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Gingival Enlargement as Initial Manifestation of Acute Myeloid Leukemia : A Case Report

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ABSTRACT
Acute myeloid leukemia (AML) is a disease of hematopoietic stem cells in the bone marrow that proliferates and differentiates abnormally. AML can develop aggressively and cause a variety of complaints due to bone marrow suppression and symptoms of inflection to individual organs. Symptoms and signs of AML can be caused due to the suppression of the bone marrow resulting in ineffective erythropoesis. The oral cavity can show the first clinical manifestations of leukemia. Individuals with leukemia may show lesions such as enlarged gums. Case Presentation: A 31-year-old female patient was referred from the Dental Polyclinic of Tabanan Hospital with complaints of enlarged gums since 1 month ago. Enlargement occurs in the gums behind which incisors enlarge rapidly. Other complaints include fever up and down, weakness, bleeding through the anus. The results of the Complete Blood test found a very high WBC value, with bicytopenia, with BMP examination showing AML with M4 morphology. Conclusions: In a 31-year-old female patient, gum enlargement was found as an early manifestation of acute myeloid leukemia (AML) accompanied by constitutional symptoms such as fever, weakness, spleenomegaly. Clinical manifestations of AML can include symptoms of suppression of the bone marrow by malignant cells, and infiltration into organ systems. Oral manifestations of AML can include enlargement of the gums, discoloration of the mucous membranes to bluish or pale, ulcers, erosion, bleeding, ecchymosis, which can be mistaken for manifestations of other diseases.
Keywords: AML, Gingival Enlargement, Oral Manifestation, M4

Introduction

Acute myeloid leukemia (AML) is a malignancy of *hematopoietic* stem cells within the bone marrow characterized by abnormal proliferation and differentiation. AML is an aggressive disorder of white blood cells that leads to symptoms associated with bone marrow failure and organ infiltration (Cammarata-Scalisi et al., 2020; DiNardo et al., 2023; Hwang, 2020; Naymagon et al., 2020; Reinhardt et al., 2022; Short et al., 2018). The disease can progress rapidly, resulting in a variety of clinical presentations caused by bone marrow suppression and specific organ involvement, and, in many cases, can become fatal and life-threatening. AML, representing approximately 1% of all cancer cases, frequently manifests as a highly aggressive disease with considerable mortality rates (Bhansali et al., 2023; De Kouchkovsky & Abdul-Hay, 2016; Qin, 2022; Stubbins et al., 2022; Weinberg et al., 2023). Most AML cases are diagnosed in older adults, commonly over the age of 60, with a reported median age at diagnosis of about 68 years. However, AML can also present in young adults aged 15–39 years, albeit at a lower incidence of 0.7 to 2.0 cases per 100,000 individuals per year.

The symptoms and signs of AML often stem from the suppression of normal bone marrow function, resulting in ineffective *erythropoiesis*. Patients may present with signs of anemia, bleeding from mucosal membranes and internal organ systems, fatigue, dyspnea, tachypnea, headache, among others (ACS, 2018; Albrecht et al., 2017; Amonoo et al., 2021; Shi et al., 2023). In addition, infiltration of leukemic cells into various organs can also occur. Typically, these symptoms develop acutely, often within days to several weeks. The oral cavity, due to its vascularity and dynamic environment, can serve as an initial site for clinical manifestations of

leukemia. Individuals with leukemia may initially present with lesions such as gingival enlargement, mucosal discoloration (bluish or pale), ulceration, erosions, spontaneous bleeding, or *ecchymosis*, which can easily be misdiagnosed as manifestations of other diseases. This case report highlights the early oral manifestations of AML encountered in daily practice to underscore the importance of early detection and management in patients with AML.

Due to its high vascularity and ongoing cellular turnover, the oral cavity often serves as an initial site for the presentation of systemic diseases, including various hematologic malignancies. Oral alterations may frequently represent the earliest clinical indicators of underlying systemic abnormalities, emphasizing the significance of comprehensive oral examinations in general health assessments. Recognizing these oral indicators is critical, as they may serve as essential clinical clues for the early identification of serious disorders such as leukemia.

Among the array of oral manifestations, gingival enlargement stands out as a notable and at times overlooked presenting sign of AML. This feature is characterized by exuberant overgrowth of the gum tissue, attributable to leukemic cell infiltration. While gingival enlargement can arise from multiple etiologies—including inflammation, hormonal changes, or certain medications—its rapid progression and distinctive appearance in the context of other systemic symptoms should prompt strong suspicion for hematologic malignancy. Numerous case reports and reviews have documented gingival enlargement as an early or even initial manifestation of AML, most notably in certain subtypes, such as acute monocytic leukemia (*M5*) and acute myelomonocytic leukemia (*M4*). The present case report, detailing "Gingival Enlargement as Initial Manifestation of Acute Myeloid Leukemia," underscores the value of this oral finding as a gateway to timely diagnosis. Prior research emphasizes that dental professionals are frequently the first healthcare providers to encounter patients exhibiting these initial manifestations, underscoring their vital role in early referral and diagnosis.

