



LETTERS TO THE EDITOR

Imipramine-induced hyperpigmentation of skin – A case report



Introduction

Imipramine is a tricyclic antidepressant that is used to treat depression, anxiety, and other psychiatric illnesses. A small number of patients develop cutaneous pigmentation on sun-exposed skin, resulting in considerable cosmetic disfigurement. We report a case of imipramine therapy-induced hyperpigmentation in a 54 year old lady after 17 years of treatment.

Case report

Mrs. A, a 54 year old married lady was being seen at our hospital since 2001 on a regular basis. She had been diagnosed with dysthymia and recurrent depressive disorder. She had had 6 episodes of depression from 2001 to 2015 and was maintaining well on Imipramine 225 mg, which was started in 2001. She also had a history of hypertension since 2007 and was on half a tablet of Tab. Amlong A (Amlodipine besylate 5 mg + Atenolol 50 mg) since then. She presented in April 2017 with 6 months history of slate gray hyperpigmentation on exposed parts of the body, mainly on the forehead and both forearms. The skin lesions were not associated with pruritus or scaling. At that time, she was on Imipramine 225 mg and half dose of Tab. Amlong A. Investigations done revealed normal thyroid function levels, normal glucose levels, and hemogram. However, she was detected with low levels of Vitamin B12. As Vitamin B12 deficiency can also cause hyperpigmentation, correction was initiated and Imipramine was continued at the same dose. However, even after the correction of vitamin B12, the hyperpigmentation persisted and was a cause of concern.

A dermatology review was sought where a high possibility of it being Imipramine-induced melanosis/hyperpigmentation was considered and discontinuation of Imipramine was advised. Imipramine was discontinued and Venlafaxine 150 mg was started for the patient. Within 4 months, all of the hyperpigmentation resolved completely. The patient had not been exposed to Amiodarone, tetracyclines, phenothiazines or antimalarials anytime. Application of the Naranjo probability scale

indicated a score of 5, suggesting a probable association between the use of imipramine and the hyperpigmenting process.¹ Biopsy and histological examination could not be done.

Discussion

Hare first reported a case of possible Imipramine-induced hyperpigmentation in a 46 -year-old man who had taken Imipramine for about 8 years.² Following this, there have been a few instances of Imipramine induced hyperpigmentation reported predominantly in women.^{3,4} A case report of Imipramine induced hyperpigmentation in an adolescent girl was the first case report in India.⁵ Imipramine-induced hyperpigmentation presents as slate gray discrete macules and patches on sun-exposed skin that may appear anywhere from 2 to 22 years after initiating the medication.⁴ Affected areas include the malar cheeks, temples, periorbital areas, hands, forearms, and rarely the iris and sclera. Although the blue to slate gray coloring is the classic presentation, other colors have been described including brown, golden brown, and purple.⁴

Imipramine may lead to the deposition of an abnormal “drug metabolite-melanin complex”.³ It has been postulated that ultraviolet light may react with imipramine (as it does with chlorpromazine) to activate tyrosinase, which in turn increases the production of melanin from dihydroxyphenylalanine, trapping imipramine-free radicals.⁶

Most patients report satisfactory resolution of imipramine-induced discoloration within 1 year of stopping Imipramine or switching to a different antidepressant.

Summary

Although the use of tricyclic antidepressants has decreased in the recent years due to the popularity of selective serotonin-reuptake inhibitors and other drugs, familiarity with their possible adverse effects remains essential if clinicians are to provide the best care. Imipramine has been reported to cause hyperpigmentation rarely especially in women and on long term use. Hyperpigmentation can be both severe and persistent, causing distress to the patients. However, since several patients had considerable improvement with discontinuation of imipramine, we strongly recommend tapering and discontinuing the drug as

soon as possible after the pigmentation process begins, if other drug treatment options are available.

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Conflict of interest

The authors have no conflict of interest to declare.

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