

Case Report

# Leukemia-induced Gingival Overgrowth as an Early Manifestation in Pregnancy: A Case Report

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## Abstract

Leukemia is a neoplastic disease with early oral and periodontal manifestations such as ulceration, infection, bleeding and gingival hyperplasia. This paper describes a 39-year-old pregnant woman with a diagnosis of acute myelomonocytic leukemia (AML), with gingival enlargement in the upper and lower jaws. A gingival biopsy was performed, followed by a complete blood count and peripheral blood smear. From a histopathological view, infiltration of the neoplastic (myelomonocytoblastic) cells was observed and many immature lymphoid cells were revealed by the hematologic tests. The interesting clinical finding about this case was the absence of spontaneous bleeding and profuse bleeding on probing. This case is reported to emphasize the leukemia-induced gingival enlargement in pregnancy and the early diagnosis of AML by dentists, which results in immediate treatment and management of the patient.

**Key words:** Gingival overgrowth, Leukemia, Oral manifestation.

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## Introduction

Many systemic diseases produce oral changes in different stages of their course. Leukemia is a fatal disease of unknown etiology, which is characterized by excessive proliferation of primitive white blood cells in the bone marrow and/or blood, and its presence as leukemic infiltrates has been reported in the lungs, kidneys, bowels, breasts, testes, eyes,

meninges, lymph nodes, liver, skin and the oral cavity.<sup>1</sup> Leukemias are divided into chronic and acute forms clinically, which in turn, are classified according to the type of the white blood cell involved, i.e. lymphoid and myeloid.<sup>2</sup> The association between leukemia and pregnancy is not common.<sup>3</sup> Most leukemias diagnosed during pregnancy are acute.<sup>4</sup> It is not surprising that in some patients the management of acute leukemia will be complicated by a coexis-

tent pregnancy. However, the association of leukemia and pregnancy is uncommon.<sup>5</sup> Its prevalence is low at ~1 in 10,000 pregnancies, and as a result data are limited to small retrospective series and case reports, rendering evidence-based recommendations for management strategies difficult.<sup>6</sup> Oral changes are non-specific in patients with chronic leukemia. Oral manifestations of acute leukemia include gingival swelling, oral ulceration, petechiae, candidiasis, ulcerative necrotic lesions and hemorrhage.<sup>2</sup>

This paper presents a case of acute myelomonocytic leukemia (AML) with manifestations of gingival hyperplasia in the upper and lower jaws. In fact our aim is to provide dentists with early manifestations of leukemia and gingival hyperplasia in pregnancy for immediate treatment and management of patients.

### Case Report

A 39-year-old pregnant woman (gestational age = 12 w + 6 d) with a diagnosis of gingival hyperplasia was referred to the Department of Periodontology, Isfahan University of Medical Sciences, complaining of gingival enlargement that had started and developed during the last 21 days.

### Medical History

Systematically she had a feeling of weakness and fatigue and except for OCPs (oral contraceptives) she had not used any other medications over the past year.

### General Examinations

The patient did not have other lesions on her skin or any other abnormality.

### Extraoral Examinations

She had a submental lymphadenopathy (1 cm in diameter) that compromised both breathing and swallowing and could be palpated from skin (Figure 1).

### Oral Examinations

Gingival hyperplasia was observed on the buccal, lingual and palatal aspects of all the teeth, which re-



Figure 1. Submental lymphadenopathy

sulted in mouth breathing and an open bite occlusion. The gingiva was bulbous and pale. Her gingival consistency was firm, with no spontaneous bleeding or excessive bleeding by palpation or probing, accompanied by fetor oris with a necrotic layer around the gingiva of the anterior teeth and an escharotic lesion in the buccal vestibule of lower anterior teeth. Her oral hygiene was fair (Figure 2).