Despite substantial literature addressing oral manifestations of AML, a significant gap persists regarding a comprehensive understanding of the diagnostic pathway initiated by dental practitioners and long-term outcomes for patients whose primary symptom is gingival enlargement. While case reports provide isolated descriptions, a more systematic exploration is needed of diagnostic algorithms, interprofessional collaboration, and the resulting patient prognoses in such presentations. Additionally, further research is warranted on strategies to empower dental practitioners in identifying and responding to subtle, yet critical, indicators of systemic disease.

The urgency of this research is underlined by the aggressive progression of AML, where early diagnosis and prompt initiation of therapy are closely linked to improved outcomes and survival rates. Diagnostic delays due to nonspecific or underestimated oral symptoms can result in disease advancement and poorer clinical trajectories. Thus, heightened awareness and improved detection of oral manifestations as potential early signs of AML are essential for effective intervention.

This study augments current knowledge by offering an in-depth examination of a case with gingival enlargement as the initial finding, illuminating the diagnostic process and subsequent clinical management. The novelty of this research lies in its in-depth focus on oral presentation and its pivotal role in the early detection of AML, highlighting the need for increased vigilance among dental professionals. It addresses an existing research gap by discussing the

practical implications of interpreting seemingly isolated oral symptoms as potential hallmarks of a severe systemic condition.

The primary aim of this research is to underscore the diagnostic relevance of gingival enlargement as an early clinical sign of AML, and to advocate for its recognition as a critical diagnostic cue. It seeks to demonstrate how timely identification of oral features by dental professionals can substantially reduce diagnostic delays and contribute to improved patient outcomes.

Specifically, the objectives are: (1) to provide a detailed description of the clinical presentation and diagnostic progression of a patient whose AML diagnosis originated from consultation regarding gingival enlargement; (2) to highlight the importance of interprofessional collaboration between dentistry and medicine for timely and precise diagnosis; and (3) to advocate for the incorporation of thorough oral examinations into routine health screenings, particularly when systemic disorders are suspected.

Ultimately, this research offers multiple benefits, including enhanced awareness among dental professionals regarding the importance of unusual oral findings as potential indicators of systemic malignancy such as AML, promotion of proactive patient care, and encouragement of closer communication and collaboration between dentistry and hematology. These advances are expected to accelerate diagnosis, improve clinical outcomes, reduce morbidity, and increase the likelihood of life-saving intervention for patients with acute myeloid leukemia.

RESEARCH METHODS

A 31-year-old female patient was referred from the Dental Polyclinic of *Rumah Sakit* Tabanan with a chief complaint of gingival enlargement that had developed over the preceding month. The enlargement primarily affected the gums posterior to the incisors. Initially, the gingival swelling was mild but progressively increased in size, reaching approximately 5 cm within one month. The enlargement was associated with bleeding provoked by toothbrushing. This significant gingival swelling severely impaired the patient's ability to eat and speak. Additional complaints included intermittent fever and marked fatigue, both of which had been present for ten days prior to hospitalization. The patient also reported bleeding per rectum during defecation, which had occurred over the past five days.

At the dental polyclinic, intraoral radiography and a complete blood count (CBC) were performed. The dental X-ray revealed no significant abnormalities; however, the CBC demonstrated marked leukocytosis. Due to these findings, the patient was referred to the Medical Hemato-Oncology Polyclinic of *Rumah Sakit* Tabanan.

On physical examination, the patient appeared moderately ill. Vital signs were as follows: blood pressure 130/80 mmHg, pulse rate 109 beats per minute, temperature 38.6°C, and respiratory rate 23 breaths per minute. Examination revealed conjunctival pallor, absence of icteric sclera, no palpable lymphadenopathy (*kelenjar getah bening* enlargement [-]), and splenomegaly (Scuffner grade 2). There was a 2 cm ulcer present on the buttocks, with a muscular base and irregular margins.

