

Gingival Hypertrophy in Acute Megakaryoblastic Leukemia

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Gingival hypertrophy occurs in some cases of acute leukemia. Most commonly, this association is with acute monocytic and myelomonocytic leukemia¹. We report a case of gingival hypertrophy and hypothesize some reasons to explain such an occurrence in acute megakaryocytic disease.

Case Report

A 32 year old previously healthy woman presented to the University Hospital of Jacksonville (Florida) with a three week history of weakness, low grade fever, shortness of breath and easy bruising. There was no history of medication or illicit drug usage, allergies, or any important facts in her family history. The menstrual history was normal except for recent metrorrhagia. She had given birth to two children aged 5 and 7 who were in good health. Physical examination revealed a well developed, well nourished, moderately obese black woman with normal vital signs. The gingiva showed marked hypertrophy and inflammation (Figure 1).



Figure. Showing the patient with gingival hypertrophy.

Multiple ecchymoses were present on the extremities. The lungs were clear and the cardiac examination was normal. There was no palpable abdominal organomegaly and the patient was intact neurologically. Laboratory findings revealed WBC $2.7 \times 10^3/U$, RBC $3.1 \times 10^6/\mu l$, Hgb 9.0 gm/dl, Hct 28%, reticulocyte count 6.1%, platelet count $14 \times 10^3/U$. Differential WBC count showed neutrophils 8%, bands 2%, lymphocytes 74%, monocytes 11% and atypical lymphocytes 5%. The peripheral blood smear demonstrated abundant nucleated red cells (NRBC) (35 NRBC/100 WBC), anisocytosis and an occasional white cell with an immature nuclear pattern. Other laboratory tests including direct and indirect Coombs test were negative. Cytomegalovirus titer was 1:16. Prothrombin and partial thromboplastin time was normal; total serum protein 7.4 gms/dl; albumin 4.0 gni/dl; normal liver function tests; serum iron 54; transferrin 188; serum ferritin 238. Serum IgM 572; IgG 1560. HIV serology test by ELISA was negative. Urine and blood cultures were negative. A bone marrow aspirate was performed with a "dry" aspirate and the biopsy revealed myelofibrosis with areas of

undifferentiated atypical megakaryocytes consistent with acute megakaryoblastic leukemia. Immunoperoxidase stain for Factor VIII related antigen demonstrated positivity both in the abnormal cells and the large undifferentiated cells consistent with a megakaryocytic lineage. Many of the smaller cells in clusters also stained positive and these were also morphologically recognizable as megakaryocytes. There were however no recognizable myeloid or erythroid precursors in the bone marrow. Chromosome analysis done on the peripheral blood showed a normal female karyotype (46 XX) based on an analysis of 20 metaphase cells examined from 24 hours of unstained peripheral cell culture. A chromosome analysis performed on bone marrow cultures failed. Radiographs of the sternum, pelvis, skull and chest were normal. Computerized tomography of the abdomen was normal with no evidence of hepatosplenomegaly. The patient was treated with supportive therapy including platelet and red blood cell transfusions. Because of the known poor prognosis in megakaryoblastic leukemia, the patient underwent an HLA identical sibling related bone marrow transplant. The patient unfortunately succumbed during the transplant confinement to infectious complications.

Discussion

A number of clinical conditions can be associated with gingival hypertrophy. These include pregnancy^{2,3}, drugs such as diltiazem, cyclosporine and nifedipine^{4,5}, other rare conditions⁶ and non-malignant hematologic disease may also cause gingival hypertrophy^{7,8}. Oral manifestations of acute leukemia are well recognized clinically. These manifestations include bleeding from the mouth, but in some cases marked hypertrophy of the gingiva also occurs. Hypertrophy of the gums is thus an interesting physical finding in acute leukemia but its clinical significance is dubious. This is usually ascribed to infiltration of the area with neoplastic cells and parallels the hematologic course of the acute leukemia⁹⁻¹¹. In 1958 Duffy described the oral manifestation in 38 cases of leukemia and of these, 17 patients had gingival hypertrophy. No hematologic subtype of the leukemias were however described. Gingival hypertrophy has been described in the acute monocytic, myelomonocytic, myelocytic¹¹, but to our knowledge not in acute megakaryocytic leukemia and or the related entity of acute myelofibrosis. A number of publications have expanded this clinical spectrum which remains closely related and inter-twined with acute megakaryoblastic leukemia. Acute megakaryoblastic leukemia belongs to the M-7 category of the FAB classification of the acute leukemias. Acute megakaryoblastic leukemia is rare and accounts for only 1% of all the cases of AML¹². The M-7 subset of acute myeloid leukemia has admittedly been a difficult diagnosis in the past and has been the subject of some hematologic difficulty because of varying diagnostic criteria which are employed. In order to diagnose this entity, one needs the appropriate bone marrow findings and other corroborative immunochemical evidence e.g., a demonstration of factor VIII related antigen in the blasts and or other tests if available. A significant finding which is observed in the M7 FAB subset of acute myeloid leukemia cases is bone marrow fibrosis^{12,13}. These patients are often pancytopenic and both the bone marrow and the peripheral blood contains few cells. It is believed on the basis of clinical and experimental evidence that this bone marrow fibrosis is related to the secretion of multiple growth factors by the megakaryocytic cells line. In a recent paper Terui showed that megakaryoblasts from a patient with leukemia secreted transforming growth factor beta (TGFβ)¹⁴. TGFβ in this patient stimulated the production of collagen from the bone marrow fibroblasts. TGFβ is a substance of diverse activity whose functions include cellular suppression and fibrous tissue deposition. Platelets also release other substances e.g., platelet derived growth factors which could be related etiologically to bone marrow fibrosis as well. Altered collagen metabolism has been reported in nifedipine induced gingival overgrowth as well¹⁵. If as we feel, that our patient's gingival enlargement was not due to cellular infiltration, then its explanation may be in the ability of the leukemic cell line to cause gingival

hypertrophy. It is unlikely that cellular infiltration was the cause of this finding because the patient had bone marrow fibrosis, hypocellularity and importantly severe peripheral pancytopenia. It is possible that growth factors secreted by the malignant megakaryocytic cell line could affect the gingiva either systemically or due to the local proximity of the gingiva to the leukemia in the facial and jaw bones.

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