### Radiographic Examinations

There was no bone loss or abnormality on the panoramic radiograph. Due to the general medical status of the patient, moderate plaque accumulation, lack of calculus and rapid enlargement of gingivae, we avoided any periodontal treatment and a biopsy from anterior gingiva of the upper jaw was taken on the same day. Because of the clinical picture and since leukemia may appear during pregnancy, the patient was referred to an oncology center to be under the supervision of a hematologist. She was advised to undergo a complete blood count test, peripheral blood smear and bone marrow biopsy. Within a span of two weeks we were informed that unfortunately she had died. Therefore, it took only 5 weeks from the appearance of the first signs of the disease for her to die.



Figure 2. Generalized diffuse gingival hyperplasia

### Histopathology

In the present histopathological study, neoplastic proliferation of myelomonocytoblastic cells with pleomorphism, atypism, severe hyperchromatism of nuclei, vesicular nuclei, multiple mitotic figures, lobulated and bean-shaped nuclei and occasionally eosinophilic cytoplasm associated with two or three nucleated giant cells were seen diffusely in the lamina propria up to the striated squamous epithelium. With a CD33 marker (marker of early myeloid cells and monocytes), staining intensity was evaluated as 2<sup>+</sup>. In the blood smear study, multiple large-sized cells with convoluted nuclei, fine chromatin and occasionally containing nucleoli, were seen, in addition to a decrease in platelet counts. According to these findings, a diagnosis of acute myelomonocytic leukemia (AML) was suggested. For a definitive diagnosis, further studies with bone marrow biopsy, bone marrow aspiration and flow cytometry were suggested but unfortunately the patient died from the disease (Figures 3-5).

### Hematologic Values

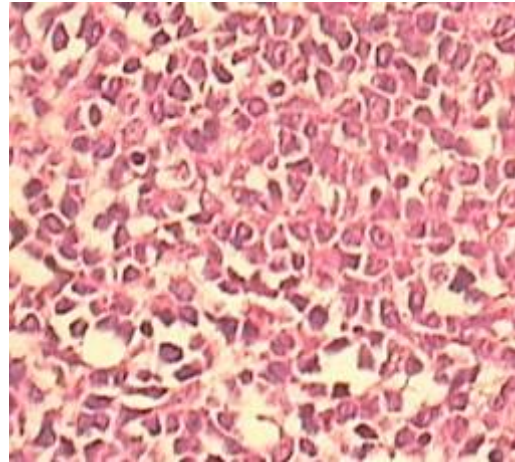
The hematologic reports revealed that the patient had a white blood cell count of 155,900/ $\mu$ L, red blood cells count of 2.40 million/ $\mu$ L, platelet count of 28,000/ $\mu$ L, hemoglobin (Hb) value of 8.6 g/dL, MCH value of 35.8/pg and MCHC value of 36.4 g/dL. In the peripheral blood smear (PBS), severe leukocytosis with many immature lymphoid cells, severe thrombocytopenia, anisocytosis (+), anisochromia (few) and poikilocytosis (mild) were seen. The results of hematologic tests confirmed the diagnosis of acute myelomonocytic leukemia (Figure 6).

### Discussion

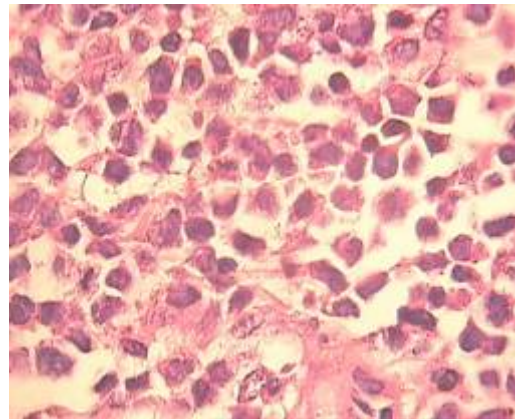
There are many systemic conditions with unvarying manifestations in the gums and deep periodontium. Leukemia has varying rates of development and in most cases a reserved prognosis. Acute leukemias are a group of neoplastic diseases with proliferation of immature white blood cells, especially in the bone marrow, spleen and lymph nodes. Acute myelomonocytic leukemia (AML) is an aggressive hematopoietic neoplasm, characterized by clonal proliferation of immature myeloid cells. Due to its high rate of morbidity, early diagnosis and treatment is essential because it can lead to death within a few days. Some of the typical manifestations of AML are paleness of the oral mucosa with gingival bleeding, which can in turn develop to painless gingival hyperplasia, marrow failure, cytopenia, fever, fatigue, mucosal pallor, petechiae and oral infection.<sup>7</sup> The

diagnosis is confirmed by tissue biopsy or fine needle aspiration cytology.<sup>8</sup>

