JAMA Dermatology Clinicopathological Challenge

Hypertrichotic Plaque in a 17-Month-Old Boy

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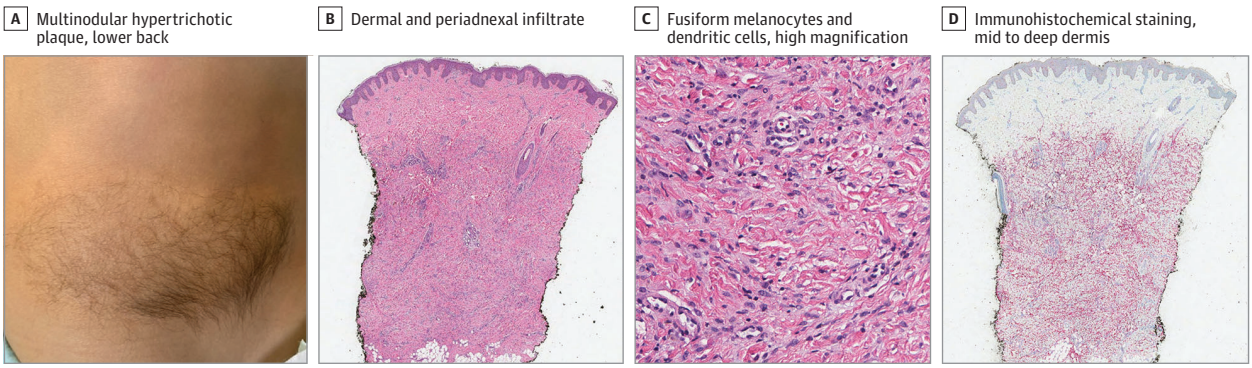

Figure. A, Large, well-defined, firm yellow to skin-colored multinodular hypertrichotic plaque on the left lower back. B, Hematoxylin-eosin staining demonstrates diffuse dermal infiltration of spindle cells, predominantly encircling terminal folliculosebaceous units (original magnification ×4). C, Higher-power magnification highlights a mix of partially fusiform melanocytes and dendritic cells with glassy, eosinophilic cytoplasm (hematoxylin-eosin, original magnification ×40). D, Immunohistochemical staining reveals diffuse and periadnexal S100 positivity in the mid to deep dermis (original magnification ×4).

A 17-month-old boy was referred to pediatric dermatology for evaluation of a slow-growing, nontender plaque on the lower back. The child's mother reported that, on discovery, the plaque was initially 1 × 1 cm and had since grown in size with the child. She was uncertain if the plaque was present at birth. The patient's medical history was significant for dermal melanocytosis of the right hip and mid back, increased head circumference (97th percentile), and expressive language delay. There was no family history of congenital birthmarks or neurofibromatosis type 1 or 2.

Physical examination revealed a well-appearing boy with normal vital signs and Fitzpatrick type III skin type. On the left lower back, there was a 15 × 5-cm indurated skin-colored to yellow, firm, multinodular plaque with hypertrichosis, extending from the midline to the left lower flank (**Figure**, A). There were additional blue-gray patches on the back and right hip, as well as a small café au lait macule on the right lower back. Limited neurologic examination was within normal limits. A 4-mm punch biopsy was performed for further diagnostic evaluation (Figure, B-D).

WHAT IS YOUR DIAGNOSIS?

A. Becker nevus

B. Neurocristic hamartoma

C. Smooth muscle hamartoma

D. Plexiform neurofibroma

Quiz at jamacmelookup.com

Diagnosis

B. Neurocristic hamartoma

Microscopic Findings and Clinical Course

Histopathologic evaluation findings demonstrated a diffuse dermal proliferation of partially fusiform spindled cells in the mid to deep dermis with entrapped enlarged terminal folliculosebaceous units. Immunohistochemical staining was positive for S100, CD34, and SOX-10 and negative for desmin, SMA, and CD1a. Partial expression of Melan A and epithelial membrane antigen stains were noted. This combination of clinical and histopathologic examination findings led to a diagnosis of neurocristic hamartoma.

