

# Diagnosis of acute myeloid leukemia in a dental hospital; report of a case with severe gingival hypertrophy

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## Abstract

Acute myeloid leukemias (AMLs) are aggressive hematopoietic neoplasms that, if untreated, can lead to death within days. Owing to its high morbidity rate, early diagnosis and appropriate medical therapy is essential. Oral lesions may be the presenting feature of acute leukemias and are, therefore, important diagnostic indicators of the disease. Erythematous or cyanotic gingival hyperplasia with or without necrosis is reported to be the most consistent symptom leading to a diagnosis of acute leukemia that directs the patient to seek early dental consultation. This report refers to a patient with AML that was provisionally diagnosed in the dental hospital due to severe gingival enlargements.

**Key words:** Acute myelocytic-monocytic leukemia, acute myeloid leukemia, gingival hyperplasia, gingival overgrowth

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## Introduction

Leukemia is a hematologic disorder that is characterized by disordered differentiation and proliferation of abnormal hemopoietic stem cells.<sup>[1,2]</sup> This results in marrow failure, depressed blood cell count, and death as a result of infection, bleeding, or both.<sup>[3]</sup> There are many etiologic factors of leukemia, including genetic factors, certain carcinogens like benzene, tobacco smoke, ionizing radiation, advancing age, immune deficiency, viruses like Epstein-Barr virus, and oncogenes.<sup>[4]</sup> According to the clinical behavior leukemias are classified into acute or chronic forms and characterized as lymphocytic and myelocytic, referring to their histogenetic origin.<sup>[1]</sup> Acute myeloid leukemia (AML) can present as leukemic infiltrates in many sites including gingival enlargement, mucosal and skin nodules.<sup>[5]</sup> Oral lesions occur both in acute and chronic forms of all types of leukemias, however, oral manifestations are more common in the acute stages of the disease. Such lesions may occur due to direct leukemic infiltration of tissues, or be secondary to immunodeficiency, anemia and thrombocytopenia.<sup>[6]</sup>

Erythematous or cyanotic gingival hyperplasia with or without necrosis is reported to be the most consistent symptom leading to a diagnosis of acute leukemia that directs the patient to seek early dental consultation. Other oral findings include; petechiae, ecchymosis, mucosal ulcers, hemorrhage, herpetic infections and candidiasis.<sup>[2,6]</sup> This report refers to a patient with AML that was provisionally diagnosed in the dental hospital as a result of severe gingival enlargements. This case shows the importance of dentists' awareness about leukemic infiltration as a cause for gingival lesions.

## Case Report

A 30-year-old male patient was referred to the Department of Oral and Maxillofacial Radiology after visiting a dentist with the chief complaint of swollen, painful bleeding gingiva with 10 days of evolution. He treated with parenteral antibiotics for presumed oral infection. However his condition

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**Figure 1:** Generalized gingival hyperplasia covering the crown of the teeth. Ulcerations and bleeding of gingiva can be observed

deteriorated. Patient also gave a history of fatigue, mild weight loss and loss of appetite from last few months. He had no systemic diseases related to gingival enlargements such as sarcoidosis, Wegener's granulomatosis, Crohn's disease or tuberculosis and was not using any medications including phenytoin, anticonvulsants, immunosuppressants or calcium channel blockers. He gave no family history of hematological disease. At the physical examination, the patient was pale, with fever and malaise. He had pain and tenderness in submandibular lymph nodes. Intraoral examination revealed generalized gingival enlargement involving the buccal, palatal and lingual region covering the crowns of the teeth. The gingiva was hemorrhagic, swollen, ulcerative, fragile, painful and bled easily [Figure 1]. The color of the gingiva was reddish to purple. Hard and soft palatal mucosa showed a large area of ecchymosis [Figure 2]. Moreover, the patient had fetor oris. No positive findings were noted on the radiographs. Differential diagnoses of acute leukemia and human immunodeficiency virus (HIV) infection were considered for this patient.

However, clinical symptoms strongly favored the diagnosis of leukemia based on the severity and extent of gingival alterations, history and duration of gingival overgrowth, gingival bleeding and the palatal ecchymosis.

He was urgently referred to Hematology Department at Faculty of Medicine for full blood count (FBC). Further tests were done by hematology clinic and patient was diagnosed as AML M4 (French American British [FAB] classification) according to peripheral blood smear, bone marrow biopsy and flow cytometry. Tests for HIV infection/AIDS were negative. The peripheral blood smear showed white blood cells (WBC) count of 35,000/mm<sup>3</sup>, platelet count of 30,000/mm<sup>3</sup> and red blood cells count of 2.7 million/mm<sup>3</sup>. The differential WBC count showed more than 30% of blast cells, mainly myeloblasts and monoblast, which is consistent with a diagnosis of AML M4 variety, i.e. acute myelocytic-monocytic leukemia. Patient was hospitalized,



**Figure 2:** Hard and soft palatal mucosa showed large area of ecchymosis

and treatment commenced with broad spectrum intravenous antibiotics and then chemotherapy. Presently, patient has completed three courses of chemotherapy, and he is followed-up. Oral hygiene instruction was given to the patient and 0.2% chlorhexidine was prescribed. Periodontal therapy and gingivectomy were postponed since the treatment needs a minimum platelet count of 60,000 in this condition.

