

Hyperpigmented patch of the left hemithorax



Adam Levin, BS,^a Harib Ezaldein, MD,^b Robert M. Rothbaum, MD,^b and Gregory R. Delost, DO^b
Downers Grove, Illinois, and Cleveland, Ohio

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A 6-hour-old infant was found to have large irregularly bordered brown patches on the trunk, neck (Fig 1), and buttocks. The infant otherwise had a normal-term delivery without any concerning findings.

Question 1: Which of the following syndromes typically presents with lesions featuring the morphology seen here?

- A. McCune-Albright syndrome
- B. LEOPARD syndrome
- C. Neurofibromatosis type 1
- D. Peutz-Jeghers syndrome

E. Legius syndrome

Answers:

A. McCune-Albright syndrome — Correct. McCune-Albright syndrome is characterized by abnormalities in endocrine function, polyostotic fibrous dysplasia, and café-au-lait spots. The café-au-lait spots are generally large, respect the midline, and often have irregular, jagged borders, resembling

From the Chicago College of Osteopathic Medicine^a and the Department of Dermatology, University Hospitals Cleveland Medical Center.^b

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Correspondence to: Gregory R. Delost, DO, Department of Dermatology, UH Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 3500, Cleveland, OH 44106. E-mail: Gregory.Delost@UHhospitals.org; Gregorydelost@gmail.com.

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the coast of Maine. These spots are the presenting finding.¹

B. LEOPARD syndrome — Incorrect. LEOPARD syndrome is a rare inherited disorder associated with multiple congenital anomalies also known as multiple lentigines syndrome. LEOPARD is an acronym for the major findings in this disease: multiple Lentigines, EKG (electrocardiogram) conduction abnormalities, Ocular hypertelorism, Pulmonic stenosis, Abnormal genitalia, Retardation of growth, and sensorineural Deafness.

C. Neurofibromatosis type 1 — Incorrect. The café-au-lait spots found in patients with neurofibromatosis type 1 typically have regular borders resembling the coast of California, are often smaller, and do not respect the midline. Although linear segmental variants of neurofibromatosis type 1 can present with larger, segmental café-au-lait spots, these lesions also typically have more regular borders.

D. Peutz-Jeghers syndrome — Incorrect. Patients with Peutz-Jeghers syndrome have multiple perioral lentigines and intestinal polyps and a predisposition for gastrointestinal tract and other malignancies. These patients do not typically have café-au-lait spots.

E. Legius syndrome — Incorrect. Almost all patients with Legius syndrome present with 6 or more café-au-lait spots. These café-au-lait spots are similar to those present in neurofibromatosis type 1, with their regular borders, smaller size, and crossing of the midline.

Question 2: Which of the following is NOT an endocrine abnormality associated with the syndrome that has this cutaneous finding?

- A.** Precocious puberty
- B.** Cushing syndrome
- C.** Hypophosphatemic rickets
- D.** Hyperthyroidism
- E.** Hyperparathyroidism

Answers:

A. Precocious puberty — Incorrect. Precocious puberty is reported to be associated with McCune-Albright syndrome.¹

B. Cushing syndrome — Incorrect. Cushing syndrome is reported to be associated with McCune-Albright syndrome.¹

C. Hypophosphatemic rickets — Incorrect. Hypophosphatemic rickets is reported to be associated with McCune-Albright syndrome.²

D. Hyperthyroidism — Incorrect. Hyperthyroidism is reported to be associated with McCune-Albright syndrome.¹

E. Hyperparathyroidism — Correct. Precocious puberty, Cushing syndrome, hypophosphatemic rickets, and hyperthyroidism are all reportedly associated with McCune-Albright syndrome. Hyperparathyroidism is the only endocrinologic sequelae listed that has not been reported to be associated with McCune-Albright syndrome.³

Question 3: If this finding were associated with a syndromic condition, what gene mutation and mode of inheritance would be expected in this patient?

- A.** *SPRED1*; postzygotic mutation
- B.** *GNAS1*; autosomal dominant
- C.** *PTPN11*; autosomal dominant
- D.** *GNAS1*; postzygotic mutation
- E.** *STS*; X-linked recessive

Answers:

A. *SPRED1*; postzygotic mutation — Incorrect. Although McCune-Albright syndrome is caused by a postzygotic mutation, it is not a mutation in the *SPRED1* gene. Legius or NF1-like syndrome is caused by a postzygotic mutation in the *SPRED1* gene.

B. *GNAS1*; autosomal dominant — Incorrect. Although McCune-Albright syndrome is caused by a mutation in the *GNAS1* gene, it is not inherited in an autosomal dominant manner. Albright hereditary osteodystrophy is caused by a mutation in the *GNAS1* gene and is inherited in an autosomal dominant manner.

C. *PTPN11*; autosomal dominant — Incorrect. LEOPARD syndrome and not McCune-Albright syndrome is caused by a mutation in the *PTPN11* gene. The former is inherited in an autosomal dominant manner.

D. *GNAS1*; postzygotic mutation — Correct. McCune-Albright syndrome is caused by a nonheritable postzygotic mutation in the *GNAS1* gene. This mutation is found only in individuals demonstrating mosaicism.⁴ The protein product of the *GNAS1* gene, G_sα, is activated in excess as a result of this mutation, which overstimulates adenylyl cyclase,

leading to an overproduction of intracellular cyclic adenosine monophosphate.⁵

E. *STS*; X-linked recessive — Incorrect. X-linked ichthyosis and not McCune-Albright syndrome is caused by a mutation in the *STS* gene. The former is inherited in an X-linked recessive manner.

REFERENCES

1. Dumitrescu CE, Collins MT. McCune-Albright syndrome. *Orphanet J Rare Dis*. 2008;3:12.
2. Yamamoto T, Miyamoto K-I, Ozono K, et al. Hypophosphatemic rickets accompanying McCune-Albright syndrome: evidence that a humoral factor causes hypophosphatemia. *J Bone Min Metab*. 2001;19(5-6):287-295.
3. Hammami M, Al-Zahrani A, Butt A, Vencer L, Hussain S. Primary hyperparathyroidism-associated polyostotic fibrous dysplasia: Absence of McCune-Albright syndrome mutations. *J Endocrinol Invest*. 1997;20(9):552-558.
4. Vasilev V, Daly AF, Thiry A, et al. McCune-Albright Syndrome: A detailed pathological and genetic analysis of disease effects in an adult patient. *J Clin Endocrinol Metab*. 2014;99(10). <https://doi.org/10.1210/jc.2014-1291>.
5. Schwindinger WF, Francomano CA, Levine MA. Identification of a mutation in the gene encoding the alpha subunit of the stimulatory G protein of adenyl cyclase in McCune-Albright syndrome. *Proc Natl Acad Sci U S A*. 1992;89(11):5152-5156.