

**Shiraz E-Medical Journal**  
**Vol. 12, No. 3, July 2011**

<http://semj.sums.ac.ir/vol12/jul2011/89049.htm>

**Imatinib Induced Facial Skin Hyperpigmentation in a Case of  
Chronic Myelogenous Leukemia.**

Valizadeh N.

Assistant Professor, Section of Hematology and Medical Oncology, Department of Medicine, Urmia University of Medical Sciences, Urmia, Iran.

Correspondence: Dr. N. Valizadeh, Department of Medicine, Urmia University of Medical Sciences, Urmia, Iran. Telephone: +98(441) 337-0234, Fax: +98(441) 346-9935, Email: nседaha0@gmail.com

Received for Publication: December 24, 2010, Accepted for Publication: May 3, 2011.

**Background:**

Imatinib is a tyrosine kinase inhibitor (TKI) which targets BCR-ABL protein in patients with chronic myelogenous leukemia (CML) and c-kit in patients with gastrointestinal stromal tumors (GISTs). Skin hypopigmentation is reported during Imatinib therapy. We present a case of CML who developed skin hyperpigmentation in the face during treatment with Imatinib which found chloasma-like appearance.

**Keywords: Imatinib, Skin, Hyperpigmentation, Chloasma.**

**Introduction:**

Imatinib mesylate (Gleevec) is a tyrosine kinase inhibitor which targets BCR-ABL protein in patients with chronic myelogenous leukemia (CML) and c-kit and platelet-derived growth factor receptor (PDGFR) in patients with gastrointestinal stromal tumors.<sup>(1)</sup> Common dermatologic side effects of Imatinib are: pruritus, skin

edema, skin rashes. Rare dermatologic side effects are erythema multiform, exanthematous pustulosis, epidermal necrolysis, Stevens-Johnson syndrome and skin pigmentary changes.<sup>(2)</sup> We want to present a 28 y/o male, a case of CML who developed skin hyperpigmentation in his face during Imatinib therapy.

**Case Report:**

A 28 years-old male presented with abdominal pain, dizziness and falling down. Past medical history was unremarkable. Family history was negative. He had history of opium addiction in inhaler form. Physical examination revealed: temperature=38 °C, pulse rate=120/min, blood pressure=80/55mmHg, orthostatic changes, filliform pulses, cold sweating, pallor, tachycardia, diffuse abdominal tenderness and guarding and huge splenomegaly.

**Laboratory findings on admission are included:**

WBC count=280,000/ $\mu$ l (high) (Neutrophil =80%, Lymphocyte= 5%, Band=5, Eosinophil=5%, Basophil=5%), hemoglobin =10 g/dl (low), platelet counts=350,000/ $\mu$ l. PT =17 second (high), PTT=36 second, AST=88 U/L (high), ALT=62 U/L (high). Cr, BUN, Blood sugar, Calcium, Phosphore, Na , K, ESR, Alkaline phosphatase, total and direct bilirubin, albumin and total protein were normal. HBS Ag and HCV Ab were negative. ACTH level is not available in our center so, we did not check it.

Urine analysis showed many amorphurate crystals, WBC=20-25, RBC=25-30 and 2 plus blood in it. Result of urine culture was negative.

Chest X ray was reported normally and ECG showed only sinus tachycardia.

In hospital course, 12 hour after admission, his systolic blood pressure was dropped to 70 mmHg, urinary output markedly decreased and hemoglobin level was dropped to 7.5 gr/dl. Urgent surgical consultation was performed and clinical diagnosis of splenic rupture was

made and blood transfusion was started. He underwent laparotomy and an urgent splenectomy. After splenectomy, his vital signs were stabilized and he was transferred to Hematology ward again. Bone marrow aspiration and biopsy was performed several days after operation and revealed hypercellular marrow. Cytogenetic study was positive for Philadelphia chromosome (translocation of 9:22 Chromosomes). We started Imatinib mesylate 400 mg daily and followed him up after discharge in clinic. He achieved hematologic response after 3 weeks and cytogenetic response after 6 months but, during Imatinib therapy, he developed skin hyperpigmentation of the face which slowly increased and looked like chloasma (Picture1).



Picture 1, Facial appearance of the patient.

**Result:**

This young man with CML, developed skin hyperpigmentation of the face 6 month after starting imatinib therapy which slowly increased and found chloasma-like appearance after one year.

**Conclusion:**

Although skin hypopigmentation is a well-known side effect of Imatinib, but skin hyperpigmentation is another side effect of Imatinib.

#### Discussion:

The common dermatologic side effects of Imatinib are included: pruritus, skin edema, skin rashes<sup>(2)</sup> and hypopigmentation.<sup>(3)</sup> Although skin hypopigmentation is reported in patients on Imatinib<sup>(4)</sup>, but imatinib-induced skin hyperpigmentation is rarely reported.<sup>(1,4)</sup> There are case reports regarding imatinib-induced skin repigmentation of vitiligo lesion<sup>(5)</sup>, imatinib induced nail pigmentation<sup>(6)</sup> and imatinib induced dental pigmentation.<sup>(7)</sup>

A possible explanation for skin hypopigmentation is C-kit expression in melanocytes.<sup>(4)</sup> It plays a role in melanogenesis and pigmentation<sup>(8)</sup> that is a target for imatinib, but the molecular mechanism for hyperpigmentation is not known.<sup>(6)</sup> Chloasma-like skin hyperpigmentation is another dermatologic side-effect of Imatinib.

Author not declaring conflicts of interest.

#### Aknowledement:

We want to thank Dr Ali Eishi Oskuie, Associate professor at section of Hematology and Medical Oncology in Urmia

University of Medical Sciences, who helped us in management of this patient.

#### References:

- Alexandrescu D T, Dasanu C A, Farzanehmehr H, Kauffman C L. Persistent cutaneous hyperpigmentation after tyrosine kinase inhibition with imatinib for GIST. *Dermatology Online Journal*.2008; 14 (7): 7
- Up to date 17.3, 2009. Drug information: Imatinib.
- O'Brien SG, Guilhot F, Larson RA, Gathmann I, Baccarani M, Cervantes F, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic phase chronic myeloid leukemia. *N Engl J Med* 2003; 348: 994-1004
- Arora B, Kumar L, Sharma, Wadhwa J, Kochupillai V. Pigmentary changes in chronic myeloid leukemia patients treated with imatinib mesylate. *Ann Oncol* 2004; 15: 358-9.
- Hui H, Yang-yang Y, Yu-houng W, Imatinib mesylate-induced repigmentation of vitiligo lesions in a patient with recurrent gastrointestinal stromal tumors. *JAAD*.2008; 59 (5): S80-83
- Prabhash K, Biswas Gh, Prasad N, Karant N, Sastry PS, Parikh PM. Imatinib-induced nail hyperpigmentation in chronic myeloid leukemia. *Indian J Dermatol Venereol Leprol*. 2006; 72 (1): 63-4
- Singh N, Bakhshi S. Imatinib-induced dental hyperpigmentation in childhood chronic myeloid leukemia. *J Pediatr Hematol Oncol*. 2007; 29 (3): 208-9
- Tsao AS, Kantarjian H, Cortes J, O'Brien S, Talpaz M. Imatinib mesylate causes hypopigmentation in the skin. *Cancer*.2003; 98: 2483-7.