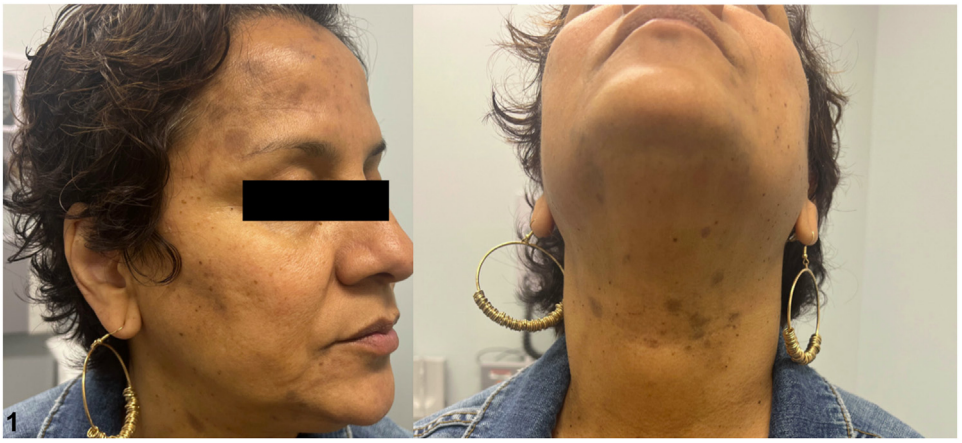
Gray-brown macules on the face and neck

Julian Cortes, BS, Brian Hinds, MD, and Genevieve Kaunitz, MD

Key words: cutaneous immune-related adverse events; lichen planus pigmentosus; PD-1 inhibitor; pembrolizumab.



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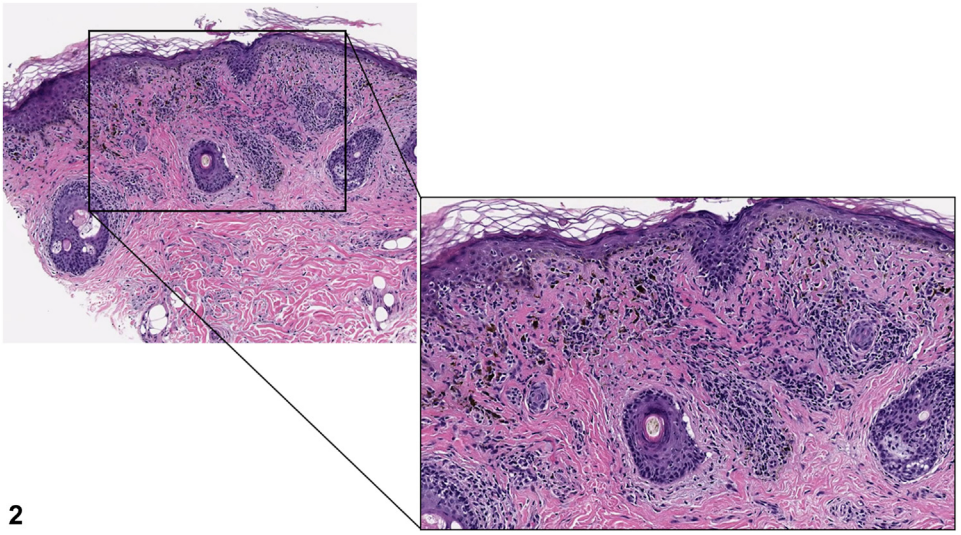

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From the Department of Dermatology, University of California San Diego, San Diego, California.

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Correspondence to: Genevieve Kaunitz, MD, Department of Dermatology, University of California San Diego, 8899 University Center Lane Unit 350, San Diego, CA 92122. E-mail: gkaunitz@health.ucsd.edu.

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CASE DESCRIPTION

A 56-year-old woman with stage IV colon adenocarcinoma presented with new brown patches on her face and neck approximately 3 weeks after starting pembrolizumab/talazoparib (Fig 1). She had previously been treated with a clinical trial medication and standard chemotherapy. Otherwise there were no new medications or topical exposures. Physical exam showed gray-brown macules and patches on the forehead, temples, lateral cheeks, upper lip, and anterior neck. The patient was started on a medium-potency topical steroid. After 2 weeks with minimal improvement, a 3-mm punch biopsy was performed from the lateral forehead (Fig 2).

Question 1: What is the most likely diagnosis?

