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A 29-year-old Vietnamese woman presented with a 4-year history of darkening of the sun-exposed areas of her skin. She had been taking chlorpromazine 200 mg daily for 14 years. On examination, there was a bluish-gray pigmentation on her face, neck, upper chest, and dorsal hands and feet.

## What is your diagnosis?

## The Diagnosis: Hyperpigmentation Due to Long-term Chlorpromazine Use



Chlorpromazine is a phenothiazine antipsychotic. Hyperpigmentation, which develops most commonly in sun-exposed areas, is a rare side effect of long-term chlorpromazine use. Patients at greatest risk are women who have been taking between 500 and 1500 mg of chlorpromazine daily for 3 or more years.<sup>1</sup> In addition to skin pigmentation, the cornea and lens also may develop anomalous pigmentation. Autopsies have demonstrated pigment deposits in the lungs, heart, liver, kidneys, gastrointestinal tract, and adrenal glands.<sup>2</sup>

Histologically, skin that is hyperpigmented due to chlorpromazine use has been shown to contain golden-brown, melanin-positive, pigment granules within the papillary and upper reticular dermis, predominantly within perivascular macrophages of the superficial plexus.<sup>3</sup> Electron microscopy reveals dense inclusion bodies extracellularly, as well as in dermal histiocytes, pericytes, endothelial cells, and Schwann cells.<sup>3</sup> Energy-dispersive x-ray microanalysis of the granules shows a striking peak for sulfur, one of the elements that comprises the chlorpromazine molecule. Thus, the granules most likely contain chlorpromazine or one of its metabolites in addition to melanin.<sup>3</sup> Chlorpromazine-melanin complexes have been found in neutrophils and monocytes, which presumably distribute the pigment to internal organs, thereby staining them as well.<sup>2</sup>

There is no effective treatment for chlorpromazine-induced hyperpigmentation. However, some patients have experienced a very slow disappearance of the pigmentation after discontinuing chlorpromazine.<sup>2</sup>

## REFERENCES

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