Enlarging Nodule on the Back

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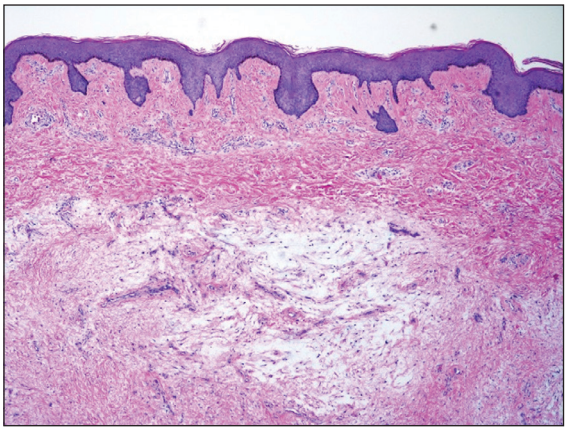

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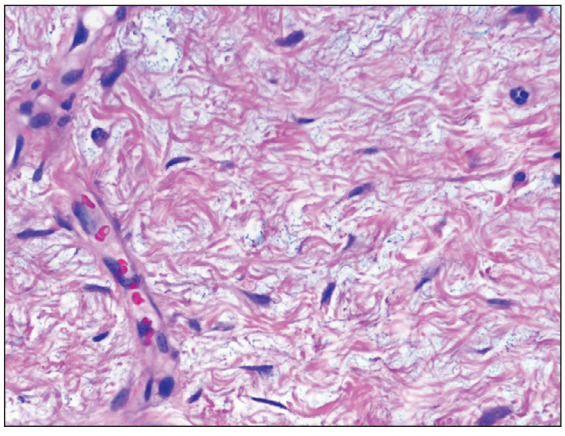

H&E, original magnification ×40.

A 43-year-old man with an unremarkable medical history presented to our clinic with an enlarging painful nodule on the upper back that was present for years without bleeding or ulceration. He denied prior treatment or any similar lesions. Physical examination was notable for a 2×1.5-cm, pedunculated, flesh-colored nodule on the left upper back. A shave excision of the lesion was performed.

THE BEST **DIAGNOSIS IS:**

a. cutaneous myxoma
b. nerve sheath myxoma
c. neurofibroma
d. nodular fasciitis
e. spindle cell lipoma

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THE **DIAGNOSIS:** Cutaneous Myxoma

Microscopic analysis showed features of cutaneous myxoma (quiz images). The epidermis was essentially unremarkable. Stellate to spindle cells with bland nuclear chromatin were present in the dermis with abundant pools of myxoid stroma. Colloidal iron staining highlighted the markedly increased dermal mucin.

Cutaneous myxomas (also referred to as superficial angiomyxomas) are rare, well-demarcated tumors of the dermis and subcutis.[1,2] They can present as solitary, flesh-colored nodules on the trunk, lower extremities, head, or neck, and they often measure between 1 and 5 cm.[2,3] Histologically, cutaneous myxomas are hypocellular with some stellate fibroblasts, occasional epithelial structures, and an abundant myxoid stroma, with notable thin-walled small blood vessels.[2,4] These lesions contain pools of mucin and are positive for mesenchymal mucin stains such as colloidal iron and Alcian blue.[1] Moreover, perivascular neutrophils are a distinguishing characteristic of cutaneous myxomas.[4]

Multiple cutaneous myxomas should raise concern for Carney complex,[1,5] a genodermatologic syndrome that arises due to a mutation in the protein kinase CAMP-dependent type I regulatory subunit alpha gene, *PRKAR1A*, on chromosome 2.[1,5] Additional cutaneous manifestations include blue nevi, lentigines, and café-au-lait macules.[5] Carney complex also is known for endocrine overactivity and cardiac myxomas, which can cause serious embolic complications.[1]

Recommended management is complete excision with close follow-up, as these lesions may recur in up to one-third of cases. Although there is a potential for recurrence, metastases are uncommon.[3] Even without recurrence in the presenting location, follow-up should include screening for manifestations of Carney complex.[1,3]

The clinical and histological differential for cutaneous myxoma may include nerve sheath myxoma or neurofibroma. A nerve sheath myxoma is a dermal tumor that manifests as a solitary, flesh-colored nodule, measuring less than 2 cm. These lesions commonly present on the head, neck, and upper body.[6] Cutaneous myxomas can grow larger than 2 cm, but these two lesions have a great deal of overlap in their other features.[3,6] Thus, histology can be used to distinguish them.

