# Diltiazem-Induced Hyperpigmentation

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*A healthy-appearing 66-year-old black woman presented with a 5-year history of facial hyperpigmentation that was unresponsive to topical sunscreen, hydroquinone, tretinoin, and azelaic acid. Her medications included extended-release diltiazem for hypertension for the past 7 years, rofecoxib for arthritis, and pantoprazole for esophagitis. On examination, the woman displayed hyperpigmented patches and papules involving most of her face. The punch biopsy findings from a hyperpigmented papule on the right temple revealed compact hyperkeratosis, follicular dilation, and dense inflammatory infiltrate along the dermal-epidermal junction with abundant dying keratinocytes. Her diltiazem therapy was discontinued, which led to gradual resolution of her hyperpigmentation.*

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## Case Report

A healthy-appearing 66-year-old black woman presented with a 5-year history of facial hyperpigmentation. The patient presented to our clinic for a second opinion and possible laser therapy. For 5 years, she was under the care of a physician who treated her unsuccessfully with topical sunscreen, hydroquinone, tretinoin, and azelaic acid. Despite these therapies, her pigmentation continued to progress.

Her medical history was significant for hypertension and osteoporosis. Her medications included extended-release diltiazem for hypertension for the previous 7 years, rofecoxib for arthritis, and pantoprazole for esophagitis.

On examination, the patient was healthy-appearing with Fitzpatrick skin type V with coalescing hyperpigmented patches and papules involving most of her face (Figure 1A). Her hands, neck, trunk, and bilateral upper and lower extremities were unaffected.

The punch biopsy findings from a hyperpigmented papule on the right temple revealed compact hyperkeratosis and follicular dilation. In addition, there was a dense inflammatory infiltrate along the dermal-epidermal junction with abundant dying keratinocytes (Figure 2). Pigment incontinence was marked. There was an intense superficial to mid-dermal perivascular and perifollicular lymphocytic infiltrate. Laboratory findings, including a wintrobe erythrocyte sedimentation rate, antinuclear antibody, anti-DNA, hepatitis screen, Ro (SS-A), and La (SS-B), were all negative or within reference range.

Extended-release diltiazem was discontinued. Four months after discontinuation of the drug therapy, the patient displayed lightening of the hyperpigmentation and flattening of the papules (Figure 1B).

## Comment

When a patient presents with hyperpigmentation of the face, many diagnoses may be suspected, including melasma, exogenous ochronosis, postinflammatory hyperpigmentation, drug-induced hyperpigmentation, erythema dyschromicum perstans, Riehl melanosis, acquired immunodeficiency syndrome, systemic lupus erythematosus, alkaptonuria, macular amyloidosis, Addison disease, and hemochromatosis. When a lichenoid infiltrate or interface dermatitis is present, a histologically different set of diagnoses should be considered including actinic lichen planus, dermatomyositis, and lichenoid drug reactions (gold, antimalarials, penicillamine, thiazide diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, and nonsteroidal anti-inflammatory drugs). We propose that extended-release diltiazem should be added to the list of lichenoid drug reactions, especially when associated with intense hyperpigmentation.

Diltiazem hydrochloride is a widely used calcium channel–blocking agent for treatment of hypertension and angina, especially among the black population. Diltiazem has been noted to cause serious cutaneous manifestations such as toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema

