Generalized reticulated hyperpigmented patches interspersed with hypopigmented macules

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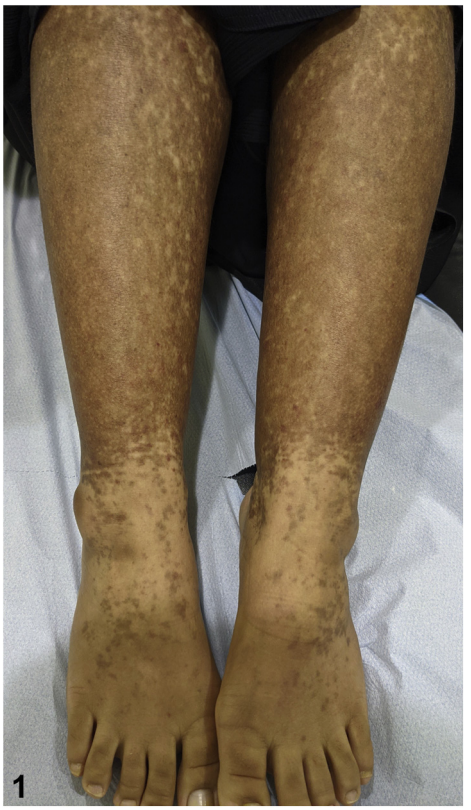

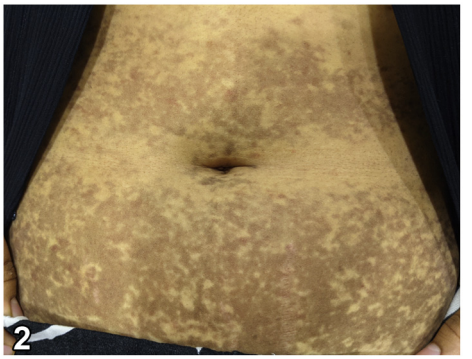

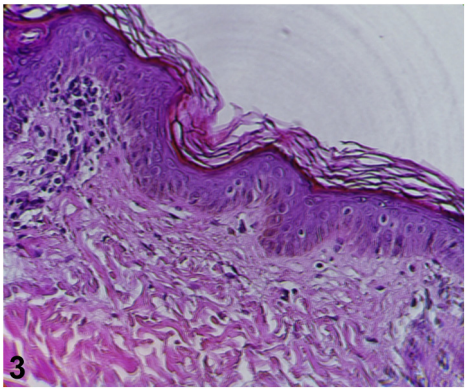

A 21-year-old Saudi girl with nonconsanguineous parents complained of skin dyspigmentation since she was 8 years old. It started in both lower extremities and then spread to the upper extremity and trunk over the past few years. Face, palms, and soles were spared. Her mucous membranes, teeth, hair, and nails appeared normal. Her developmental milestones and school performance were average. There was no history of exposure to any chemicals. Symptoms such as headache, seizures, blurred vision, night blindness, eye pain, postural hypotension, palpitation, joint pain or swelling, morning stiffness, tinnitus, or hearing impairment were absent. There was a family history of a similar condition in 2 sisters and 1 brother. On examination, reticulated hyperpigmented patches interspersed with hypopigmented macules were observed over both shins, thighs, arms, and abdomen (Figs 1 and 2). Skin biopsy from the hyperpigmented patch showed mild epidermal atrophy, hyperpigmentation of the basal layer with mild vacuolar interface change, and scanty perivascular lymphocytic infiltrate with no amyloid deposit in the papillary dermis (Fig 3).

Question 1: Which of the following is the most likely diagnosis?

