

Case Report

Acquired Melanonychia and Mucocutaneous Hyperpigmentation with Hydroxyurea Therapy for the Treatment of Blast Crisis of Chronic Myeloid Leukaemia: A Case Report

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Abstract:

Hydroxyurea is an antineoplastic agent used to treat chronic myeloid leukaemia (especially in accelerated phase and blast crisis). We report this unique case of a 60 year old lady who was diagnosed case of chronic-phase of chronic myeloid leukaemia was getting imatinib and well suited. As a consequence of imatinib noncompliance, she developed blast crisis and was subsequently hydroxyurea initiated. At her 3rd month follow-up she presented with blackening of her exposed parts of the body, all three mucocutaneous areas especially skin of her hands, feet, fingernails, toenails and oral mucosa in some extent.

Hydroxyurea-induced melanonychia and mucocutaneous hyperpigmentation is rarely reported. To the best of our knowledge, this is one of the few published reports of hydroxyurea induced mucocutaneous hyperpigmentation and melanonychia involving all 20 nails. The mainstays of treatment are withdrawal of the drug and sun-avoidance; laser therapy is a hope for cure in small percentage of permanent cases. A correct diagnosis is essential to prevent undue fears in the patient. Proper advice to the patient regarding adverse reactions of particular agent and close monitoring after prescribing should be ensured to prevent harm to patients. Always should remember, drugs not only save life, but can even take it.

Keywords: Chronic myeloid leukaemia, Hydroxyurea, Acquired Melanonychia, Mucocutaneous hyperpigmentation.

Introduction

Hydroxyurea (Hydroxycarbamide USP) is an antineoplastic drug used preferably in myeloproliferative disorders (chronic myeloid leukaemia, polycythemia vera, essential thrombocythemia)^{1,3}. Number of adverse effects of this drug has been reported: alopecia, leg ulcer, lichenoid eruption, mucositis, myelosuppression, secondary leukaemia and notably hyperpigmentation for instance². Among the entire, latest one is a rare side effect of hydroxyurea therapy^{4,5,8}. Hydroxyurea-induced hyperpigmentation and melanonychia are not commonly reported.

CASE REPORT

A 60 years old postmenopausal non-diabetic, normotensive lady with dark complexion hailing from a poor family of Chattak, a rural area under Sylhet division, Bangladesh a diagnosed case of chronic-phase of chronic myeloid leukaemia was getting imatinib following diagnosis of her malignancy. She was well suited with this drug and responded dramatically evident by clinical (weight gain, regression of spleen size, and general well-being) and hematological (normalization of blood picture) improvement. She could not continue imatinib due to her limited wealth and consequently stopped taking imatinib after two years. Few months later, she attended us and confessed of imatinib noncompliance.

Immediate work-up was done with complete blood count, peripheral blood film, and sonographic examination of abdomen which revealed a picture resemble of blast crisis. Considering indication and affordability (hydroxyurea is cheaper than imatinib) hydroxyurea was prescribed at a dose of 1 g/day (20 mg/kg/day)^{1,4,7}. She continued this drug for nearly three months. At follow-up after three months she presented with blackening of her exposed parts of the body, especially her hands, feet, fingernails, toenails and oral mucosa in some extent (Figure-1). There was no evidence of any other side effects. At that time she was not on any medications causing hyperpigmentation and all the causes of hyperpigmentation such as Addison's disease, Cushing's syndrome, scleroderma, haemosiderosis, hyperthyroidism and vitamin B₁₂ deficiency were also ruled out. Finally, a diagnosis of acquired melanonychia and mucocutaneous hyperpigmentation with hydroxyurea therapy was made. The acute onset of the symptoms following therapy lent support to the diagnosis also. The offender was withdrawn with re-institution of imatinib therapy and awaited her next follow-ups and found hyperpigmentation was resolved gradually over three months. Figure-2 showed improvement of appearance of feet & toe nails after withdrawal of hydroxyurea.



Figure 1: At presentation



Figure 2: After hydroxyurea withdrawal

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DISCUSSION

Hydroxyurea is indicated in chronic myeloid leukaemia as a single agent to those patients presenting in accelerated phase and who has already received imatinib⁶. The mechanism by which hydroxyurea produces its beneficial effects are uncertain. However, various studies support the hypothesis that, it interferes with synthesis of DNA by acting as a ribonucleotide reductase inhibitor, with no effect of synthesis of RNA or protein⁷. The drug is mostly metabolized by liver (60%), leaving behind urea and CO₂. Major portion is excreted through kidney⁷. Number of adverse effects have been reported of this drug, includes nausea, vomiting, diarrhea, alopecia, leg ulcer, lichenoid eruption, mucositis, myelosuppression, secondary leukaemia, hyperpigmentation³. Among the adverse effects caused by hydroxyurea, melanonychia and mucocutaneous hyperpigmentation is rare^{4,5,8}. It produces hyperpigmentation in about 10% of persons, especially those who are dark-skinned⁷. The mechanism of hydroxyurea induced melanonychia and mucocutaneous hyperpigmentation is not known; potential causes include toxicity affecting the nail bed or nail matrix, focal stimulation of nail-matrix melanocytes, and photosensitization⁴. The mainstays of treatment are withdrawal of the drug and sun-avoidance. Pigmentation may last for a long time or may even become permanent in some cases. But laser therapy gives rise to hope of a cure nowadays⁹.

CONCLUSION

Every drug produces adverse reactions to some extent. Sometimes few become overt in respect to age, sex, and ethnicity of individual. So, gathering sound knowledge about the preferred drug should be deeply concerned before prescribing. Proper advice to the patient about adverse reactions of particular agents and close monitoring after prescribing should be ensured also. So that immediate and necessary steps can be taken to prevent further harm to patients. Always should remember, drugs save life, drugs can even take it.

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