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## RESEARCH ARTICLE

# IMATINIB INDUCED SWEET SYNDROME IN THE PATIENT OF CHRONIC MYELOID LEUKEMIA

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**ABSTRACT**

Imatinib mesylate is the first line tyrosine kinase inhibitor and the main chemotherapeutic agents currently used to treat patients with chronic myeloid leukemia (CML). Although various cutaneous reactions to this drug are well known, but only few case reports are there documenting sweet syndrome (Ayirookuzhi *et al.,* 2005).



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## INTRODUCTION

Imatinibmesylate, a derivative of 2-phenyl- aminopyridine, is a molecular inhibitor of tyrosine kinase and is used in the treatment of CML because of its specific inhibition of BCR-ABL (Deininger *et al.,* 1997). The most common adverse effects include nausea, edema, rash, myalgias, and diarrhea. Skin rash is one of the most common adverse effects of imatinib, and estimates of incidence range from 7% to 88.9% (Basso *et al.,* 2009). Sweet's syndrome (acute febrile neutrophilic dermatosis) is characterized by an acute onset of erythematous plaques, fever, and leukocytosis. This syndrome has been reported to be associated with leukemia including chronic myelogenous leukemia (CML). Sweet's syndrome seen in patients with leukemia is usually associated with active and/or refractory disease. Imatinib induced Sweet syndrome in patient of chronic myeloid leukemia in chronic remission accounts only for few cases in literature.

**Case Report:** A60 year oldman presented with lump left upper abdomen and easy fatigablity in October 2014. Clinical examination and laboratory testing revealed splenomegaly, an elevated white blood cell (WBC) count of 1,30000/cumm, and a platelet count of 1,50000/cumm. A peripheral blood smear showed predominant neutrophils, promyelocyte, myelocytes, metamyelocytes, and basophils with less than 10% myeloblasts. Bone marrow showed hypercellular marrow with hyperplasia of granulocytic and megakaryocytic lineages. All the above mentioned features are consistent with the diagnosis of chronic myeloid leukemia (CML).

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A diagnosis of CML was further confirmed when the patient tested positive for the presence of the BCR-ABL fusion gene (transcript). Patient was started on Imatinibmesylate therapy with dose of 400mg OD. He had a good hematologic and minor cytogenetic response with 40% Ph chromosome positive cells at 6 month of treatment with Imatinib. Findings of a repeated bone marrow biopsy showed no new abnormalities but were consistent with CML in the chronic phase with persistence of the BCR-ABL defect. After 7 months of start of treatment, he developed an abrupt onset tender and erythematous skin plaques and nodules onhis upper extremities, face and upper back along with moderate grade fever. Patient was in remission at this time. Imatinib therapy was withheld and patient was given topical steroids. The skin lesions resolved with hyperpigmentation. This was the first time he had developed such skin lesions and was suspected due to any exanthematous illnessand it was not immediately evident that they were secondary to Imatinib therapy. The skin lesions of this patient manifested as an abrupt onset of tender and painful erythematous plaques and small nodules. The lesions were multiple, bilateral, and asymmetrical, involving the face, neck, and upper back (Figure 1, 2, 3). The lesions healed with residual pigmentation. A skin biopsy specimen showed edema and perivascular acute neutrophilicdermatosis extending into deep dermis with epidermal sparing with mild hyperkeratosis, focal atrophy of dermis and focal spongiosis consistent with Sweet syndrome (Figure 4, 5). Imatinib was restarted to optimize therapy, and within a week, the patient was admitted with complaints of skin lesions identical to those of the prior episode.. He had a WBC count of 11500/cumm, a platelet count of 156000/cumm, and a single temperature spike of 39°C. Imatinib treatment was discontinued, and therapy with prednisone led to resolution of the skin lesions although with residual pigmentation.

