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IMIPRAMINE MONOTHERAPY-INDUCED HYPERPIGMENTATION IN AN ADOLESCENT GIRL

Sir,

We report an adolescent girl who, being continuously on tablet imipramine for 5 years, developed hyperpigmentation in the photo-distributed areas.

Ms A, a 20-year-old fair complexioned girl, was registered with a 3-year history of feeling sad with low-confidence levels, early insomnia, and decreased appetite. She met the DSM-IV criteria for major depressive disorder and was treated with tablet imipramine 100 mg/day as a monotherapy for 6 months. Subsequently, the dose of imipramine was titrated to 75 mg/day and she was stabilized on this dose for the past 4 years, except on two occasions when she had recurrences of depressive symptoms, when the dose of imipramine was increased to 125 mg/day for 3 and 5 months, approximately 3 and 2 years back, respectively.

After continuing imipramine therapy for approximately 4 years, she started complaining of change in the color of skin and her face. There was no history of preceding skin disorder before the initiation of imipramine therapy, nor was there any history of exposure to any other psychotropic medication or other drugs including amiodarone, monocycline, and antimalarials, which could have explained the hyperpigmentation. Both the patient and her family members stated noticing the dark complexion of her face. Physical examination revealed gray pigmentation of the face and extensor parts of forearms. Relatively no hyperpigmentation was noticed in the sclera, mucus membrane, nails, or teeth. The results of all routine investigations including serum iron level, blood glucose, liver and renal function, electrolytes, complete blood count, and sedimentation rate were within normal limits.

Dermatologist opinion confirmed this as a case of hyperpigmentation. Skin biopsy showed focal thinning of epidermis, upper epidermis, and on staining revealed melanin. Mild mononuclear infiltration and fibrosis of deeper dermis was noticed. Pigmentation incontinence was stained for iron but it was negative. There was no basal layer degeneration or band-like inflammatory infiltrate suggestive of lichen planus pigmentosus. The probability of adverse drug reaction assessed by using Naranjo probability scale indicated a possible association between the use of imipramine and

the pigmenting process. Subsequently imipramine was totally stopped and replaced with sertaline 150 mg/day. The depressive symptoms remitted, and there was mild improvement in hyperpigmentation over the next 6 months.

We could find only 12 published case reports of hyperpigmentation associated with imipramine in the existing literature and notably, all except two occurred in females.[1,2] From these reports, it was difficult to conclude that only imipramine was the causative agent because most patients were prescribed other drugs also. Contrary to our report where hyperpigmentation is noticed in an adolescent girl with a low dose of imipramine, the previous reported cases were in the 45–75 years age group and were taking imipramine in the dose range between 150 and 375 mg. In our case, the cutaneous pattern of distribution of pigmentation and biopsy report were similar to that described in review literature.[1,3,4]

The previous review concluded that imipramine may lead to the deposition of an abnormal 'drug metabolite melanin complex.'[1] This may be an irreversible side effect and hence, one needs to be aware of this adverse effect of imipramine even with low to moderate dosages.

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