, the results of the two tests were in coherence [Figures 5 and 6].

The patient underwent blood and blood product transfusions followed by chemotherapy induction with cytosine arabinoside (Ara-C, 200 mg/m² continuous intravenous infusion for 7 days) and idarubicin hydrochloride (idarubicin, 12 mg/m²/day for 3 days). The patient was also concomitantly injected with antiemetics, analgesics, prophylactic antibiotics and antifungals, vitamins and folic acid supplements. Two weeks after chemotherapy, the patient underwent bone marrow aspiration that revealed hypocellularity with <5% blast cells seen.

One month after the completion of chemotherapy induction, resolution of gingival enlargement was observed. Staining of teeth was observed due to the use of chlorhexidine mouthwash. After remission was achieved, the patient was referred to a cancer hospital where he continues to be on follow-up [Figure 7].

DISCUSSION AND REVIEW OF LITERATURE

Acute monocytic leukemia (M5b) accounts for 3%–6% of all AML cases. In the US, it is estimated that there will be 21,380 new cases of AML and an estimated 10,590 people will die of this disease in 2017. AML is more common in older adults and among men compared to women. AML is a relatively rare disease. The number of new cases of AML in the United States was only 4.2 per 100,000 men and women per year based on 2010–2014 cases.^[10]

The highest incidence of AML in adults is in North America, Western Europe and Oceania and the lowest in Asia and Latin America. The highest rate of childhood AML is in Asia and the lowest in North America and India.^[11] According to the National Cancer Registry Program, India, the projected number of myeloid leukemia cases for the year 2020 are 16,522 and 10,679 among men and women, respectively.

In 1967, Lynch and Ship did a clinical study with sample size of 155 patients seen over a 10-year period. They found that petechiae or bleeding (56%), ulceration (53%) and gingival enlargement (36%) were the most common initial diagnostic manifestation of leukemia.^[12] Lynch and Ship conducted another study in 1967 and stated that



Figure 1: Initial presentation. Anterior labial view showing enlargement of gingiva in maxillary and mandibular arches



Figure 2: Orthopantomogram revealing generalized horizontal bone loss

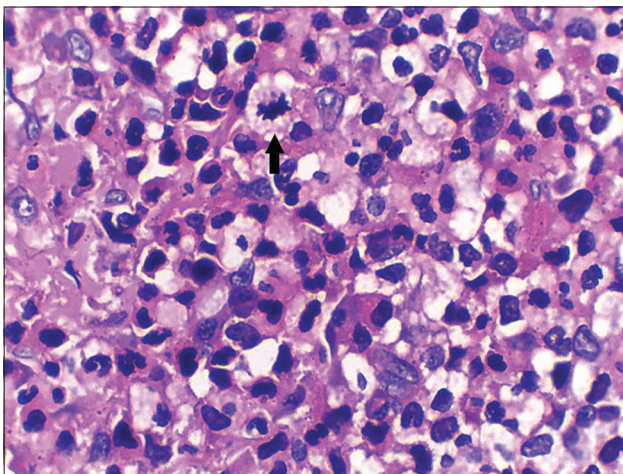


Figure 3: Histopathology study. Section showing an arrow pointed at a bizarre mitotic figure among immature tumor cells (H&E, original magnification $\times 1000$)

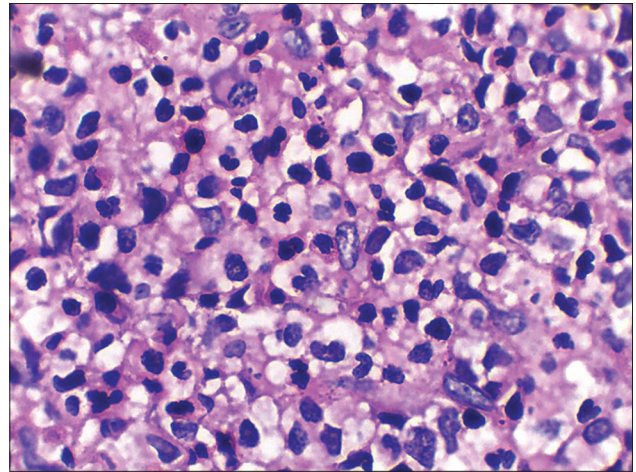


Figure 4: Histopathology study. Section showing band cells and metamyelocytes (H&E, original magnification $\times 1000$)

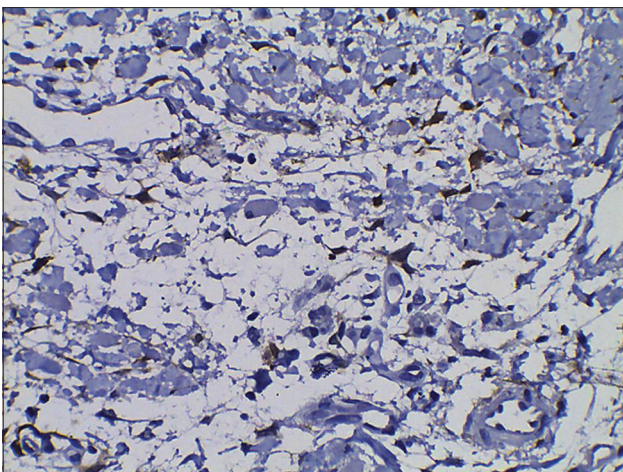


Figure 5: Immunohistochemistry study. Section demonstrating antibody against CD117 showing "focal" immunopositivity in tumor cells. (Original magnification $\times 1000$)

