

# Progressive Axillary Hyperpigmentation

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A 50-year-old Hispanic woman presented with asymptomatic, progressive, brown hyperpigmentation involving the axillae, neck, upper back, and inframammary areas of 5 years' duration. She had no other notable medical history; family history was unremarkable. She had been treated with topical hydroquinone and tretinoin by an outside physician without improvement. Physical examination revealed reticulated hyperpigmented macules and patches involving the inverse regions of the neck, axillae, and inframammary regions. Additionally, acneform pitted scars involving the perioral region were seen. A 4.0-mm punch biopsy of the right axilla was performed.

## WHAT'S YOUR DIAGNOSIS?

- a. acanthosis nigricans
- b. confluent and reticulated papillomatosis
- c. Dowling-Degos disease
- d. granular parakeratosis
- e. inverse psoriasis

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The authors report no conflict of interest.

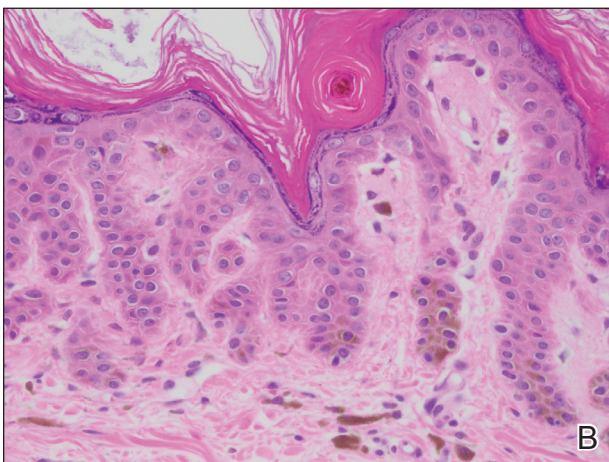
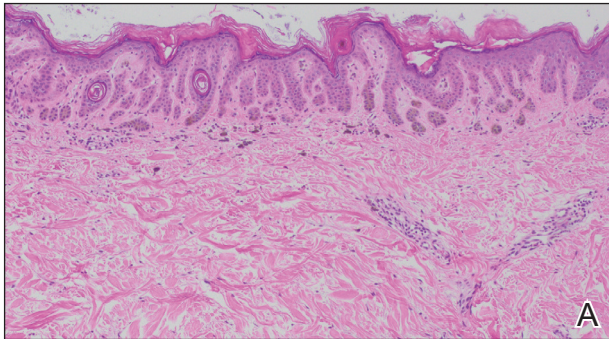
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## THE DIAGNOSIS: Dowling-Degos Disease

**H**istopathology demonstrated elongation of the epidermal rete ridges with increased basal pigmentation, suprapapillary epithelial thinning, dermal melanophages, and a mild lymphocytic infiltrate (Figure). Given the clinical and histologic findings, a diagnosis of Dowling-Degos disease (DDD) was made. The patient was counseled on the increased risk for her children developing DDD. Treatment with the erbium:YAG (Er:YAG) laser subsequently was initiated.

Dowling-Degos disease (also known as reticulate pigmented anomaly of the flexures) is an uncommon autosomal-dominant condition characterized by reticular hyperpigmentation involving the flexural and intertriginous sites. Classic DDD commonly is caused by loss-of-function mutations in the keratin 5 gene, *KRT5*<sup>1</sup>; however, DDD also may result from loss-of-function mutations in the protein O-fucosyltransferase 1, *POFUT1*, and protein O-glucosyltransferase 1, *POGLUT1*, genes.<sup>2</sup>



Histopathology showed elongation of the rete ridges with increased pigmentation within the basal layer, suprapapillary epithelial thinning, and a mild perivascular infiltrate (H&E, original magnifications  $\times 10$  and  $\times 40$ ).

Rare cases of DDD associated with hidradenitis suppurativa are caused by mutations in the presenilin enhancer protein 2 gene, *PSENEN*.<sup>3</sup>

Of note, a missense mutation in *KRT5* is implicated in epidermolysis bullosa simplex with mottled pigmentation. Onset of DDD typically occurs during the third to fourth decades of life. Reticulated hyperpigmented macules initially occur in the axillae and groin and progressively increase over time to involve the neck, inframammary folds, trunk, and flexural surfaces of the arms and thighs. Patients additionally may present with pitted perioral scars, comedolike lesions on the back and neck, epidermoid cysts, and hidradenitis suppurativa. Keratoacanthoma and squamous cell carcinoma rarely have been reported in association with classic DDD.<sup>4,5</sup>

Dowling-Degos disease usually is asymptomatic, though pruritus seldom may occur in the affected flexural areas. Histologically, the epidermal rete ridges are elongated in a filiform or antlerlike pattern with increased pigmentation of the basal layer and thinning of the suprapapillary epithelium. Dermal melanosis and a mild perivascular lymphohistiocytic infiltrate also are present with no increase in the number of melanocytes.<sup>6,7</sup> Galli-Galli disease is a variant of DDD that shares similar clinical and histologic features of DDD but is distinguished from DDD by suprabasilar nondyskeratotic acantholysis on histology.<sup>8</sup>

Regarding other differential diagnoses for our patient, acanthosis nigricans may be distinguished clinically by the presence of velvety and/or verrucous plaques, commonly in the neck folds and axillae. Histologically, acanthosis nigricans is distinct from DDD and involves hyperkeratosis, acanthosis, and epidermal papillomatosis. Our patient had no history of diabetes mellitus or insulin resistance. Granular parakeratosis presents with hyperpigmented hyperkeratotic papules and plaques classically confined to the axillary region; however, the involvement of other intertriginous areas may occur. Histologically, granular parakeratosis demonstrates compact parakeratosis with small bluish keratohyalin granules within the stratum corneum. Confluent and reticulated papillomatosis presents with red-brown keratotic papules that initially appear in the intermammary region and spread laterally forming a reticulated pattern. Histology is similar to acanthosis nigricans and demonstrates hyperkeratosis, acanthosis, and papillomatosis. Inverse psoriasis presents with symmetric and sharply demarcated, erythematous, nonscaly plaques in the intertriginous areas. The plaques of inverse psoriasis may be pruritic and/or sore and occasionally may become macerated. Inverse psoriasis shares similar histologic findings compared to classic plaque psoriasis but may have less confluent parakeratosis.

Treatment of DDD essentially is reserved for cosmetic reasons. Topical hydroquinone, tretinoin, and corticosteroids have been used with limited to no success.<sup>5,9</sup> Beneficial results after treatment with the Er:YAG laser have been reported.<sup>10</sup>

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