These changes are consequences of neoplastic proliferation of white blood cells, which affects the normal production of erythrocytes, leukocytes and



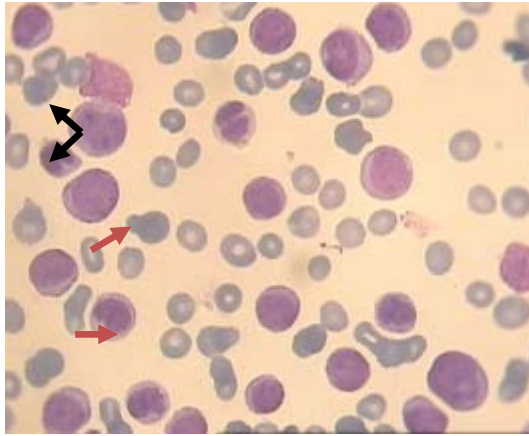
**Figure 3. Neoplastic proliferation of myelomonocytic cells with pleomorphism (magnification x 100 ) H&E**



**Figure 4. Neoplastic proliferation of myelomonocytic cells with pleomorphism (magnification x400) H&E**



**Figure 5. Immunohistochemistry (IHC) with marker of CD33 shows large early myeloid cells (magnification x400)**



**Figure 6. Peripheral Blood Smear (PBS) shows severe leukocytosis with many immature lymphocoid cells. Black arrows represent early myeloid cells and red arrows show lymphocytes (magnification  $\times 1000$ ).**

platelets. Since oral manifestations of acute leukemia occur early in the course of the disease, about 65% of acute leukemia patients consult a dentist. Thus, since acute exacerbation has been reported after such surgical interventional procedures, dental personnel should be alert to these findings and avoid such procedures.<sup>9</sup> Differential diagnoses that are considered in relation to gingival enlargement include conditional enlargement in pregnancy, drug-induced, vitamin C deficiency-induced and inflammatory and hereditary gingival enlargement. Clinical examinations of the gingiva, including color and consistency, rule out the source of vitamin C deficiency and pregnancy because in these situations lesions are clinically deep red or bluish red, soft and friable with a smooth shiny surface that bleeds easily.<sup>10</sup>

Considering the medical history of the patient, drug-induced gingival hyperplasia could not have been the cause of enlargement. The rapid growth of the gingivae rules out the chronic inflammatory enlargement. In hereditary gingival hyperplasia, there is a family history of gingival enlargement that usually begins with eruption of both primary and permanent teeth.<sup>11</sup> In the presented case, the resemblance of the lesions to fibrotic enlargement might have led to misdiagnosis. The change in gingival morphology and its cyanotic appearance may be a result of reactive hyperplasia, dense leukemic infiltration of connective tissue and compression of local vasculatures, causing ischemia.<sup>12</sup> The susceptibility of gingival tissues to leukemic cell infiltration is attributed to their microanatomy and expression of endothelial adhesion molecules, increasing infiltration of leukocytes.<sup>13</sup>

The extent of gingival overgrowth ranges from mi-

nimal to complete tooth coverage, creating functional and esthetic concerns.<sup>8</sup> Leukemic gingival infiltration appears to be limited to dentate subjects, implying a potential role for tooth-associated local factors. In a recent research performed by Chelghoum et al in 2005 on acute leukemia in pregnant women, it was confirmed that 84% of patients had AML and 16% had ALL, with 76% of patients diagnosed during the second or third trimesters.<sup>4</sup> Gingival enlargement represents a 5% frequency as the initial presenting complication of AML.<sup>12</sup>

### Conclusion

In our case the chief complaint of the patient was gingival hyperplasia and respiratory problems. In general, early diagnosis of AML by dentists results in prompt treatment and management of the patient.

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