



Case Report

Unveiling acute myeloid leukemia through gingival enlargement: A case report

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Abstract

Gingival enlargement might be result from many conditions like local irritation, mouth breathing drug consumption, leukemias, Wegner’s granulomatosis, sarcoidosis etc. The consistency could be fibrotic, inflammatory or mixed. Such oral manifestation like gingival enlargement might be key factor to early diagnose and prompt treatment of fatal cases. Here is a case report of 30-year-old female who was suffering from slow, progressive gingival enlargement with lots of discomfort while chewing and speaking and later diagnosed with acute myeloid leukemia (AMLs). Acute myeloid leukemia is aggressive hematopoietic neoplasm shows high morbidity if left untreated could lead to death. So, there is crucial role of dentist when commencing the deadly disease like leukemia.

Keywords: Gingival enlargement, Acute myeloid leukemia, Monoblasts, leucocytosis, Monocytic differentiation.

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1. Introduction

Leukemia is a clonal malignancy of any of the blood-forming cellular elements, consisting largely of immature precursors (blasts), preferentially involving the blood, bone marrow, or both. The disease course progresses over weeks to months, ultimately culminating in bone marrow failure.¹

According to the most recent World Health Organization Classification of Tumours of Hematopoietic and Lymphoid Tissues, leukemia is classified based on clinical behaviour,

1. Acute
2. Chronic

The primary hematopoietic cell line affected,

1. Myeloid
2. Lymphoid

The four principal diagnostic categories are,

1. Acute myelogenous leukemia (AML)
2. Acute lymphocytic leukemia (ALL)
3. Chronic myelogenous leukemia (CML)
4. Chronic lymphocytic leukemia (CLL).

1.1. Acute leukemia

Acute leukemia may be lymphoblastic or myeloid. ALL most commonly seen in small children and young adults while AML most commonly seen in adults.^{1,2}

1.1.1. FAB and WHO Classification for acute myeloid leukemia-

Two staging systems are commonly used for acute myeloid leukemia. The French-American-British (FAB) Classification system is based on morphology to define specific immunotypes. World Health Organization (WHO) classification shows chromosome translocations and evidence of dysplasia.^{1,2}

FAB Subtype	Name
M0	Undifferentiated acute myeloblastic leukemia 5%
M1	Greater number of myeloblasts with <10% granulocytic differentiation
M2	Myeloblasts in great number with granulocytic differentiation >10%, NSE <20%

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M3	Promyelocytes that are hyper granular with many Auer rods on CAE or Wright-stain and variant form cells with reniform nuclei, multilobed or bibbed, primeval cells with multiple Auer rods or relative scarcity of hyper granular promyelocytes.
M4	>20% but <80% NSE-butyrate positivity in monocytic cells
M5	Monocytic cells with >80% NSE positivity. (a) Monocytic cells predominantly monoblasts (>80%) Acute Monoblastic Leukemia (b) A mixture of monoblasts and promonocytes (<80% blasts)
M6	>30% of myeloblasts with more than 50% erythroblasts, eliminating the erythroid cells.
M7	Acute megakaryoblastic leukemia <5%

than 2/3rd of the crown of teeth to the buccal, palatal and lingual aspects. Loss of normal contour of gingiva with generalized tenderness and pseudopockets were present associated with bleeding on probing. Poor oral hygiene with presence of stains and calculus. So, provisional diagnosis given was Leukemic gingival enlargement.

2.2. Oral manifestations

1. Generalized gingival enlargement covering more than 2/3rd of the crown of teeth.
2. Bleeding from the gingiva on probing.
3. Pale oral mucosa was present.

2.3. Investigations

Radiological Investigation- An OPG had taken place, and there was no bone loss, or any abnormality elicited. (Figure 4)

Specimen: Peripheral blood EDTA-1, Heparin-1 vacutainers labelled.

Haematological investigation

Haemoglobin	7.1 g/dl
Haematocrit	22.4 %
MCV	108.5 fL.
RDW-CV	19.6%
MCH	34.5 pg.
WBC Count	101.2 x 10 ³ µl
RBC Count	2.07 x 10 ⁶ µl
MCHC	31.8 g/dL
Platelet Count	82 x 10 ³ µl

2.3.1. Peripheral blood smear examination

RBCs: Normocytic normochromic with anisocytosis.
WBCs: Leucocytosis with blasts and promonocytes (blast equivalents). Blasts are large 4-5 times the size of small lymphocytes, abundant cytoplasm, round to oval nucleus, fine chromatin with prominent nucleolus. Blasts equivalents are large, abundant cytoplasm, indented/ lobulated, irregular nucleus with open chromatin, prominent nucleoli.
Platelet: Thrombocytopenia