A. Reticulate acropigmentation of Kitamura

B. Dyschromatosis symmetrica hereditaria

C. Dyschromatosis universalis hereditaria

D. Amyloidosis cutis dyschromica

E. Acquired brachial cutaneous dyschromatosis

Answers:

A. Reticulate acropigmentation of Kitamura—Incorrect. Reticulate acropigmentation of Kitamura is an autosomal dominant disease manifesting with atrophic reticulated or lentigo-like hyperpigmented macules without hypopigmented macules and favoring the dorsal aspects of the hands and feet, sometimes accompanied by palmoplantar pits.[1]

B. Dyschromatosis symmetrica hereditaria—Incorrect. Dyschromatosis symmetrica hereditaria is an autosomal dominant disease manifesting with small, irregular hypopigmented and hyperpigmented macules on the dorsal aspects of the distal extremities, especially the hands and feet, without significant involvement of the trunk.[1]

C. Dyschromatosis universalis hereditaria—Correct. Dyschromatosis universalis hereditaria (DUH) is a rare disorder of dyspigmentation characterized by hypo- and hyperpigmented macules in a generalized distribution developing on the head, neck, extremities, and trunk and potentially involving the palms and soles as well as the dorsal aspects of the hands and feet; however, it spares the mucous membranes.[1] Autosomal dominant, recessive forms, and sporadic cases of DUH have been reported.[2]

D. Amyloidosis cutis dyschromica—Incorrect. Amyloidosis cutis dyschromica is a rare disorder manifest with generalized guttate leukoderma plus reticulated hyperpigmented macules primarily in sun-exposed skin.[1] However, small foci of amyloid deposits in the papillary dermis are usually seen, which were not found in our patient when tested using Congo red stain.

E. Acquired brachial cutaneous dyschromatosis—Incorrect. Acquired brachial cutaneous dyschromatosis is an acquired disorder of elderly Caucasian women characterized by chronic, asymptomatic gray-to-brown patches with geographic borders interspersed with hypopigmented macules on the dorsal aspect of the forearms. Patients usually have a history of chronic sun exposure.[3]

Question 2: Which of the following gene mutations is a possible underlying cause of this disease?

A. *ADAR*

B. *ABCB6*

C. *ABCB4*

D. *ABCC6*

E. *ADAM10*

Answers:

A. *ADAR*—Incorrect. Dyschromatosis symmetrica hereditaria is caused by heterozygous mutations in *ADAR* (DSRAD), which encodes double-stranded RNA-specific adenosine deaminase.[1]

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B. *ABCB6*—Correct. A subset of DUH is due to mutations in *ABCB6*, which encodes an ATP-binding cassette transporter protein that is expressed in keratinocytes and melanocytes.[1]

C. *ABCB4*—Incorrect. A mutation in *ABCB4,* which encodes the bile transporter protein, has been reported as a predisposing factor for intrahepatic cholestasis of pregnancy.[1]

D. *ABCC6*—Incorrect. Loss-of-function mutations in *ABCC6* can be identified in most patients with pseudoxanthoma elasticum. *ABCC6* encodes an ATP-binding cassette transporter predominantly expressed in the basolateral membrane of hepatocytes, where it serves as an efflux pump.[1]

E. *ADAM10*—Incorrect. Heterozygous loss-of-function mutations in the a disintegrin and metalloproteinase 10 gene (*ADAM10*), which encodes a zinc metalloproteinase that activates Notch signaling, have been found to be associated with reticulate acropigmentation of Kitamura.[1]

Question 3: Which of the following extracutaneous manifestations is reported with this disease?

A. Seizures

B. Short stature

C. Deafness

D. Glaucoma

E. All of the above

Answers:

A. Seizures—Incorrect. Although seizure has been reported in association with DUH, these are not the only extracutaneous manifestations of DUH.[4,5]

B. Short stature—Incorrect. Although short stature has been reported in association with DUH, it is not the only extracutaneous manifestation of DUH.[4,5]

C. Deafness—Incorrect. Although deafness has been reported in association with DUH, it is not the only extracutaneous manifestation of DUH.[4,5]

D. Glaucoma—Incorrect. Although glaucoma has been reported in association with DUH, it is not the only extracutaneous manifestation of DUH.[4,5]

E. All of the above—Correct. Extracutaneous abnormalities reported in isolated cases of DUH include learning difficulties, severe mental retardation, oral leukoplakia, short stature, high-tone deafness, abnormalities in erythrocytes, platelets, and tryptophan metabolism; bilateral glaucoma, unilateral cataract, seizures, and insulin-dependent diabetes mellitus.[4,5]

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Abbreviation used:

DUH: dyschromatosis universalis hereditaria

Conflicts of interest

None disclosed.

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