Acute Myelomonocytic Leukemia with Gingival Enlargement: A Case Report
Laxmi G Doddamani, Mubeen Khan, Suman B

Abstract
Oral manifestations are the early indicators of many systemic diseases. Leukemia is one among such systemic diseases which shows characteristic oral manifestations. This report describes the case of a 40 year old female who presented with gingival enlargement and bleeding. Initially a provisional diagnosis of generalized inflammatory gingival enlargement was made and based on this oral prophylactic management of the patient was carried out. However, persistent gingival swelling even after periodontal therapy made the clinicians to suspect leukemic enlargement which was confirmed on further investigations. This case outlines the role of dental professionals in identifying such underlying pathology and make early referrals to appropriate health professionals for early diagnosis and intervention reducing the patient morbidity.

Key Words: Leukemia; Acute Myelomonocytic Leukemia; Gingival Enlargement; Oral Manifestations.

Introduction
Leukemia was first discovered by a pathologist Rudolf Virchow in 1845 observing an abnormally large number of WBCs in a blood sample from a patient and coined the term Leukemia derived from Greek words Leukos (white) and Haima (blood). In 1869 Neuman concluded that bone marrow problem was responsible for the abnormal blood of leukemia patients. Thus it can be defined as a hematological disorder resulting from the proliferation of a clone of abnormal hematopoietic cells with impaired differentiation, regulation and programmed cell death.1

The 13% of global population unfortunately suffer from this deadly disease leukemia and accounts for 4% of all cancer deaths. The incidence is 13 in 100,000 people per year. Has higher incidence in men than in women with most chronic leukemia’s occurring in adults. Acute Lymphoid Leukemia more common in children whereas Acute Myeloid Leukemia is more common in adults.

This article reports a case of Acute Myelomonocytic Leukemia (AMMoL) having gingival enlargement as an oral manifestation in a 40 year old female and the importance of carrying out thorough investigations at initial visits of patients.

Case Report
A 40 year old female patient reported to our department with vague symptoms of gum swelling and bleeding since one month without any significant history of fever, pain and trauma. There was neither significant medical and family history nor any history of medication present. On general physical examination patient was healthy. Head and neck examination revealed mild facial asymmetry with diffuse swelling in the right cheek region. No abnormalities were noted in the skin, eyes, nose and ears. Mouth opening was adequate with no other abnormalities obvious in relation to temporomandibular joint. Right submandibular lymph node was palpable, mobile, enlarged, non-tender and soft in consistency.

Routine hard tissue examination of the oral cavity revealed generalized deposits of calculus and stains, generalized attrition, grade II mobility in relation to tooth #14, 15, 16, 17, 46, & 47. Soft tissue examination revealed generalized gingival enlargement and pseudo pockets (Fig 1a). Boggy, erythematous enlargement noted in the gingivae of both the arches with prominent bulbous enlargement of buccal gingiva in relation to 15, 16 & 17 (Fig 1b & c). No abnormalities were noted in the rest of the oral mucosa. On palpation swollen gingivae were soft, edematous, non-tender and bleeding could be elicited. Based on the history and clinical findings provisional diagnosis of chronic generalized inflammatory gingival enlargement was established. Various other conditions considered for differential diagnosis were...
fibrous gingival enlargement and Leukemic gingival enlargement.