Blasts	25 %
Neutrophils	06 %
Promonocytes	52 %
Lymphocytes	15 %
Monocytes	02 %

2.3.2. Flow cytometric immunophenotyping

Specimen: Peripheral blood

1.2. Etiology

1. Two Risk factors for AML include genetic changes (such as familial mutations of CEBPA, DDX41, RUNX1; Fanconi anemia; Bloom’s syndrome; and trisomy 21).¹⁻³
2. Exposure to environmental factors including ionizing radiation of ≥1 Gy is known to cause leukemia also with prolonged radiation therapy.^{1,2}
3. Chemotherapy and exposure to some chemicals like benzene, phenylbutazone and chloramphenicol.¹⁻³
4. Tobacco, smoking and certain chemicals.¹⁻³
5. Some cases of AML arise from myelodysplastic syndrome and other myeloproliferative neoplasms.¹⁻³
6. Previous haematological disorders.^{1,2}

2. Case Report

A 30-year-old female reported to the department of Oral Medicine and Radiology with a chief complaint of gums swelling and bleeding from the gums since 2 months. The swelling was spontaneous in origin and slowly progressed in size to cover all the teeth. She also gave the history of typhoid 2 months back for which she had been hospitalized to her family physician. She had high fever which increased at night with chills and swelling. She also had a loss of appetite, and sudden weight loss. General examination revealed shortness of breath, fatigue, febrile and signs of anemia. No significant medical, dental, or family history was found.

2.1. Patient shows following features

2.1.1. Extraoral examinations

Bilateral submandibular lymph nodes are slightly enlarged, palpable and pain on palpation present.

2.1.2. Intraoral examinations- (Figure 1-3)

Teeth present - All teeth were present
Generalized, diffuse, pink, firm, bulbous gingival enlargement presents in upper and lower jaws involving more

Gate Strategy (ics): FSC/SSC and CD45/SSC Gated Population(s): Blast region

Gated population	Expression (CD34 positive)	Expression (CD34 negative)
CD45	Dim positive	Moderate positive
Non-lineage specific antigen		
CD34	Moderate Positive	Negative
HLA-DR	Variable Positive	Moderate Positive
CD38	Variable Positive	Moderate Positive
B-lymphocytic antigen		
CD19	Negative	Negative
CD10	Negative	Negative
CD20	Negative	Negative
CD22 (Surface)	Negative	Negative
T-lymphocytic antigen		
CD2	Negative	Negative
CD3 (Cytoplasmic)	Negative	Negative
CD5	Negative	Negative
CD7	Negative	Negative
CD56	Negative	Negative
Myeloid Antigens		
CD11c	Dim positive	Moderate positive
CD13	Dim positive	Moderate positive
CD14	Negative	Variable positive
CD15	Negative	Dim positive
CD33	Dim positive	Moderate positive
CD117	Moderate positive	Negative
CD64	Dim positive	Moderate positive
CD36	Negative	Moderate positive
Myeloperoxidase (cytoplasmic)	Negative	Negative

2.4. Summary

Flow cytometric immunophenotyping revealed 2 population of blasts, CD34 positive and CD34 negative.

2.4.1. CD34 positive

Moderate CD13, CD33, CD45, CD64, CD11c
Variable HLA-DR, CD38

And negative for CD14, CD15, CD36, CD7, CD56, CD5, CD2, CD19, cytoplasmic CD3, cytoplasmic MPO, CD22, CD10 and CD20

2.4.2. CD34 negative

Moderate CD38, CD13, CD33, HLA-DR, CD64, CD11c, CD45, CD26 Dim CD15

Variable CD14

And negative for CD117, CD2, CD5, CD7, CD56, CD19, CD20, CD10, cytoplasmic CD3, cytoplasmic MPO and CD22

2.4.3. Final impression

Morphological and immunophenotypic analysis suggestive of Acute Myeloid Leukemia with monocytic differentiation.

2.4.4. Differential diagnosis

1. Chronic inflammatory gingival enlargement
2. Leukemic gingival enlargement
3. Plasma cell gingivitis

2.4.5. Final diagnosis

According to FAB Classification- M5b Acute Myeloid Leukemia with Monocytic Differentiation

Treatment regimen

1. Systemic
 - a. Induction therapy = Tb Cytarabine 7 days + (Daunorubicin or idarubicin) IV 3 days for (7+3) ^(19,20)
 - b. Patient was with poor prognosis so, given CPX-351 or Hypomethylating agent ^(19,20)

The patient was referred to an oncology center for chemotherapy as above but unfortunately passed away within three months.