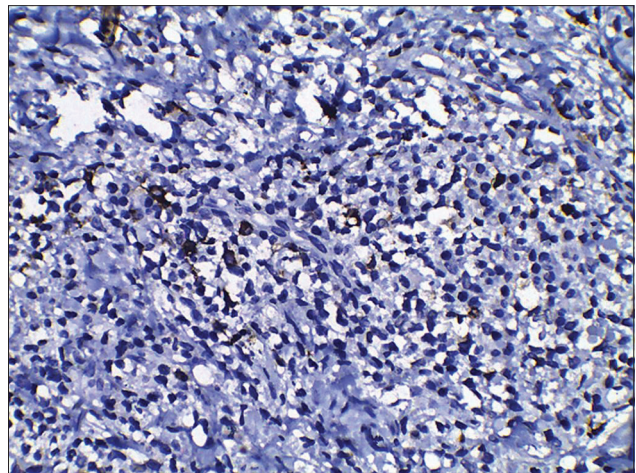


Figure 6: Immunohistochemistry study. Section demonstrating antibody against myeloperoxidase enzyme to be positive (Original magnification $\times 1000$)

the most common oral sign of leukemia occurring in the postdiagnostic period was oral bleeding or petechiae. They

also found that patients with acute leukemia who had oral petechiae or bleeding in the initial or postdiagnostic periods tended to have shortened survival time as compared to those patients with acute leukemia who did not have petechiae or bleeding.^[13] In a retrospective review of



Figure 7: 1-month follow-up showing resolution of gingival enlargement. Stains are seen due to the use of chlorhexidine mouthwash

Table 1: The French-American-British classification of acute myeloid leukemia^[9]

FAB subtype	Name
M0	Undifferentiated leukemia
M1	Acute myeloblastic leukemia
M2	Acute myeloblastic leukemia with maturation
M3	Acute promyelocytic leukemia
M4	Acute myelomonocytic leukemia
M5	Acute monocytic leukemia
M6	Acute erythroblastic leukemia

FAB: French-American-British

Table 2: Hematological findings at the time of gingival biopsy

	Patient	Normal
WBC ($\times 10^3/\mu\text{L}$)	44.78	4.00-11.00
RBC ($\times 10^3/\mu\text{L}$)	1.47	4.00-6.00
HGB (g/dL)	4.9	13.5-17.5
HCT (%)	14.5	42-52
PLT ($\times 10^3/\mu\text{L}$)	65	150-450

WBC: White blood cell, RBC: Red blood cells, HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet

500 cases in 1980, Stafford and associates also concluded that most oral manifestations were more common in patients with acute leukemia than in those with chronic leukemia.^[14] Oral changes in patients with chronic leukemia are nonspecific in contrast to those in patients with acute leukemia.^[15]

Dreizen *et al.* found that cases with acute monocytic leukemia had the highest incidence of gingival infiltrates (M5) (66.7%) followed by acute myelomonocytic leukemia (M4) (18.5%) and acute myeloblastic leukemia (M1, M2) (3.7%).^[16] In 1937, Osgood concluded that gingival enlargement was one of the most consistent features in monocytic leukemia, noted in 80% of his 58 cases. He also reported that in comparison to other cases of acute leukemia, a considerable number of the patients consulted a dentist before going to a physician.^[17] Swollen gingiva, ulceration, spontaneous gingival bleeding, petechiae, pale mucosa and infections were found to be among the commonly reported manifestations of the disease.^[14,18] Other oral signs such as hemorrhagic bullae on the tongue, cracked lips, parotid swelling, palatal pigmentation, tooth pain and mobility were less commonly reported.^[19,20]

Leukemic gingival infiltration in edentulous individuals is unreported, indicating a potential role of local irritation and trauma in the pathogenesis.^[16] The gingival findings are reported to be partially dependent on the inflammatory condition of the tissues.^[21] Poor oral hygiene predisposes the patient to oral pain, bleeding, superinfections and tissue necrosis.^[22] Advanced cases may also present with malaise, cervical lymphadenopathy, laryngeal pain and fever.^[20] The 3-year overall survival according to Tallman *et al.* was 31% for all M5 patients, 33% for M5a and 30% for M5b and 30% for non-M5. They concluded that disease-free survival and overall survival of patients with M5a, M5b and non-M5 appear not to differ with currently available therapy.^[23]

Periodontal treatment of leukemia patients necessitates the physician's consent. The scaling and root planning should be covered by prophylactic antibiotics.^[8] Patients should be advised 0.2% chlorhexidine mouth rinses after oral hygiene procedures. However, certain complications of chemotherapy and radiation such as mucositis, xerostomia, hemorrhage and recurrent HSV infection should be identified and the treatment plan accordingly modified.^[22]

Literature suggests that gingival hyperplasia resolves completely or at least partly with effective leukemia chemotherapy.^[24] Wu *et al.* reported resolution of gingival enlargement in 10 days whereas Demirer *et al.* reported resolution after 8 weeks.^[25,26] However, Menezes and Rao reported that no resolution or increase in the enlargement was observed after chemotherapy although the time period was not specified.^[27] Hence, it is derived that the role of oral hygiene and other factors influencing the resolution of enlargement in leukemia patients needs to be further studied and investigated.

This case reinforces the fact that oral health-care professionals should be aware of the oral manifestations of systemic diseases. Acute leukemia often compels the patient to seek dental care first,^[14] making dentists responsible for initiating the diagnosis in 25%–33% of patients with AML.^[28] To aid in early diagnosis and subsequent early management, the dental practitioner must clearly recognize the pathology and fully investigate it by requesting additional tests or referring the patient to a higher center.

Acknowledgments

The authors wish to thank Dr. Priya Kumar, Dr. Jeyaseelan Augustine and Dr. Aadithya B Urs from the Department of Oral and Maxillofacial Pathology,

Maulana Azad Institute of Dental Sciences, New Delhi, for providing images of the biopsied specimen.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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