Melasma: A rare adverse effect of clomipramine
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Abstract:
Melasma is a hyperpigmented dermatological condition common in females. Drugs such as steroids, cosmetics, and photosensitizing agents are known to cause melasma. We report here a case of an adult male with obsessive-compulsive disorder, receiving clomipramine, who developed melasma.

Key words:
Clomipramine, melasma, obsessive-compulsive disorder

Melasma, a dermatological condition that commonly affects females is characterized by hypermelanosis of the sun-exposed body parts, particularly face. Approximately 10–20% of all acquired hyperpigmentation are drug-induced phenomenon. Drug-induced hyperpigmentation results by various mechanisms such as excess melanin deposition, drug-mediated excess synthesis of pigments, inflammatory process in the skin, direct drug influence, and damage of dermal vasculature.

Chemicals (cosmetics), steroids, and photosensitizing drugs may produce melasma. Drugs get bound to the melanin pigments of skin, eye, and ear causing pigmentation. Individuals with more content of pheomelanin in their skin are probably at higher risk to develop pigmentation. This case study discusses the possible role of antidepressant clomipramine in the development of melasma.

Case Report
A 35-year-old male, diagnosed with obsessive-compulsive disorder (OCD) for the past 5 years was prescribed on fluoxetine up to 80 mg/day. He was receiving this treatment for the past 1 year with partial improvement of symptoms despite adequate compliance. Cognitive behavior therapy was not possible due to transportation inconvenience. Due to the persistence of symptoms, despite a high dose of fluoxetine, augmentation with clomipramine (up to 100 mg/day) was done. After few days of the addition of clomipramine, the patient had reported dark pigmentation over face localized to both malar eminences. Other than hyperpigmentation, there were no other dermatological complaints. The dermatological consultation was sought for this hyperpigmentation; a diagnosis of “melasma” was made.

His routine hemogram, thyroid function test, and serum cortisol levels were within normal limits. Due to poor tolerance to clomipramine (excessive sedation and severe constipation), dose of clomipramine was reduced to 50 mg/day. Due to the persistence of OCD symptoms, the patient was switched from fluoxetine to fluvoxamine (200 mg/day). This resulted in improvement in OCD symptoms over next 3 months; however, the skin pigmentation and severe constipation persisted. Clomipramine dose was reduced to 25 mg/day for next 2 months and persistence of constipation resulted in its stoppage. Melasma resolved after stoppage of clomipramine. Assessment score on Naranjo adverse drug reaction (ADR) probability scale was six, which was suggestive of probable ADR. Assessment on the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) system for standardized case causality assessment also suggestive of “probable” ADR with clomipramine.

The adverse effect was reported to Pharmacovigilance Programme of India with ADR report no. 2016-29974.

Discussion
In our patient, the pigmentation is confined to the malar eminences of the face, with sparing...
of rest sun-exposed areas of the body. This adverse effect of clomipramine is not life-threatening, but can be a reason of concern from cosmetic sense. In our patient, clomipramine was not acceptable due to constipation and excessive sedation, although he was worried about melasma. Stoppage of clomipramine resulted in improvement of sedation, constipation as well as melasma. Causality assessment is an important evaluation to establish the link between an adverse event with a particular drug.\textsuperscript{[6]} Causality assessment has been done on Naranjo ADR probability scale and the WHO-UMC system, which revealed probable ADR (i.e., the adverse event followed exposure to drug and disappeared following drug discontinuation, it is unlikely attributable to disease or other drugs).

In a study, it was found that the prevalence of severe ADR being 1.4\% in general; higher with the tricyclic antidepressant (TCA) group and lower with monoamine oxidase inhibitors and selective serotonin reuptake inhibitors.\textsuperscript{[7]} Among the TCAs, clomipramine has the highest (2.1\%) prevalence rate. Allergic exanthematous cutaneous reactions are known with TCAs. However, there is description of a single case of 60-year-old female suffering from depressive episode, who developed pigmentation over light exposed areas of the body with the use of clomipramine.\textsuperscript{[8]} There are few case reports of such pigmentation with the use of imipramine, a congener of clomipramine.\textsuperscript{[9]} This is probably the second case study, reporting the rare side effect of clomipramine. Clinicians must be aware of probable hyperpigmented cutaneous ADRs like melasma with clomipramine. It may not be life-threatening but definitely disfiguring cosmetically.

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Conflicts of Interest
There are no conflicts of interest.

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