

CONTACT POINT

Dorsal hand skin hyperpigmentation following oral olanzapine (Zyprexa) use

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CASE REPORT

A 39-year-old, Fitzpatrick Type IV female with a history of atopic dermatitis and schizophrenia (unspecified type) presented to our clinic with a 2-week history of marked hyperpigmentation over the dorsal surfaces of her hands, despite minimal sun exposure, appearing 5 months after beginning olanzapine (Zyprexa) and lurasidone (Latuda) dual therapy. The rash appeared as a symmetrical, diffuse slate-grey to black hyperpigmentation limited to her bilateral dorsal hands and clearly demarcated at her wrists. The lesion resembled the hyperpigmentation pictured in Jhirwal et al,¹ and had no prior erythema or associated pruritus per the patient and her brothers. Following dual therapy discontinuation, the dorsal hand hyperpigmentation decreased; 9 months later, there was 80% improvement.

It is of note that the patient's history also included a previous allergic reaction to aripiprazole (Abilify), in which she developed extensive facial swelling and an erythematous rash for 2 months over her face, her neck, and the dorsal surfaces of her hands. The rash appeared dissimilar from the presenting hyperpigmentation, and resolved completely following aripiprazole discontinuation before the patient was started on olanzapine and lurasidone therapy.

DISCUSSION

Drug-induced hyperpigmentation is responsible for approximately 10% to 20% of all cases of acquired hyperpigmentation, with psychiatric medications such as tricyclic antidepressants, mood stabilizers and typical antipsychotics commonly being implicated.^{2–4} Chlorpromazine is the most frequently involved drug, typically causing violet or purple-grey metallic pigmentation over the extremities and face.⁵ Other presentations include slate-grey, blue-grey or brownish

pigmentary changes, and additional locations include the sclera, cornea, lens of the eye, and nail beds.^{4–6}

There are several possible mechanisms of drug-induced hyperpigmentation, including: accumulation of melanin with or without the drug/drug metabolite, accumulation of the drug itself, drug-induced synthesis of special pigments, and iron accumulation from damaged dermal vessels.⁵

Drug-induced hyperpigmentation may be grouped into pigment deposition, photoirritancy, and photoallergy. Photoallergic reactions are more extensive delayed-type reactions involving adaptive immunity that require prior sensitization and re-exposure to a photoallergen in the presence of ultraviolet irradiation, whereas phototoxic reactions may activate the innate immune system following initial exposure to a photoirritant in the presence of ultraviolet irradiation.⁷ Phototoxic reactions most often resemble acute sunburn, whereas systemic photoallergy usually presents with an eczematous reaction.⁷

Lurasidone has a limited side-effect profile, with no adverse cutaneous events having been reported before it was marketed.¹ Conversely, olanzapine has been associated with cutaneous adverse drug reactions, including a similar incidence of hyperpigmentation reported by Jhirwal et al.^{1,3} We believe that drug-induced hyperpigmentation is a rare side-effect of olanzapine, but physicians should be aware of it.

Although it is possible that the patient's hyperpigmentation resulted from pigment deposition caused by olanzapine, we cannot rule out the possibility of a photoirritant or photoallergic reaction. We were unable to photopatch test the patient, but remain interested in the possibility of systemic photoallergy presenting with hyperpigmentation.

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