A. Postinflammatory hyperpigmentation

B. Lichen planus pigmentosus (LPP)—like drug eruption

C. Pigmented contact dermatitis

D. Exogenous ochronosis

E. Idiopathic eruptive macular pigmentation

Answers:

A. Postinflammatory hyperpigmentation — Incorrect. Postinflammatory hyperpigmentation is a sequela of inflammatory skin conditions or external trauma, which lead to increased melanocyte activity and overproduction of melanin.[1] Clinically postinflammatory hyperpigmentation presents with hyperpigmented macules or patches in the distribution of the initial inflammation or injury. Hyperpigmentation in the epidermis will appear tan to brown, while dermal pigmentation will present as blue-gray.[1] While there is overlap with the findings described in this case, there is no mention in the history of a preceding inflammatory dermatosis.

B. LPP—like drug eruption — Correct. The gray-brown macules and patches in a sun-exposed distribution are characteristic for LPP, a rare variant of lichen planus.[2] Lichenoid eruptions are among the most common cutaneous immune-related adverse events (cirAEs) associated with immune checkpoint blockade, and numerous subtypes of lichen planus have been described. This is the first known case of LPP in association with anti—programmed cell death protein 1 therapy. Lichenoid cirAEs tend to occur approximately 6 to 12 weeks after initiation of therapy, although this can range from 3 to 52 weeks depending on the study.[3] Our patient's time to onset was in keeping with this timeline, although at 3 weeks is earlier than average for a lichenoid eruption.

C. Pigmented contact dermatitis — Incorrect. The patient's history does not provide sufficient indication to suspect a contact dermatitis.

D. Exogenous ochronosis — Incorrect. The patient did not indicate any prior use of hydroquinone or other skin-lightening topical medications, which would make this diagnosis unlikely.[4]

E. Idiopathic eruptive macular pigmentation — Incorrect. Although the clinical presentation can be similar, idiopathic eruptive macular pigmentation more commonly appears in young children and adolescents and is characterized by brown-black macules on the neck, trunk, and proximal extremities.[2]

Question 2: What features might be expected in histopathological analysis?

A. Dermal proliferation of pigmented dendritic melanocytes

B. Absence of functioning melanocytes

C. Increased melanin in the basal layer

D. Ochre or yellow brown comma-shaped fibers in the dermis

E. Dermal pigment incontinence

Answers:

A. Dermal proliferation of pigmented dendritic melanocytes — Incorrect. This describes a blue nevus, which clinically presents with solitary blue to black papules or nodules.

B. Absence of functioning melanocytes — Incorrect. This description is characteristic for vitiligo. Although vitiligo has been described in association with immune checkpoint inhibitors, the clinical description would not be consistent with this diagnosis.[3]

C. Increased melanin in the basal layer — Incorrect. LPP does present with an interface dermatitis; however, an increase in melanin at the basal layer is more consistent with idiopathic eruptive macular pigmentation.[2]

D. Ochre or yellow brown comma-shaped fibers in the dermis — Incorrect. This feature is pathognomonic for exogenous ochronosis.[4]

E. Dermal pigment incontinence — Correct. The histology of LPP is characterized by a band-like infiltrate, vacuolization of the basal cell layer, and scattered melanophages.[2] The histology of lichenoid cirAEs can be distinguished from idiopathic lichen planus by the presence of parakeratosis, spongiosis, and eosinophils, although these features were not prominent in our case.[3]

Question 3: What is the most appropriate first step in treatment?

A. Topical calcineurin inhibitor

B. Cessation of immunotherapy

C. High-potency topical corticosteroid

D. Q-switched laser

E. Topical hydroquinone

Answers:

A. Topical calcineurin inhibitor — Correct. LPP is often refractory to treatment; however, topical calcineurin inhibitors are typically the first line therapy given their antiinflammatory effect and potential for longer-term use on sun-exposed skin.[2] Topical corticosteroids are often used in the management of cirAEs; however, this would be less optimal as a first step in treatment given LPP tends to affect the face and neck.

B. Cessation of immunotherapy — Incorrect. While dose reduction or cessation of immunotherapy may be indicated in the setting of severe cutaneous adverse events, mild toxicities can be managed with topical therapies.[3]

C. High-potency topical corticosteroid — Incorrect. Although high-potency topical corticosteroids may be appropriate in some cases of LPP and/or lichenoid cirAEs, they would not be recommended for long-term use on the face and neck given the risk of atrophy and further dyspigmentation.

D. Q-switched laser — Incorrect. Q-switched laser has been shown mild to moderate efficacy in treating LPP but can be costly and time-consuming.[2] Other treatment options should be explored prior to treating with Q-switched laser.

E. Topical hydroquinone — Incorrect. Topical hydroquinone may be used in the treatment of LPP, but it is most appropriate in combination with other treatment options such as a topical calcineurin inhibitor.[2] In addition, hydroquinone when used incorrectly can lead to exogenous ochronosis and paradoxical worsening pigmentation.[4]

Abbreviations used:

cirAEs: cutaneous immune-related adverse events
LPP: lichen planus pigmentosus

Conflicts of interest

None disclosed.

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