A Case of Diffuse Gingival Enlargement in Acute Myeloblastic Leukemia (AML M1)

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INTRODUCTION

Leukemia is a heterogenous group of hematological disorders that arises from a hematopoietic stem cell characterised by a disordered differentiation and proliferation of neoplastic cells.¹ Acute leukemias result from malignant transformation of immature hematopoietic cells followed by clonal proliferation and accumulation of the transformed cells. This neoplastic proliferation in marrow may result in pancytopenia leading to symptoms of anemia, granulocytopenia and thrombocytopenia. Also, the leukemic cell proliferation may be observed in organs such as lymph nodes, spleen, gingiva, central nervous system and skin.²

Leukemia is categorised into acute or chronic forms, based on its clinical behavior, and into lymphocytic and myelocytic, based on its histogenetic origin. Acute myelocytic leukemia (AML), which is also known as; acute granulocytic leukemia, acute myeloblastic leukemia or acute non-lymphocytic leukemia, is commonly classified under 8 subgroups according to the French-American-British (FAB) classification system including 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 erythroleukemia), and M7 (acute megakaryoblastic leukemia).³ However in 1997, the World Health Organization proposed 4 groups in the AML category 1) AML with recurrent cytogenetic translocations; 2) AML with myelodysplasia-related features; 3) therapy-related AML and myelodysplastic syndromes; and 4) AML not otherwise specified (NOS).³

Leukemias occur in all human races, but are more common in Caucasians. Leukemia is the most common childhood cancer in India with relative proportion varying between 25 and 40%. Sixty to 85% of all leukemias reported are acute lymphoblastic leukemia (ALL).⁵ Oral lesions associated with leukemia have been well documented.⁶ Signs and local symptoms of leukemia in the oral cavity include paleness of the oral mucosa with gingival bleeding, gingival enlargement, and ulcerative necrotic lesions.⁷ Here, we
report an unusual case of diffuse gingival hypertrophy in a 15 year old Asian female which led to laboratory studies, which in turn led to a rapid and relatively early diagnosis of acute myeloblastic leukemia (AML M1).

**CASE DESCRIPTION**

A 15-year old girl reported on 19th July 2012 to Department of Periodontology and Oral Implantology, Government Dental College and Hospital, Jaipur with the complaint of swollen gums in 10-15 days time and associated pain. Her clinical examination revealed fever and signs of anemia. Her medical history was non-contributory and she was not on medication for any chronic illness.

Oral examination of the patient demonstrated generalized diffuse enlargement of maxillary and mandibular gingiva covering about 2/3rd of the crown structure involving buccal, lingual and palatal aspects. Color of gingiva appeared reddish blue with loss of stippling. Further intraoral examination revealed an ulcer on dorsal and ventral aspect of tongue. Palatal petechiae were also noted. Palpation and probing was avoided due to unusual history and clinical findings. The same day, blood investigations were advised.

**INVESTIGATIONS**

Complete blood count revealed a marked increase of white blood cells, a decrease in red blood cells with lowered hematocrit and haemoglobin levels and a low platelet count indicative of leukocytosis, anemia and thrombocytopenia. An abnormal leukocyte differential displayed 03% segmented neutrophils, 95% blasts, 0% monocytes, 02% lymphocytes and 00% eosinophils. Peripheral blood smear displayed leukocytosis with numerous blasts having irregular nuclear margins, prominent nucleoli and immature chromatin, reduced platelets in number and anisopoikilocytotic, microcytic RBCs suggestive of an acute leukemia. Subsequent bone marrow biopsy demonstrated 90% hypercellularity, predominated by sheets of blast cells. Therefore the diagnosis of acute myeloid leukemia M1 was established and the patient was referred to Department of Pediatrics, SMS Medical College and Hospital, Jaipur.

**TREATMENT**

Oral hygiene instructions were given to the patient and 0.2% chlorhexidine was prescribed. Scaling and root planing was postponed since the treatment needs a minimum platelet count of 60000 in this condition. She was hospitalised with a diagnosis of AML M1 type. After 7 days her hematologic profile was as presented in Table 2. After a period of 12 days while receiving therapy, she succumbed to the disease due to respiratory arrest.

**DISCUSSION**

The differential diagnosis of a patient presenting with gingival enlargement would include chronic gingivitis, drug-induced hyperplasia, idiopathic gingival enlargement or neoplastic processes. Hyperplastic gingivitis secondary to local factors such as periodontal infection or trauma tends to demonstrate erythematous and boggy gingiva localized to a focal area. Drug-induced hyperplasia can be caused by calcium channel blockers such as nifedipine and verapamil hydrochloride; the anticonvulsant such as phenytoin sodium; or the immunosuppressant cyclosporin. Gorlin et al. described several genetic syndromes involving gingival fibromatosis presenting as generalized gingival enlargement, such as Cross syndrome, Ramon syndrome, Rutherford syndrome, and others. However, the enlargement typically occurs before the age of 20 and often correlates with tooth eruption and mental retardation. Gingival swellings may manifest as a localized metastatic deposit or haematological disorder such as lymphoma or a leukemic infiltrate.

