Chronic Myeloid Leukemia presenting with extramedullary disease as gingival hyperplasia

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Introduction

Granulocytic sarcoma (GS) is a rare and frequently under/mis-diagnosed extramedullary tumor composed of extramedullary granulocytic cells. It may be seen in different malignant blood diseases involving the granulocytic series, acute non lymphoblastic leukemia (ANLL) being the most frequent, followed by myelodysplastic syndromes (MDS) and chronic myeloproliferative syndromes, including chronic myeloid leukemia (CML). Extra-Medullary Involvement (EMI) in CML usually occurs during the accelerated phase or blast crisis and has been reported in the soft tissues, lymph nodes and body cavities as GS. However, diffuse gingival infiltration in chronic phase CML at the time of diagnosis has not been reported previously. We report a case of CML who presented with maxillary gingival hyperplasia and diffuse infiltration of the gingival tissue with myeloid cells as evidence by her tissue biopsy. The patient showed an excellent response to imatinib mesylate with normalization of blood counts and complete resolution of gingival disease.

Case

A 36-year-old African-American woman with a history of uncontrolled diabetes mellitus was admitted to our institution for further evaluation of a large generalized swelling of the upper gingiva which had developed over a period of four months. Physical examination remarkable for generalized gingival hypertrophy and moderate splenomegaly. Bacterial infection was suspected and the patient was started on empirical antibiotics.

Initial complete blood count (CBC) showed a hemoglobin level of 12.5, platelet count 193,000 and a white blood cell count of 62,000 (Neutrophils 23900, lymphocytes 5700, monocytes 6800, basophils 1100 and eosinophils 600). Peripheral smear examination revealed immature granulocytes in all stages of myeloid differentiation with occasional blasts. Fluoresence in situ hybridization (FISH) on peripheral blood using the dual color dual fusion LSI BCR/ABL probe revealed fusion in 92% of interphase cells. A BCR-ABL1 fusion transcript coding for 210kDa protein was detected using qualitative PCR. Flow cytometry on peripheral blood revealed 20% myeloblasts with 25% monocytes expressing CD13, CD33 & CD34, raising suspicion of CML transforming into acute myelomonocytic leukemia (AMML). A bone marrow biopsy was then performed which showed hypercellular marrow (90%) with trilinear hematopoiesis and an increase in myelocytogenesis. Analysis of 20 metaphase cells revealed a Philadelphia positive female karyotype in all cells, sealing the diagnosis of CML.

The intra-oral soft tissue swelling failed to respond with treatment using antibiotics and non-steroidal anti-inflammatory drugs. A gingival tissue biopsy of the involved lesion was then performed which revealed sheet-like proliferation of myeloperoxidase (MPO) and CD 34 positive myeloblasts, consistent with extramedullary involvement by CML.

Therapy was instituted with 400mg/day of Imatinib mesylate which resulted in a wonderful response with disappearance of splenomegaly & normalization of leukocyte count, 9700, within two weeks of treatment (ChR). Also, the gingival soft-tissue swelling decreased in size with treatment and completely disappeared by 1 month of follow-up. She has completed four months of treatment and has had a complete cytogenetic response (CyR) with Imatinib as evidenced by complete disappearance of BCR-ABL fusion transcripts on peripheral blood FISH.

Discussion

Gingival infiltration of leukemic cells is most commonly seen in acute monocytic leukemia (M5) and acute myelomonocytic leukemia (M4). Dreizen et al studied the clinicopathologic and histopathologic features of leukemic gingival and cutaneous "infiltrates" in 1,076 adults hospitalized for cancer chemotherapy but found no cases of gingival involvement with CML making this case particularly interesting. To our knowledge, this is the first report of gingival mucosal involvement as the presenting feature of CML.

Extra-medullary involvement with myeloid cells in CML is a rare histopathology that may precede or occur concurrently with acute or chronic myeloid leukemia. The commonest sites involved with extra-medullary disease are lymph nodes (10-61% of cases), followed by bone (around 33-37 %) and soft tissues (30 %). EMD in CML has been reported in body cavities, including pleura and peritoneum. Hepatosplenomegaly in CML is not considered as EMD. In a retrospective study by Paydas et al before the imatinib era, 11 out of 32 reported cases of GS had CML (six in chronic, three in accelerated and two in blastic phase).

In most reported patients, EMD was indicative of impending progression of CML and a median survival of 3-5 months. This was well before the dawn of imatinib era. Unfortunately, most published studies involving the use of Imatinib in CML donot mention about the presence of EMD and its treatment response. The IRIS study comparing Imatinib with interferon and low-dose cytarabine for newly-diagnosed chronic-phase CML excluded patients with EMD. In the study by Sawyers et al, 10% patients had lymph node involvement and 3% had chloromas. The details of these lesions was not reported and the response of EMD to imatinib was not described separately. However, considering the excellent response to imatinib in our case and previously reported case by aleem et al, it is possible that the clinical outcome of this patient subset will improve substantially with imatinib.