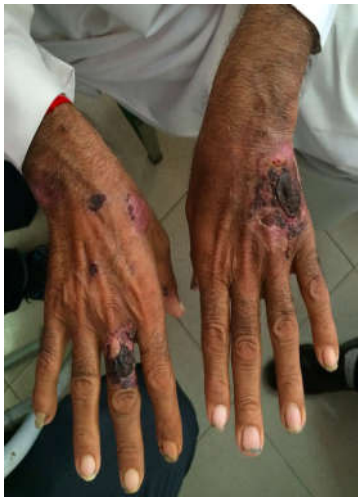
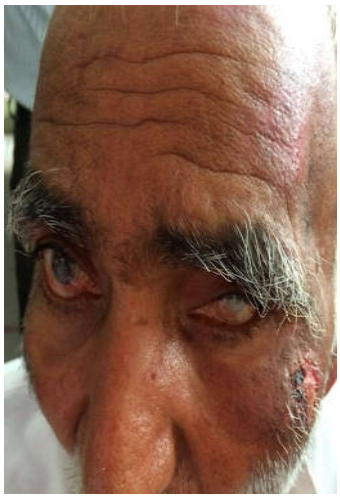
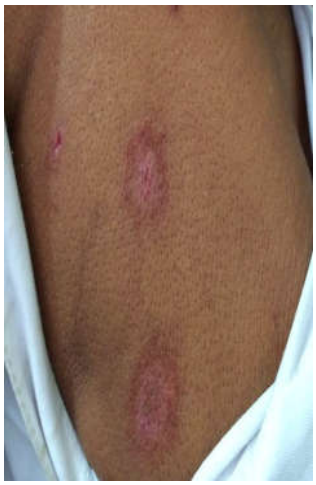

**Fig. 1,2,3. Erythematous plaque over hands, face, and upper back due to sweet syndrome**

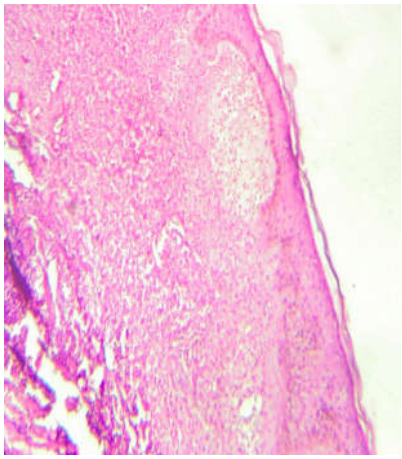
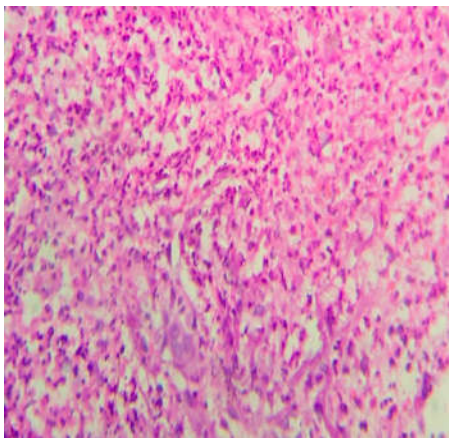

**Fig. 4,5. Showing 200X and 400X histopathological slide showing neutrophillic infilterates in epidermis and deep dermis along with lymphocytes and histiocytes. Hyperkeratosis and spongiosis also present ie suggestive of sweet syndrome**

## DISCUSSION

Various skin reactions have been reported with the use ofimatinib. These can be nonspecific, such as macular-papular rash, superficial edema, or pruritus, or less frequently, rash with clinically distinctive characteristics (lichenoid, Stevens-Johnson syndrom [SJS], psoriasiform, acute generalized exanthematouspustulosis, etc) (Pretel-Irazabal *et al.,* 2014). Sweet syndrome has been rarely associated with chronic myeloid leukemia (Cohen and Kurzrock, 1989). First-line agents in the treatment of SS include oral prednisolone, potassium iodide, cholchicine, and IV methylprednisolone. Usually, these lesions show dramatic response to systemic steroids. However, rarely there may be a need to add second-line drugs like dapsone, indomethacin, cyclosporine, clofazimine and cyclophosphamide in resistant or steroid-dependant cases (Akhil Kapoor *et al.,* 2014). Sanjay J. Ayirookuzhi *et al* also reported a case of neutrophilicdermatosis after imatinib therapy in the patient of CML-chronic phase in molecular remission (Ayirookuzhi *et al.,* 2005). In present case the patient of CML-chronic phase at the time of molecular remission developed sweet syndrome after Imatinib therapy. Furthermore, the distribution of the lesions on both occasions was consistent with Sweet syndrome. Therapy with prednisone at 40 mg/d led to complete resolution, which is suggests the diagnosis of Sweet syndrome. Blood cultures and bacterial, fungal, and mycobacterial cultures of the skin as well as special stains on the skin biopsy specimen failed to reveal any microbiological cause for the lesions.

**Conclusion:** The temporal association of both outbreaks with the administration of imatinib suggests causality. It is particularly important because the patient reported no history of skin reactions or lesions during the natural course of her CML other than after therapy with imatinib. Great awareness regarding the skin related side effects due to imatinib therapy can lead to proper characterization of skin lesion and time related proper treatment.

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