Oculocutaneous albinism in a Puerto Rican patient

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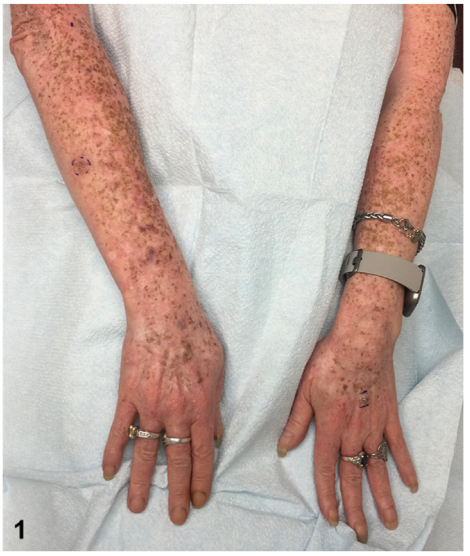

A 58-year-old Puerto Rican female with a history of easy bruising, decreased visual acuity and cutaneous squamous cell carcinoma presented to our dermatology clinic for treatment of a biopsy-proven SCC on the right arm. In addition to this finding, the patient was noted to have Fitzpatrick skin phototype I with multiple actinic keratoses, lentigines, and small ecchymoses on her upper extremities (Fig 1). Examination also demonstrated light blonde hair, blue-gray irises, and horizontal nystagmus (Video 1, available on www.jaad.org). She stated that she cannot take aspirin due to increased bleeding time and that members of her family have the same condition.

Question 1: What is the most likely diagnosis?

A. Chediak–Higashi syndrome (CHS)

B. Hermansky–Pudlak syndrome (HPS)

C. Oculocutaneous albinism type 3 (OCA3)

D. Griscelli syndrome (GS)

E. Phenylketonuria (PKU)

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Answers:

A. CHS – Incorrect. CHS is an autosomal recessive condition featuring silvery hair and skin as well as immunodeficiency due to a mutation in LYST. Although nystagmus is common in CHS, patients usually have normal visual acuity.[1]

B. HPS – Correct. HPS is a group of disorders most commonly seen in patients of Puerto Rican descent that are characterized by pigmentary dilution of the skin, hair, and eyes. Other features that can be observed in HPS subtypes include prolonged bleeding, pulmonary fibrosis, granulomatous colitis, renal failure, cardiomyopathy, immunodeficiency, conductive hearing loss, and seizures.[1]

C. OCA3 – Incorrect. Patients with OCA3, also known as "rufous" OCA, classically present with red hair and red-bronze skin color but do not have problems with bleeding.[1]

D. GS – Incorrect. Like CHS, patients with Griscelli syndrome are characterized by their silvery hair. There are 3 subsets of Griscelli syndrome.[1]

E. PKU – Incorrect. Patients with PKU can present with generalized hypopigmentation of the hair, skin, and/or eyes due to deficient phenylalanine hydroxylase, which prevents the conversion of phenylalanine to tyrosine. However, ocular findings in PKU do not typically include nystagmus, according to 1 study.[2]

Question 2: Which of the following is most likely deficient in this patient?

A. BLOC-3

B. AP-3

C. Tyrosinase

D. Pink-eyed dilution (P) protein

E. Lysosomal trafficking regulator

Answers:

A. BLOC-3 – Correct. BLOC-3 is a protein complex of HPS1 and HPS4, which is involved in the regulation of melanosomes, platelet dense bodies and lung lamellar bodies. HPS1 mutations are seen in 82% of Puerto Ricans with HPS, making it the most common cause in this demographic.[1]

B. AP-3 – Incorrect. AP-3 is a protein involved in mediation of lysosomal protein trafficking and is defunct in HPS-2 and HPS-10. These patients can have recurrent bacterial and viral infections because of congenital neutropenia and deficient natural killer cell cytotoxicity.[1]

C. Tyrosinase – Incorrect. A complete absence of tyrosinase or decreased levels of this enzyme are seen in OCA1A and OCA1B, respectively.[1]

D. Pink-eyed dilution (P) protein – Incorrect. P protein is absent in type II albinism (OCA2), which results in impaired melanosome biogenesis as well as processing and transport of tyrosinase and tyrosinase-related protein 1.[1]

E. Lysosomal trafficking regulator – Incorrect. Mutations in LYST result in impaired fusion of primary lysosome-like structures, which is seen in CHS.[1]

Question 3: Which of the following is the characteristic microscopic finding in this condition?

A. Large, irregularly-spaced macromelanosomes on light microscopy of hair shafts

B. Regularly-spaced giant melanosomes on light microscopy of hair shafts

C. Epidermis and hair bulbs completely lacking melanin and melanocytes on both light and electron microscopy

D. Small melanosomes, which are unmelanized and reduced in number on electron microscopy

E. Absent dense bodies of platelets on electron microscopy

Answers:

A. Large, irregularly-spaced macromelanosomes on light microscopy of hair shafts – Incorrect. This finding is a characteristic of GS and is useful when attempting to distinguish this condition from CHS.[1]

B. Regularly-spaced giant melanosomes on light microscopy of hair shafts – Incorrect. This finding is a characteristic of CHS and is useful when attempting to distinguish this condition from GS.[1]

C. Epidermis and hair bulbs completely lacking melanin and melanocytes on both light and electron microscopy – Incorrect. These findings are characteristics of the leukodermic skin in piebaldism.[3] Piebaldism results from errors in melanoblast migration from the neural crest and differentiation into melanocytes from these precursors.[1]

D. Small melanosomes, which are unmelanized and reduced in number on electron microscopy − Incorrect. The hypopigmented macules and patches of tuberous sclerosis complex are characterized by this finding.[3] Three or more of these hypopigmented macules or patches, if greater than or equal to 5 millimeters in size, are a major criterion for this autosomal dominant genodermatosis.[1]

E. Absent dense bodies of platelets on electron microscopy − Correct. The lack of platelet dense bodies is a pathognomonic feature of HPS.[4] Because of their platelet defect, patients with HPS should avoid aspirin and trauma.

Abbreviations used:

CHS: Chediak−Higashi syndrome
GS: Griscelli syndrome
HPS: Hermansky−Pudlak syndrome
OCA: oculocutaneous albinism type 3
PKU: phenylketonuria

Conflicts of interest

None disclosed.

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