A magnetic resonance image of the lumbar spine was obtained, which showed a contrast-enhancing cutaneous lesion extending between the L3 and L5 spinal segment, with branches of enhancement extending into the paraspinous soft tissues of the L4 and the deep subcutaneous tissues of the L3 spinous process. There was no evidence of spinal involvement or dysraphism. Because the lesion extended into the deep subcutaneous tissue of the L3 to L5 spinal segments, annual magnetic resonance imaging surveillance was recommended, with a low threshold for rebiopsy if pigment or new features emerged.

Discussion

Neurocristic hamartomas (NCHs) are rare collections of dermal neuromesenchymal cells of neural crest origin. While NCHs were initially thought to be variants of blue nevi, they are now known to have unique clinical and histologic features.[1] Neurocristic hamartoma is derived from the aberrant differentiation of pluriopotent neural crest cells into Schwann cells, melanocytes, and pigmented dendritic cells.[2] While typically congenital, NCH may be acquired from sites of constant pluripotent-cell activation.[2]

Neurocristic hamartomas present similarly to blue nevi, typically as blue-to-black hyperpigmented plaques on the head or neck with fo-

cal alopecia.[3] While the majority of cases are seen on the scalp, NCHs have been reported to occur on the back and face.[4] Neurocristic hamartomas may overlap with other disorders of neural crest, including neurofibromatosis type 1 (NF1) and neurocutaneous melanosis.[2] Of 32 cases of NCH reported in the literature, 12 (38%) had malignant transformation into melanoma and 6 (19%) metastasized.[4-6] Genetic analysis of malignant NCH has demonstrated a lack of *BRAF*, *GNAQ*, *NRAS*, and *KIT* mutations, suggesting a separate mechanism for malignant transformation compared with malignant melanoma.[6] Histologically, NCHs have overlapping features with blue nevi, including heavily pigmented spindled cells with a fusiform appearance and a predilection for adnexal structures.[1] However, NCHs have additional neural and Schwann cell differentiation.[1] Neurocristic hamartomas stain positive for S100, HMB-45, and CD-34 markers in the stroma.[2,4]

Becker nevus (BN) is a solitary hyperpigmented plaque with male predilection that may involve any region of the body. Becker nevus arises during the first decade of life, often developing hypertrichosis during the second decade of life because of its androgen-dependent nature. Becker nevus may be associated with hypoplasia or hyperplasia, or asymmetry of the affected area.[7] In this patient, while both BN and the NCH appeared in the first decade with hypertrichosis, BN exhibits epidermal hypermelanosis and acanthosis with few melanocytes in the dermis. Smooth muscle hamartoma (SMH) is a congenital, solitary hyperpigmented and hypertrichotic plaque commonly involving the trunk, buttocks, and lower extremities. These are distinguished from similar lesions by a positive pseudo-Darier sign. Malignant transformation has not been reported.[8] While both NCH and SMH can present as solitary hyperpigmented and hypertrichotic plaques, SMHs display as collections of spindled smooth muscle cells throughout the dermis, in contrast to the collection of neural crest–derived cells in NCH. Plexiform neurofibromas (PNs) are associated with NF1 and present as tender, firm subcutaneous nodules with a "bag of worms" consistency that span along the length of peripheral nerves. Superficial PNs may be characterized by hyperpigmentation and hypertrichosis, easily confused for congenital melanocytic nevi. Approximately 8% to 12% of patients with NF1 develop malignant peripheral nerve sheath tumors from PNs, with the potential to infiltrate into nerves, muscle, and fascia.[9] Although both PNs and NCHs can demonstrate S100 positivity, the patient described herein had a diffuse proliferation of spindled cells in contrast to the clear fascicles present in PN.

Neurocristic hamartoma is a rare diagnosis that should be considered on the differential for hypertrichotic plaques in children as well in cases of focal alopecia, such as aplasia cutis, especially because that is a more common clinical presentation. Owing to the paucity of reported cases, long-term management is not well understood. However, given the possibility of malignant transformation, periodic skin examinations are recommended.

ARTICLE INFORMATION

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