Figure 1: Shows Generalized gingival enlargement in upper and lower jaw.



Figure 2: Shows Gingival enlargement in upper jaw including marginal, attached gingiva with interdental papilla of labial and buccal aspects of the teeth.



Figure 3: Shows Gingival enlargement in lower jaw including marginal, attached gingiva with interdental papilla of labial, buccal and lingual aspects of the teeth.



Figure 4: No bone loss seen, or any abnormality detected in OPG.

3. Discussion

Leukemia is a malignancy of the WBCs found to occur due to disorganized proliferation and increased viability of WBCs (Blasts). Leukemias Broadly classified into lymphoid or myeloid and Acute and Chronic respectively.⁵⁻⁷ Acute and chronic depending on the onset while myeloid and lymphoid depending on the degree of differentiation of cells and maturation of cells. (6,7) Chronic leukemias are slow onset from months to years, mostly involve well differentiated WBCs.^{6,7} While acute leukemias involve poorly differentiated leucocytes. Their onset is abrupt and could be aggressive and fatal.^{7,8}

Oral lesions are more common in individuals with acute leukemia, according to Stafford et al.^{7,8} The direct infiltration of leukemic cells (primary) or underlying thrombocytopenia, neutropenia, or compromised granulocyte function may be

the cause of oral symptoms.⁷⁻⁹ The first presenting complication of AML is gingival infiltration, which occurs 5% of the time.^{8,9} Gingival infiltrates (M5) (66.7%) were most common in patients with acute monocytic leukemia, according to Dreizen et al., followed by acute myelomonocytic leukemia (M4) (18.5%) and acute myeloblastic leukemia (M1, M2) (3.7%).^{8,9}

Acute leukemias frequently present orally as petechiae, enlarged gingiva, oral ulcers, spontaneous gingival bleeding, pale mucosa, and fungal and viral infections (candidiasis and herpes).⁹⁻¹¹ The rare oral symptoms include petechiae, buccal and labial mucosa, tooth discomfort and movement, cracked lips, and hemorrhagic bullae on the anterior dorsum of the tongue.^{11,12} The degree of gingival overgrowth impedes both function and appearance and can range from little to full tooth covering.^{12,13} Since edentulous people do not exhibit leukemic gingival infiltration, teeth-associated local variables may play a part in its development. In addition to increasing the risk of mouth discomfort, bleeding, hyperinfection, and tissue necrosis, caries, calculus, and poor dental hygiene can also worsen gingival symptoms.^{13,14,16}

Allogenic bone marrow transplantation and vigorous multidrug chemotherapy are available treatments for acute leukemias. (14) Leukemic patients should always have their dental and periodontal care scheduled following a medical examination and with their doctor's approval. Scaling and root planing are examples of periodontal interventions that should be carried out while taking preventative antibiotics.^{14,15,17} Following surgery, patients are instructed to use mouthwash containing 0.12% chlorhexidine. However, unless the underlying condition completely resolves, periodontal procedures are delayed.¹⁸⁻²⁰

Our patient was advised to maintain meticulous oral hygiene by use of soft bristle tooth brush and 0.2% chlorhexidine mouth rinses. Patient was referred to oncology center for chemotherapy. The patient succumbed to death within 3 months after hospital admission.

4. Conclusion

This case highlights the critical role of oral manifestations, such as gingival enlargement, in the early detection of systemic conditions like acute myeloid leukemia (AML). Dentists, often being the first to observe such signs, play a vital role in identifying potentially life-threatening diseases. Timely recognition and referral can significantly impact patient outcomes, underscoring the importance of a multidisciplinary approach in managing oral and systemic health.¹⁹⁻²¹

4.1. Declaration of interests

1. Authors can declare that they have no known competing financial interests or personal relationships that could influence the work.

2. They can also declare any financial interests or personal relationships that could be considered competing interests.

4.2. Contributions

1. Each author can declare their contributions to the study, such as conception and design, data acquisition, analysis and interpretation, or drafting and revising the article.
2. Approval of the submitted version of the manuscript
3. Authors can confirm that all co-authors have read and approved the submitted version of the manuscript.
4. Authors can use the Elsevier Declaration Tool to save their progress and reuse information for future declarations.

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None.

6. Conflict of Interest

None.

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