Following investigations were carried out. Intraoral periapical radiograph revealed abnormally missing and thickening of lamina dura with loss of alveolar bone (Fig 1d). Complete blood count showed values within normal range with erythrocyte sedimentation rate grossly elevated. Patient underwent thorough periodontal treatment. Unfortunately patient returned to us within a span of one month with persistent gingival swelling. To rule out other causes for gingival enlargement patient was re-suggested to undergo following investigations. The orthopantamogram revealed generalized severe alveolar bone loss. Complete blood count revealed low Hemoglobin level characteristic of anemia, a low platelet count characteristic of thrombocytopenia and WBC count was markedly increased. ESR was grossly elevated and all other findings were insignificant (Table 1). Peripheral smear was advised which confirmed the diagnosis of AML revealing significant elevation of immature myeloid cells predominantly monoblasts (Fig 1e). Further investigations like chest X-ray appeared normal and ultrasound abdomen revealed mild splenomegaly with no evidence of hepatomegaly. Patient was immediately referred to Kidwai Memorial Institute of Oncology, Bangalore. Further tests such as bone marrow aspiration and cyto-chemistry were done by an oncologist. Bone marrow aspiration revealed hypercellular marrow showing blasts 80% with suppression of other marrow elements. Cytochemical staining with myeloperoxidase gave positive reaction with myeloid series of cells. Finally patient was hospitalized with a final diagnosis of Acute Myelomonocytic Leukemia and was put on chemotherapy. Unfortunately one and half months after her visit to the department, patient succumbed to death.

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>First Visit</th>
<th>Second Visit</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (gm/dl)</td>
<td>11.3</td>
<td>9.0</td>
<td>11.5 - 16.4</td>
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<tr>
<td>PCV (%)</td>
<td>37.2</td>
<td>27.2</td>
<td>36-47</td>
</tr>
<tr>
<td>RBC count (million/cumm)</td>
<td>4.53</td>
<td>3.62</td>
<td>4.8+ or -1.0</td>
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<tr>
<td>MCV (fl)</td>
<td>77</td>
<td>75.1</td>
<td>76-96</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>26</td>
<td>24.9</td>
<td>27-32</td>
</tr>
<tr>
<td>MCHC (gm/dl)</td>
<td>33</td>
<td>33.1</td>
<td>33 + or -2</td>
</tr>
<tr>
<td>Total leukocyte count (cumm)</td>
<td>5900</td>
<td><strong>1,30,000</strong></td>
<td>4000-11,000</td>
</tr>
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<td>Differential leukocyte count (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polymorphs</td>
<td>67</td>
<td></td>
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<tr>
<td>Lymphocytes</td>
<td>25</td>
<td>---</td>
<td>30 - 40</td>
</tr>
<tr>
<td>Monocytes</td>
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<td></td>
<td>5 - 8</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>04</td>
<td></td>
<td>2 - 5</td>
</tr>
<tr>
<td>Basophils</td>
<td>00</td>
<td></td>
<td>1 - 2</td>
</tr>
<tr>
<td>Platelet count (laks/mm²)</td>
<td>1.7</td>
<td>0.6</td>
<td>1.5-4</td>
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<tr>
<td>Erythrocyte sedimentation rate (mm/hr)</td>
<td>45</td>
<td>46</td>
<td>0-7</td>
</tr>
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</table>

Table 1: Complete Blood Count at first and second visit

Discussion
Leukemias are malignancies of hematopoietic tissues and about 50% of all leukemias are acute form. Acute Myelomonocytic Leukemia (AML-M4) is a subtype of acute myeloid leukemia and is defined by more than 20% (World Health Organization classification) or more than 30% (French American British classification) of myeloblasts in the bone marrow aspiration. Moreover, 20% of non-erythroid cells are of monocytic origin.

According to the clinical behavior leukemias are classified into acute and chronic forms and characterized as lymphocytic and monocytic referring to its histogenic origin.

Thus the main types are AML, ALL, CML and CLL. Chronic leukemias involve relatively well differentiated leukocytes, and are slow in onset and run an indolent course. Acute leukemias are characterized by uncontrolled proliferation of poorly differentiated blast cells; they are abrupt in onset, aggressive and rapidly fatal if left untreated. Each of these types may be further classified into subtypes. Sub-classifications are based on morphologic, cytochemical, immunologic, cytogenetic and molecular criteria. The most commonly used classification schemata for AML are WHO system and FAB system. WHO classify AML into 4 subtypes as: AML with characteristic genetic abnormalities, AML with multi-
lineage dysplasia, AML with myelodysplastic syndrome or myelo-proliferative diseases therapy related and AML not otherwise categorized. FAB system classify AML under 8 subgroups according to their degree of differentiation along cell lines and extent of cell maturation as M0 (Undifferentiated acute Myeloid Leukemia), M1 (AML with minimal maturation), M2 (AML with maturation), M3 (Acute promyelocytic leukemia), M4 (Acute myelomonocytic leukemia), M5 (Acute monocytic leukemia), M6 (Acute erythroblastic leukemia) and M7 (Acute megakaryoblastic leukemia).