## Discussion

Oral and periodontal manifestations of leukemia consist of leukemic infiltration, bleeding, oral ulcerations, and infections. The recognition of gingival enlargement as an initial oral manifestation of leukemic infiltration is extremely important for early diagnosis of acute leukemia.<sup>[1,2]</sup>

As generally known, gingival enlargement can be either hereditary or the result of some pathological reactions (leukemic infiltrates, granulomatous disease, Crohn's disease, sarcoidosis, HIV/AIDS-associated lesions), or a secondary consequence of a chronic treatment with drugs from the following therapeutic classes: Anticonvulsants (phenytoin), antihypertensive – like calcium channel blockers type (nifedipine, verapamil, diltiazem) and immunosuppressives (cyclosporine A).<sup>[7-9]</sup>

Hereditary gingival enlargement has a definite family history and is an isolated abnormality. Gingival enlargement is inherited as an autosomal dominant trait or, rarely, as an autosomal recessive trait. It, usually, begins at the time of eruption of the permanent dentition.<sup>[10,11]</sup>

The inflammatory gingival enlargement is the most common form of gingival overgrowth and is associated with local factors, like plaque and calculus.<sup>[6]</sup> However, in this case; severity and extent of gingival alterations, duration of gingival overgrowth, gingival bleeding and the palatal ecchymosis did not favor a diagnosis of inflammatory gingival enlargement.

Odontogenic tumors, odontogenic cysts and reactive lesions of gingiva can also present themselves as gingival enlargements.<sup>[12-15]</sup> Nevertheless they are, usually, solitary, and generalized lesions have rarely been reported in the literature.<sup>[16]</sup> In the present case, there was a generalized gingival enlargement involving the buccal, palatal and lingual region covering the crowns of all teeth, and no positive findings were noted related to odontogenic tumors and cysts on the radiographs.

Systemic illnesses such as Wegener's granulomatosis, sarcoidosis and Crohn's disease have also been described in association with gingival enlargements.<sup>[17,18]</sup> However, oral lesions have been noted in only a minority of cases and rarely are the initial sign of these diseases.<sup>[19]</sup>

Human immunodeficiency virus/AIDS associated lesions like Kaposi's sarcoma (KS) can be confused by gingival enlargement and palatal ecchymoses in leukemia. KS can involve any oral site, but most commonly the palate followed by gingiva and the tongue.<sup>[6,20]</sup> The lesions typically appear focally as reddish-blue macules that progress to form purple nodules. In severe cases, as was described by Khera *et al.*, the gingival lesions may spread, resulting in diffusely erythematous and edematous gingiva.<sup>[17]</sup>

In the present case, according to patient medical history, generalized gingival enlargement resulting from drugs, granulomatous diseases and heredity were ruled out. Also, severity and extent of gingival alterations did not favor a diagnosis of inflammatory or reactive gingival overgrowth. Panoramic radiographic examination revealed no obvious abnormalities related to odontogenic tumors and cysts. Hence, the probable clinical diagnoses of acute leukemia and HIV infection were considered for this patient. Laboratory tests showed that the HIV infection/AIDS were negative, and patient was diagnosed as AML M4 according to peripheral blood smear, bone marrow biopsy and flow cytometry.

Gingival infiltration is a well-known feature of the AML but particularly those of myelomonoblastic and monoblastic lineages; subtypes M4 and M5 according to the FAB classification.<sup>[5]</sup> FAB classification system divides AML into eight subtypes, M0 through to M7, based on the cell type from which the leukemia developed and its degree of maturity.<sup>[21]</sup> A study of 1076 adult patients with leukemia showed 3.6% of the patients with teeth had leukemic gingival proliferative lesions, with the highest incidence in patients with acute monocytic leukemia (66.7%), followed by acute myelocytic-monocytic leukemia (18.7%) and acute myelocytic leukemia (3.7%).<sup>[22]</sup> Stafford *et al.* evaluated 500 leukemic patients and found 65% had some oral manifestation that caused them to seek care.<sup>[23]</sup>

Although physicians most commonly diagnose leukemia, dentists have been responsible for initiating the diagnosis

in 25-33% of patients with AML.<sup>[2]</sup> However the present case was misdiagnosed by a dentist as oral infection primarily hence his decision to treat with parenteral antibiotics over a 10 day period. As a result, the patient's condition deteriorated.

Early diagnosis allows the introduction of specific chemotherapy but also supportive treatment with blood products. Many patients present with cutaneous bleeding or bruising, but some develop life-threatening gastrointestinal or intracerebral hemorrhage.<sup>[5]</sup> Other generalized symptoms include fever, fatigue, weight loss or loss of appetite, shortness of breath, anemia, petechiae, bone and joint pain, and persistent or frequent infections.<sup>[24]</sup> In the present case the patient had a history of fatigue, mild weight loss and loss of appetite few months before presentation. Also, he had a chief complaint of generalized gingival enlargements and painful bleeding gingiva with 10 days of evolution.

A FBC is a simple and useful test in suspected cases and can help to reach a prompt diagnosis.<sup>[5]</sup> In our case failure to recognize the significance of the systemic symptoms led to a delay in the diagnosis that was potentially life-threatening for the patient. Infections and anemia are the major causes of death in leukemic patients. Untreated, acute leukemia has an aggressive course, with death occurring within 6 months or less.<sup>[6]</sup>

## Conclusion

An accurate and detailed history is very important in order to rule out other differential diagnosis of gingival enlargements. As oral lesions are one of the earlier manifestations of acute leukemia, early diagnosis and treatment can improve the patients' chances of remission. Considering the aggressive progression of the disease, dentists have a critical role in diagnosis. This case emphasizes the need for the oral health care professionals to be familiar with the clinical manifestations of acute leukemia to ensure prompt detection and referral.

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