Imatinib Mesylate Induced Skin Hypopigmentation

Sir,

Imatinib mesylate is a tyrosine kinase inhibitor that targets BCR-ABL protein in chronic myelogenous leukemia (CML).1 We present three cases of CML, treated with Imatinib who developed clinical findings of hypopigmentation. All the three patients noticed pigmentation changes after the initiation of therapy with Imatinib mesylate, which was persistent during therapy. The presence of hypopigmentation did not appear to predict or alter either leukemia cell response or clinical outcome.1 All the patients achieved a hematologic response but only two patients achieved a complete cytogenetic response. Imatinib mesylate induced hypopigmentation appears to be reversible and potentially dose related and increases with dose escalation. Patients experienced fluctuation in the intensity of hypopigmentation on interruption or reinitiation of the drug and conversely an increase on dose escalation. The exact mechanism of hypopigmentation is unclear at present. The signal transduction pathway is believed to involve the SCF ligand binding of KIT which in turn attributes to the melanocyte homeostasis and differentiation. Imatinib acts on ligand SCF which regulates melanocyte development and survival resulting in hypopigmentation.1 This is further supported by the observation that human mutations in the encoded tyrosine kinase region of KIT have shown to cause piebaldism, an autosomal dominant disorder, characterized by white hair and hypopigmented skin patches on the forehead, torso and extremities.2,3 This skin toxicity although cosmetically a problem, does not pose a substantial medical hazard. Skin biopsy was considered but due to the above rational, we were unable to ethically justify subjecting these patients to the procedure. Future translational prospective studies with skin biopsies to further evaluate and confirm the mechanism of action of this skin toxicity is recommended.

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Disseminated Cryptococcosis in a case of Idiopathic CD 4 + Lymphocytopenia

Sir,

Idiopathic CD 4 + lymphocytopenia is a very rare disease. It was first recognized in 1992 and is characterized by CD4+ T cell count < 300/ µL or < 20% of total T cells in at least two successive counts, without HIV 1, HIV 2, HTLV 1 and HTLV 2 and the absence of any defined immunodeficiency or therapy associated with decreased levels of CD 4 + T cells.1 I am reporting a case of idiopathic CD 4 + lymphocytopenia with disseminated cryptococcosis.

A 28 years unmarried male, who had exposure to pigeon and eucalyptus trees, presented with fever, myalgia and jaundice of subacute onset. Fever was remittent rising up to 102 F with chills. He had low back pain and pain of thigh muscles. He had also mild cough without expectoration. He had no history of sexual exposure and blood transfusion. He had not been treated with corticosteroids or other immunosuppressive agents for any reasons. On examination he had moderate jaundice, pallor, and oedema, enlarged cervical and axillary lymph nodes. BP was normal (120/78 mm Hg). Liver was palpable with free fluid in abdomen. He had no neurological involvement, no neck rigidity with intact sensorium. Investigation showed: malaria parasite –ve, vivax and falciparum antigen –ve, blood culture –ve, HBsAg, anti–HCV and ANF –ve. LFT showed total bilirubin 15 mg% with direct 8 mg% and indirect 7 mg%, increased SGOT, SGPT (> 3 times), decreased albumin (<2 gm%) and prothrombin time 21 seconds (control 13 seconds). His immunoglobulin levels were normal. CSF study was normal. HIV 1, HIV 2, HTLV 1 and HTLV 2 serology were –ve. Sputum AFB was negative for three consecutive samples. USG showed hepatosplenomegaly with abdominal lymphadenopathy and ascites. Scattered consolidation was seen in chest X-ray and CT thorax. Biopsy from lymph node and muscle showed massive infiltration of Cryptococcus. CD 4+ T cells count was 174/cumm with closely similar values on repetition. Patient was treated with lyposomal amphotericin B and fluconazole. Septran DS (cotrimoxazole) was given prophylactically. Patient responded initially but after stoppage of amphotericin B, it relapsed. Amphotericin B was restarted, but patient died from liver failure.

Idiopathic CD 4 + lymphocytopenia is extremely rare. Although recently identified it is probably not new. There is no evidence of a new transmissible agent that causes lymphocytopenia.2 There is no endemic zone and no evidence of inter-human
transmission. Primary failure of regeneration of stem cell precursors may be a possible cause underlying it. The clinical presentation is different from HIV infection. Although patients are susceptible to opportunistic infections, CD4 counts have relative stability over time and may manifest reductions in other lymphocyte subgroups and no hypergammaglobulinaemia occurs. Progressive multifocal leukoencephalopathy may occur rarely. Idiopathic CD4+ T lymphocytopenia is probably a primary immunodeficiency syndrome. Opportunistic infections occur according to CD4 count and cryptococcal meningitis is common. Prophylaxis is given according to CD4 count. Some cases have partial or complete spontaneous reversal in the CD4+ T cell lymphocytopenia.

This case is reported because of rarity and for its association with disseminated cryptococcosis involving muscles, liver, and lymph nodes without involving meninges and brain.

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