A unique localized eruption of rubbery flesh-colored nodules

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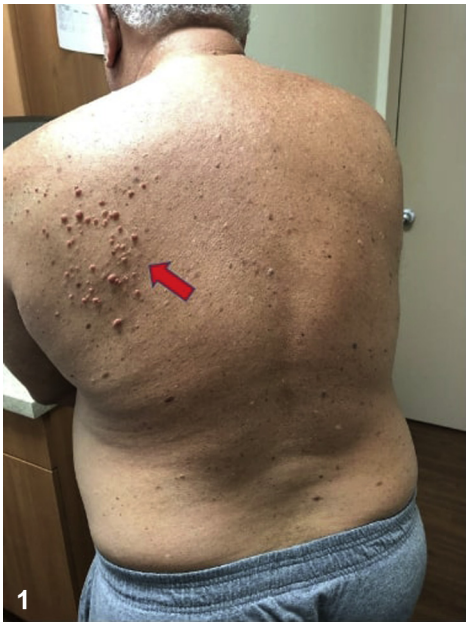

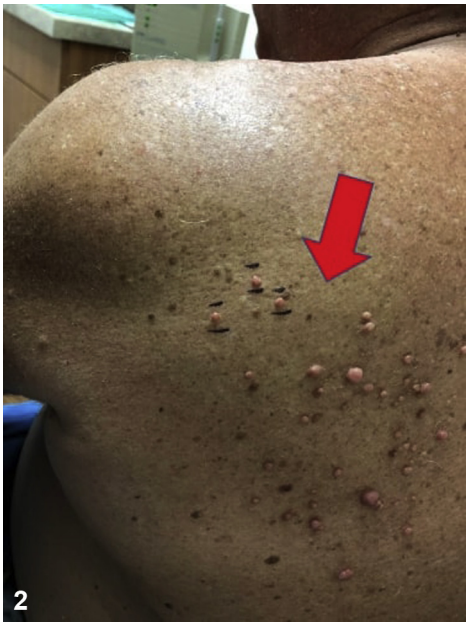

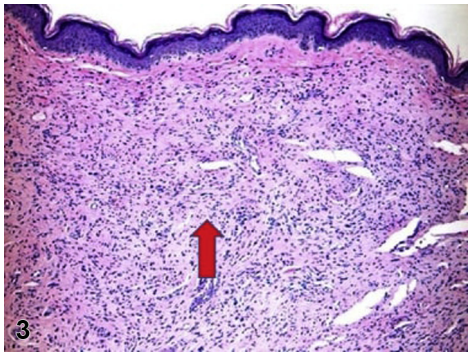

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CASE

A 63-year-old white man presented to the clinic for evaluation and management of multiple skin tags that first presented in childhood. Physical examination revealed a grouped collection of soft, nontender, pedunculated, skin-colored papules overlying the patient's left scapula (Figs 1 and 2). Although the patient initially denied any personal or family history of dermatologic disease, specific questioning revealed his siblings had similar findings to various degrees. Two shave biopsies (Fig 3) were performed to confirm the diagnosis. Referrals to a geneticist and ophthalmologist were offered but deferred by the patient because he had no plans to conceive and no active visual complaints.

Question 1: What other finding would you expect on examination and history taking in this patient?

A. Shagreen patches

B. Hemangioblastomas

C. Pectus excavatum

D. Café au lait macules

E. Ash-leaf spots

Answers:

A. Shagreen patches—Incorrect. Shagreen patches are commonly observed with tuberous sclerosis complex.

B. Hemangioblastomas—Incorrect. Hemangioblastomas are most commonly observed with Von Hippel Lindau.

C. Pectus excavatum—Incorrect. Pectus excavatum or pectus carinatum can be observed in Legius syndrome, also known as NF1-like syndrome.

D. Café au lait macules—Correct. Café au lait macules, Lisch nodules, and axillary freckling are other commonly observed cutaneous manifestations of segmental neurofibromatosis. The patient did not exhibit any other manifestations of neurofibromatosis type 1, including other eruptions of neurofibromas, axillary or groin freckling, or café-au-lait macules. Although the patient did decline a referral to ophthalmology, which may have recognized Lisch nodules, none were observed on our physical examination.

E. Ash-leaf spots—Incorrect. Ash-leaf spots are commonly observed with tuberous sclerosis complex, associated with mutations in the *TSC1* and *TSC2* genes.

Question 2: What is the mechanism of pathogenesis of this condition?

A. Loss of function mutation of the *TSC1* gene

B. Pathogenic variant of the *SPRED1* gene

C. Mutation of the *LZTR1* gene

D. Nontruncating mutation of the *SMARCB1* gene

E. Postzygotic mutation of the *NF1* gene

Answers:

A. Loss of function mutation of the *TSC1* gene—Incorrect. Mutation of the *TSC1* and *TSC2* genes is observed in tuberous sclerosis complex. This condition is characterized by ash-leaf spots and cutaneous hamartomas.

B. Pathogenic variant of the *SPRED1* gene—Incorrect. Mutation of the *SPRED1* gene is observed in Legius syndrome, which presents with café au lait macules without neurofibromas.[1]

C. Mutation of the *LZTR1* gene—Incorrect. Mutation of the *LZTR1* gene is a mechanism of pathogenesis for schwannomatosis, which is characterized by diffuse schwannomas. The most common presenting symptom is diffuse or localized pain.[2]

D. Nontruncating mutation of the *SMARCB1* gene—Incorrect. Mutation of the *SMARCB1* gene is associated with schwannomatosis. Mutations typically occur in exon 1 or the 3′ untranslated region.[3]

E. Postzygotic mutation of the *NF1* gene—Correct. Segmental neurofibromatosis is conventionally due to genetic mosaicism via postzygotic mutations in the *NF1* gene on chromosome 17.[4]

Question 3: Because of this condition, this patient is at an increased risk for developing which of the following malignancies?

A. Malignant peripheral nerve sheath tumors

B. Renal cell carcinoma

C. Basal cell carcinoma

D. Colorectal carcinoma

E. Medullary thyroid cancer

Answers:

A. Malignant peripheral nerve sheath tumors—Correct. The incidence of malignancy in a patient with neurofibromatosis has been estimated at 36% by aged 70 years. The presence of neurofibromas is

recognized as a risk factor for malignant peripheral nerve sheath tumors.[5]

B. Renal cell carcinoma—Incorrect. Renal cell carcinoma is more commonly observed in patients with tuberous sclerosis complex rather than segmental neurofibromatosis.

C. Basal cell carcinoma—Incorrect. Because of the neural crest origin of both melanocytes and Schwann cells, the incidence of malignant melanoma has been speculated to be increased in patients with neurofibromatosis. However, there is no evidence to suggest an increased incidence of basal cell carcinomas in this population subtype.

D. Colorectal carcinoma—Incorrect. Gastrointestinal tract carcinomas—specifically, colorectal carcinomas—are more commonly observed in patients with Peutz-Jeghers syndrome, an autosomal dominantly inherited disease that commonly presents in childhood but can be observed at any age.

E. Medullary thyroid cancer—Incorrect. Medullary thyroid cancer is more often observed in association with multiple endocrine neoplasia type 2B, which can also cause mucosal neuromas resembling the neurofibromas of neurofibromatosis.

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