Laboratory investigations included a repeat CBC and a planned bone marrow puncture (BMP). Initial management consisted of intravenous fluid loading with NaCl 0.9% at 1 liter followed by maintenance at 28 drops per minute, transfusion of 2 units of packed red cells (*PRC*), 1 unit of thrombocyte concentrate (*TC*), with premedication using methylprednisolone 125 mg

IV, Cefoperazone 1 g IV every 12 hours, tranexamic acid 500 mg IV every 8 hours, hydroxyurea 500 mg orally twice daily, and paracetamol 500 mg orally as needed for fever. BMP was scheduled to be performed when the patient's hemoglobin increased adequately to permit the procedure.

During hospitalization, the patient developed severe thrombocytopenia that was refractory to repeated TC transfusions. On the seventh day of treatment, she experienced a decline in consciousness and respiratory distress, subsequently progressing to death. The patient unfortunately did not receive induction therapy for AML prior to her demise.

Table 1. Serial Complete Blood Test Results

Parameters	21/2/2024	24/2/2024	27/2/2024	Reference Value
HGB	6.3	9.0	7.7	13.2-17.3
HCT	19.0	27.4	23.6	40-52
RBC	2.05	3.11	2.67	4.4-5.9
WBC	117.7	27.9	29.6	3.8-10.6
PLT	58	47	5	150-440
MCV	93	88	89	80-100
MCH	31	29	29	26-34
MCHC	33	33	33	32-36
%NEU	38	34	11.3	50-70
%LYMPH	8	8	3.7	25-40
%MONO	54	58	14.5	2-8
%EOS	0.0	0.0	0.0	2-4
%BASO	0.0	0.0	0.0	0-1

Table 2. Results of Examination of Hemostasis, Kidney Function, and Blood Glucose

Parameters	21/2/2024	Reference Value
PT	19.6	10.0 - 14.4
APTT	33.4	24 - 35
INR	1.4	0.8-1.2
Urea	10	10-50
Creatinine	1.1	Male : 0.62 - 1.10 Female : 0.45 - 0.75
GDS	119	74-106

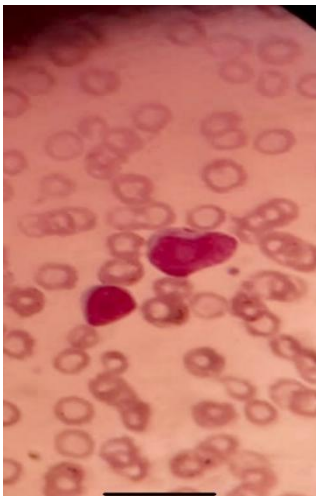

Figure 1. Auer Rod On Edge Blood Removal Examination

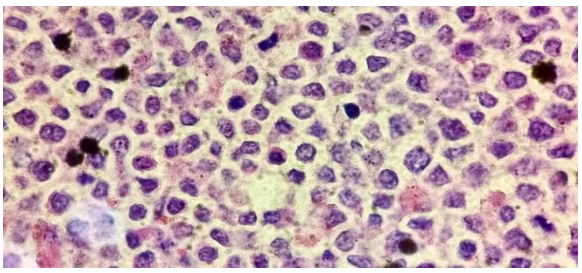

Figure 2. Dominance of myeloid series, myeloid series blast component >20% impresses M4 Acute Myeloid Leukemia

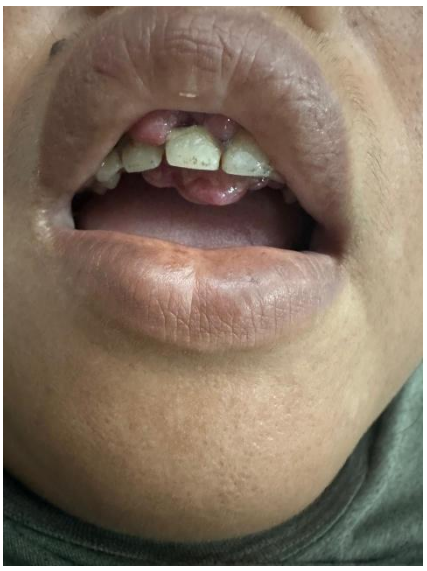

Figure 3. Gum enlargement as an early manifestation of AML patients

RESULTS AND DISCUSSION

Acute myeloid leukemia (AML) is a malignancy of hematopoietic cells of the myeloid series characterized by rapid expansion of immature myeloid cells, differentiation failure, and high cell proliferation. (7) This clonal expansion causes ineffective erythropoesis and megakaryosis resulting in failure to form red blood cells and platelets. Risk factors for AML can vary, especially in patients with myeloproliferative neoplasms such as myelofibrosis, polycythemia vera, essential thrombocytosis, and chronic myeloid leukemia that can develop into AML at some point. Environmental exposures such as smoking, radiation, and benzene can also be risk factors for developing AML. Genetic disorders known to be associated with AML include translocation (8; 21) (Q22; Q22.1), these mutations are usually associated with genetic trisomy disorders 13 and 21 that show resistance to standard induction therapy.

