A peculiar presentation of mirtazapine-induced melasma: A very rare case report

Dear Editor,

Mirtazapine is a norepinephrine and specific serotonergic antidepressant known for its cardiac safety and less sexual side effects.[1] While common side effects are weight gain, nausea, diarrhea, headaches, and tremors, hyperpigmentation is an extremely uncommon adverse effect.[2] There are only two cases of mirtazapine-induced hyperpigmentation,[3,4] although mirtazapine-induced melasma was not mentioned.

In this context, we present a case of a 40-year-old married lady from a lower-middle-class family admitted to the Psychiatry department of Assam Medical College and Hospital. She had experienced depression for 3 years but sought psychiatric help due to worsening symptoms, including low mood, crying spells, early awakening, and inability to maintain daily activities. She was diagnosed with severe depressive episode without psychotic symptoms (F32.2, ICD-10), and a daily dose of 15 mg of Mirtazapine was recommended. No other medication was prescribed. Her symptoms partially improved; however, she developed gray-brown facial patches including malar areas and the regions around the eyes within 3 weeks. She stopped the medication after 3 months, leading to the patches fading within a month, though her depressive symptoms worsened without medication. Two months before her current admission, she sought psychiatric help again and was prescribed 30 mg of mirtazapine daily. Since she did not mention her previous facial pigmentation, the higher dose was intended for a better therapeutic response. Within 2 weeks, gray-brown facial patches reappeared and darkened [shown in Figure 1]. Due to the worsening depression over the past month, she was admitted and her prescription was changed to desvenlafaxine 50 mg daily, with 2 mg of risperidone. Within a month, both the facial pigmentation and depressive symptoms improved.

Dermatologists diagnosed the facial pigmentation as melasma and advised sunlight protection, sunscreen, and topical tyrosinase inhibitor. No histopathological examination was performed due to lack of consent. Interestingly, the pigmentation began to fade once she discontinued mirtazapine even before starting the dermatological medication. Spontaneous melasma disappearance is rare, usually occurring post pregnancy or after stopping oral contraceptives.[5]

Her thyroid, blood sugar, iron, lipid, vitamin B complex, and vitamin D profiles, as well as an abdominal ultrasound, were normal. She had no history of diabetes, hypertension, menstrual irregularities, or regular medication or substance use. Additionally, she had minimal sun exposure in the past 8 months. Given these findings, the Naranjo Adverse Drug Reaction Probability Scale[6] was used, scoring 6 [Table 1], indicating mirtazapine as a probable factor in her melasma.

Mirtazapine inhibits presynaptic 5HT2, 5HT3 receptors, and alpha-2 adrenergic receptors. While effective for pruritus, it can cause severe skin reactions like toxic epidermal necrolysis, Steven Johnson syndrome, and edema.[7] However, hyperpigmentation and melasma are rare side effects.[3,4] Previously reported cases of drug-induced hyperpigmentation emerged 6 to 8 months after starting mirtazapine, while this patient's melasma developed within a month. Similar to those reports, the hyperpigmentation in our case also occurred in exposed areas. Melasma can result from pregnancy, oral contraceptives, menopause, thyroid issues, genetics, and certain drugs, typically affecting individuals aged 20 to 40.[8]

Table 1: Score in naranjo scale of our patient

Questions	Impression	Score
Are there previous conclusive reports on this reaction?	No	0
Did the adverse event appear after the suspected drug was administered?	Yes	+2
Did the adverse event improve when the drug was discontinued?	Yes	+1
Did the adverse event reappear when the drug was readministered?	Yes	+2
Are there alternative causes that could on their own have caused the reaction?	Yes	-1
Did the reaction reappear when a placebo was given?	Do not know	0
Was the drug detected in the blood or other fluids in concentrations known to be toxic?	No	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	No	+1
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Yes	+1
Was the adverse event confirmed by any objective evidence?	No	0
Total Score	6	



Figure 1: Actual photo of the patient showing melasma induced by mirtazapine

Melanin accumulation can occur due to medication, causing epidermal melanocytes to produce melanin, a nonspecific inflammatory skin response, or the formation of stable drug-melanin complexes that hinder melanin clearance in dermal macrophages, often seen perivascularly. Another mechanism involves the drug accumulating in dermal macrophages or as scattered granules in the extracellular matrix, inducing new pigments like lipofuscin, or causing iron deposition from vascular damage, resulting in pigmentation from red blood cell leakage. Sun exposure can exacerbate melanin-related darkening.[8,9]

This case highlights the rare side effects of melasma from mirtazapine, which can develop rapidly and significantly impact a patient's quality of life. Although benign, melasma can cause significant cosmetic and psychological concerns, prompting clinicians to monitor for hyperpigmentation when prescribing mirtazapine. If melasma or hyperpigmentation emerges, psychiatrists should consider switching to an alternative antidepressant. Early identification and management of such side effects can alleviate psychological distress and improve patient care. This case adds to the limited literature on mirtazapine-induced melasma and underscores the need for further research into its mechanisms. Clinicians should document and report similar cases to enhance the understanding of drug-induced hyperpigmentation, thereby guiding better clinical decision-making.

Acknowledgement

We thank our patient for providing permission to use her picture for this publication.

Declaration of patient consent

I certify that we obtain all the appropriate patient consent forms. In that consent form patient has given her consent for her images and other clinical information to be reported in the journal. Patient understands her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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