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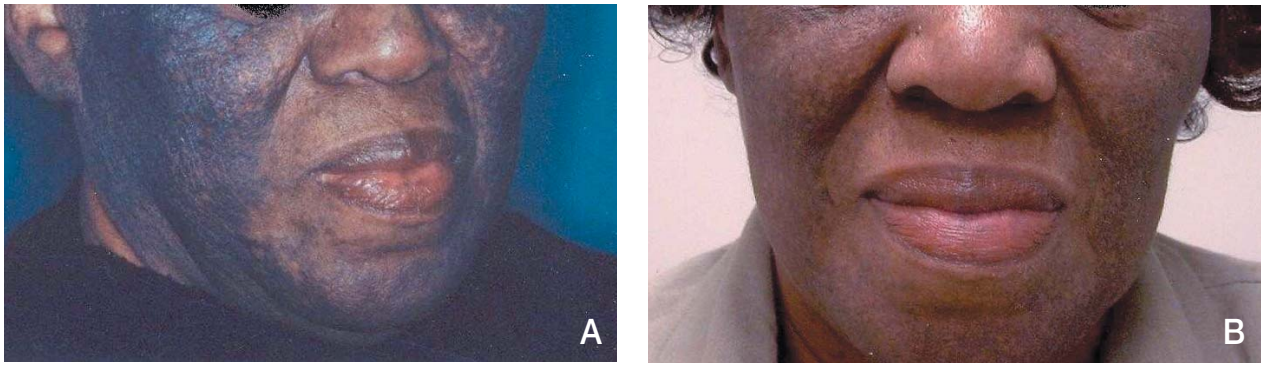


**Figure 1.** Hyperpigmented patches and papules on the face (A). Improvement following discontinuation of extended-release diltiazem (B).

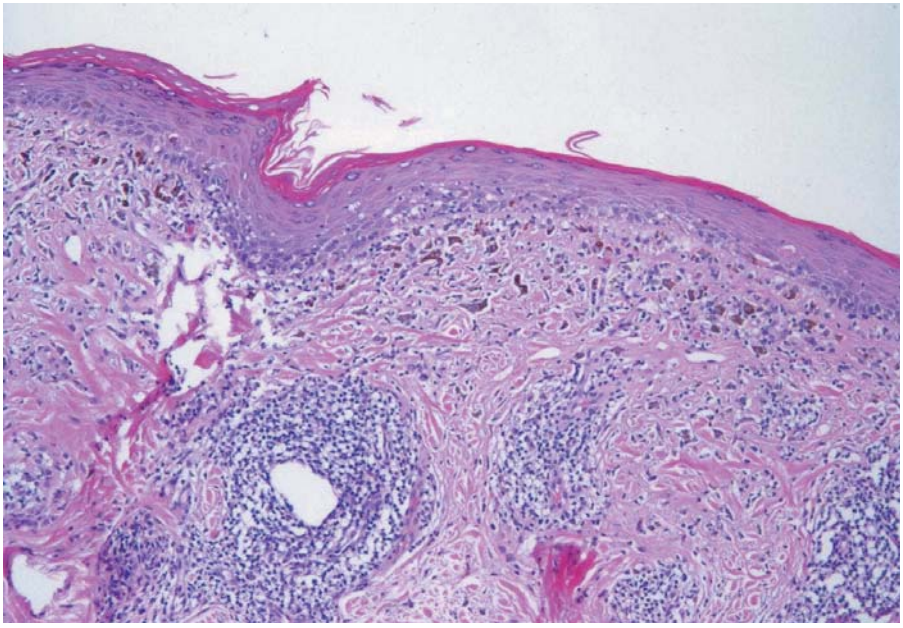

**Figure 2.** A dense inflammatory infiltrate, abundant dying keratinocytes, and compact hyperkeratosis (H&E, original magnification ×40).

multiforme.[1] In a recent case report, extended-release diltiazem was implicated histologically in causing facial hyperpigmentation in a black woman with a lichenoid infiltrate.[2] In that case, the woman was taking extended-release diltiazem for approximately 2 years before she noticed the hyperpigmentation. Scherschun et al[3] also have described 4 patients, all African American with a mean age of 62 years, with photodistributed hyperpigmentation associated with extended-release diltiazem. The mean duration of diltiazem administration prior to the development of hyperpigmentation was 8 months. Histopathologic examination in these cases also showed lichenoid dermatitis with prominent pigmentary incontinence. Discontinuation of diltiazem therapy resulted in the gradual resolution of the hyperpigmentation in these cases.[2,3]

Extended-release diltiazem–induced hyperpigmentation is the most likely diagnosis in our current patient given the improvement of her facial color less than 6 months after discontinuation of the drug. This reaction may be more common than once thought.

## REFERENCES

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