Patients with AML will generally show symptoms related to the failure of the bone marrow to produce hematopoietic cells such as anemia, manifestations of bleeding in various organ systems, DIC, infections as a result of abnormal function of leukocytes, weakness, tightness and other compensatory signs of anemia. Symptoms of infection in the form of fever and other symptoms according to the location of infection. Enlargement of organs such as hepatosplenomegaly can be found, but enlargement of lymph nodes is rarely reported. (6) In this case, the patient had a fever since 10 days before being treated, other complaints such as cough, tightness, urinary pain, diarrhea were denied. Physical examination of the abdomen found

spleenomegaly scuffner 2, without hepatomegaly being found. The initial complaint that caused the patient to seek medical help was the enlargement of the gums that was felt since 1 month. Progressive gum enlargement from a small size then enlarges until the patient has difficulty speaking and eating. Bleeding on the gums was also found but only when provoked by the activity of brushing teeth. Patients also complained of bleeding from the anus during defecation. In the patient, an ulcer was also found on the left buttocks with a size of 2 cm, along with inflammatory signs such as redness and pain.

Oral manifestations of AML have been reported by several studies including enlarged gums, discoloration of mucous membranes to bluish or pale, ulcers, erosion, bleeding, ecchymosis, which can be mistaken for manifestations of other diseases. (4, 5,8) mucosal bleeding in the form of PTEKIE and spontaneous hemorrhage was reported in 56%, mucosal ulceration in 53%, and gum enlargement in 36%. (5,8) The NCCN in 2016 provided guidelines for initial laboratory examinations for the enforcement of AML diagnosis, including complete blood tests, differential counts, coagulation factors, blood chemistry such as electrolytes, uric acid, kidney and liver function, HLA gene testing, and bone marrow examination with BMP. The purpose of the BMP examination is to assess the morphology and determine the type of cells that are malignant, and risk assessment. AML is generally identified from the number of blasts > 20% in the bone marrow. Cell morphology is usually related to the etiology of the underlying gene mutation as in t(8:21) large blasts and azurophilic granules are found. Immunophenotyping is a method to determine the lineage of the blast and assess the minimum residual disease after chemotherapy. Some of the surface markers of leukocytes that have been identified are CD33, CD14, CD56, and CD45. Some other tests such as cytogenic analysis, and mutase analysis are necessary to get the most suitable therapeutic regimen for the patient.

In the case of BMP examination and it was found that the dominance of the myeloid series, the myeloid blast component >20%, appeared to be a lot of intra myeloid and dysplasia of neutrophils with neutrophil components >20%. In accordance with the French-American-British (FAB) classification, this case tends to be classified as M4. FAB-M4 classification of monocyte precursors, mature monocytes, and also mature precursors and neutrophils >20% of the number of nucleated cells in the bone marrow or a high percentage of monocyte cells can be found in peripheral blood where in this case a high percentage of monocytes is also found.

In the early stages of diagnosis and treatment, patients may experience complications as a result of a significant increase in the number of leukocytes. This causes leukostasis due to hyperleukocytosis can be accompanied by complications of cytopenia such as infection, anemia, and bleeding manifestations. Leukostasis can occur at a high number of peripheral leukocytes (usually > 50x109/L) or at a lower number. Symptoms that can occur resemble symptoms of ischemia such as decreased consciousness, stroke, chest pain, hypoxia, etc. In this case, the patient experienced a sudden decrease in consciousness after previously complaining of sudden tightness, a brief decrease in bleeding followed by cardiac arrest, so that on the 7th day of treatment the patient was declared dead.

CONCLUSION

In a 31-year-old female patient, gingival enlargement was identified as an early manifestation of acute myeloid leukemia (AML), presenting alongside constitutional symptoms such as fever, profound weakness, and *splenomegaly*. The clinical presentation of AML often

includes signs and symptoms resulting from bone marrow suppression by malignant cells, as well as infiltration of leukemic cells into various organ systems. Oral manifestations of AML can encompass gingival enlargement, mucosal discoloration ranging from bluish to pale, ulcers, erosions, spontaneous bleeding, and *ecchymosis*, all of which may be misinterpreted as symptoms of other oral or systemic conditions. These findings underscore the importance of considering hematologic malignancies like AML when encountering unusual oral lesions, reinforcing the need for thorough oral and systemic evaluation in such cases.

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