Figure 1: The clinical picture showing generalized gingival enlargement with deposits of stains and calculus (a), with bulbous enlargement of gingiva in maxillary right posterior teeth (b) and boggy generalized gingival enlargement in mandibular arch (c). The intraoral periapical radiograph shows maxillary & mandibular alveolar bone loss (d). The photomicrograph of peripheral smear shows immature myeloid cells –monoblasts (e).

The exact etiology for leukemia is not known. However genetic, viral, chemicals, drugs and environmental factors play a role. Genetic is related to mutations in DNA. Certain mutations can trigger leukemia by activation of oncogenes and deactivation of tumour suppressor genes there by disrupting the regulation of cell death, differentiation or division leading to accumulation of leukemic blast cells in the marrow and suppression of normal hemopoietic stem cells.

Patients with AMMoL generally present with symptoms related to complications of pancytopenia, which includes fatigue, unexplained persistent low grade fever, weight loss, headache, muscle or joint pain and profuse bleeding with minor trauma. Pallor, recurrent infections, lymphadenopathy, mild splenomegaly, petechiae, ecchymosis and purpura in the skin and mucous membrane and bone tenderness are the most common physical signs. Classical oral manifestations include generalized gingival enlargement which is boggy, diffuse and soft involving marginal, attached and interdental gingiva leading to mobility of teeth, spontaneous bleeding and ulcerations, petechiae and ecchymosis in the oral mucosae and opportunistic infections like candidiasis and herpes.

Oral manifestations in patients with leukemia have been described in all subtypes of AML, CML, ALL and CLL. Oral manifestations are common in monocytic and myelomonocytic leukemias. Dreizen et.al reported that the patients with acute monocytic leukemia had the greatest incidence of gingival infiltrates (M5-66.7%) followed by acute myelomonocytic leukemia (M4-18.5%) and acute myeloblastic leukemia (M1, M2-3.2%).

Diagnosis is made from the identification of abnormal hemopoietic cells in the peripheral blood and bone marrow. Further characterization is by cytochemical staining,
immunophenotyping and cytogenetic analysis of chromosomal abnormalities. When concern arise about possible damage due to leukemia, radiographs MRI and ultrasound can help potentially to view leukemia's effect on such body parts as bones, the brain or the kidneys, liver and spleen.

Leukemias are treated with chemotherapy. Some are also treated with radiation therapy, blood and plasma transfusion. In some cases bone marrow transplant are helpful. Treatment and prognosis depends on several factors like age, WBC count, type of AML, response to induction therapy and leukemic cytogenetic abnormalities. Though there have been tremendous advances in management of leukemia, the death rate is still high. Unfortunately the life span of leukemia patients remains within six months. However survival rate depends on the type of myeloid cells involved and early diagnosis and treatment.

**Conclusion**
The academy of general dentistry has determined that more than 90% of all systemic diseases have oral manifestations. Careful examination of the oral cavity may reveal findings indicative of an underlying systemic condition. Examination should include evaluation for mucosal changes, periodontal inflammation and bleeding, and general condition of the teeth. Thus dental professionals can be the first to identify these oral manifestations and make early referrals to appropriate health professionals for early diagnosis and treatment for better prognosis, thus playing a key role in screening for such systemic conditions. In our patient the diagnosis was missed initially in the first visit. However in the second visit peripheral smear provided a correct pathway for diagnosis. It is very much essential in any clinical enlargement of gingiva to carry out thorough investigations.

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**References**

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