Dentists in clinical practice have become increasingly interested in leukemia as the oral complications are common throughout the clinical course of the disease, dental management is complex, and the oral cavity is a potential source of morbidity and mortality. Because oral signs and symptoms are common, the dentist may be the first clinician to diagnose the disease. Head and neck signs such as cervical lymphadenopathy, oral bleeding,
gingival enlargement, infections, and oral ulcers result from leukemic cell infiltration. In the most extensive review of the topic by Driezen et al, gingival hyperplasia was observed in acute myelogenous leukemia (AML) with a frequency of 3% to 5% among 1,076 patients receiving anti-leukemia chemotherapy at a referral centre.

Gingival hyperplasia is most commonly seen with the AML subtypes acute monocytic leukemia (M5) (66.7%), acute myelomonocytic leukemia (M4) (18.5%), and acute myelocytic leukemia (M1, M2) (3.7%). In this case report, rapid gingival hyperplasia was the main reason of the patient to seek dentist consultation. The examining dentist suspected a systemic disease such as one of the hematologic disorders based on the duration of gingival hyperplasia and history of spontaneous gingival bleeding, without prominent dental plaque or calculus accumulation. A hematological investigation was asked and it revealed an elevated leukocyte count. Stafford et al. evaluated 500 leukemic patients and found 65% had some oral manifestation that caused them to seek care, contributed to their reason for seeking care, or was noted at the initial physical examination.

Oral manifestations have been observed in 15% to 80% of his patients with leukemia and are more commonly seen in acute (65%) rather than in chronic leukemia (30%). Lynch and Ship found that petechiae or bleeding (56%), ulceration (53%), and gingival hyperplasia (36%) were the most common initial diagnostic and postdiagnostic manifestations of leukemia in a 10-year retrospective study of 155 patients. Other findings include pallor, infection, pain, lymphadenopathy, and pharyngitis. Extreme pallor of the oral mucosa, resulting from acute anemia, may be the only oral manifestation of acute leukemia in patients maintaining excellent plaque control.

Gordon MR reported a case of acute myelogenous leukemia diagnosed following laboratory studies initiated due to extreme gingival pallor. Gingival infiltration represents a 5% frequency as the initial presenting complication of AML. However, the development of gingival infiltration in any patient is uncertain with respect to gender and age. Leukemia cell infiltration in gingiva is not observed in edentulous patients, which implies that local irritation and trauma associated with the presence of teeth may have a role in the pathogenesis of this abnormality. However, gingival hyperplasia occurs in patients with excellent oral hygiene, indicating that adverse local conditions are not necessary requirements to promote or induce leukemic infiltration of oral tissues. Poor oral hygiene may predispose the patient to develop infections, bleeding, ulceration, and pain. Osgood noted that swelling of gingiva was one of the most constant feature in monocytic leukemias, occurring in 80% cases of his 58 cases. It is more common in monocytic than in other cases of acute leukemias and a significant number of patients consulted a dentist before going to a physician.

Pogrel MA reported a case of acute myeloblastic leukemia in which the mode of presentation was marked hypertrophy in the mandibular incisor region only, the remainder the gingivae and oral cavity being completely normal. A definite diagnosis was not made until the patient was in a final stage similar to that of present case. Vural F reported a case of CD56+ chronic myelomonocytic leukemia (CMML) who developed gingival hypertrophy simultaneously when the leukocyte count elevated. It is hypothesized that, M4–M5 monoblasts which have the capability of early maturation and migration from bone marrow could demonstrate extramedullary tissue invasion.

This CD56+ leukemic cells invasion and proliferation in extramedullary tissues, results in development of myeloblastoma. Since flow cytometric analysis of bone marrow cells was not performed in our case, similar mechanism of extramedullary tissue involvement cannot be extrapolated.

Since oral manifestations in all types of acute leukemias occur early in the course of disease, it must be emphasized that unnecessary dental intervention may aggravate the situation and give rise to exacerbation of acute symptoms. Hence, any dental therapy was avoided in our case and was referred immediately to physician. In the course of medical treatment, the patient succumbed to the disease in 12 days. The rapid and extensive enlargement in both the arches was more interesting in this case.

Figure 1: Clinical photographs of labial (a), palatal (b) and lingual (c) view at first visit. Ulcer seen on dorsal aspect of tongue in c
CONCLUSION

This case emphasizes that dentist should be well acquainted with the oral manifestations of systemic diseases and stresses the role of gingival enlargement as a diagnostic indicator of leukemia. Medical consultation must be essential in dental therapy in such cases. An accurate history is critical for diagnosis and subsequent management in all patients.

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REFERENCES


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