Nerve sheath myxomas are circumscribed nonencapsulated tumors of the dermis composed of multilobular aggregates of spindle to epithelioid cells in a mucinous matrix (Figure 1). Clefts often are present around the cell aggregates. Despite previously being termed *myxoid neurothekeomas*, nerve sheath myxomas are S-100 positive, whereas cellular neurothekeomas are S-100 negative and likely not of neural origin. Cutaneous myxomas, in contrast to nerve sheath myxomas, are S-100 negative. Nerve sheath myxomas are more cellular and lack the characteristic mucin pools compared with cutaneous myxomas.[1,2,6]

Neurofibromas frequently are flesh colored and pedunculated, as was the lesion in our patient, yet they are vastly different microscopically. The stroma of neurofibromas can vary, but cellularity typically is greater than a cutaneous myxoma and consists of increased numbers of bland spindle cells with wavy nuclei (Schwann cells) and fibrillar cytoplasm as well as mast cells and fibroblasts (Figure 2). Neurofibromas stain positively for S-100 and SOX-10 (Sry-related HMg-box 10).[2,7] In addition to café-au-lait macules, axillary freckling, optic gliomas, and

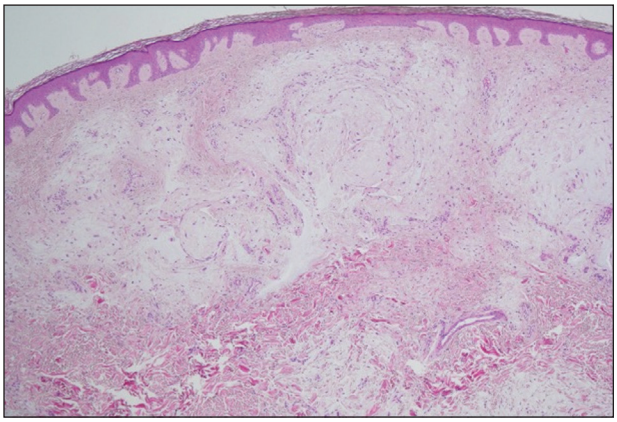

FIGURE 1. Nerve sheath myxoma. Multilobate tumors with clefts (H&E, original magnification ×10).

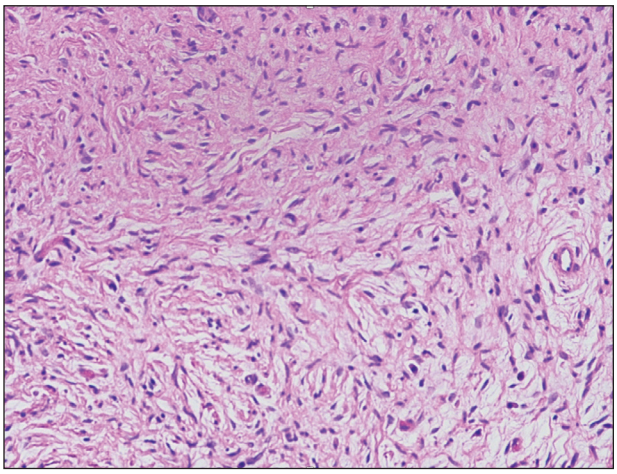

FIGURE 2. Neurofibroma. Cellular lesion of spindle cells with wavy nuclei (H&E, original magnification ×40).

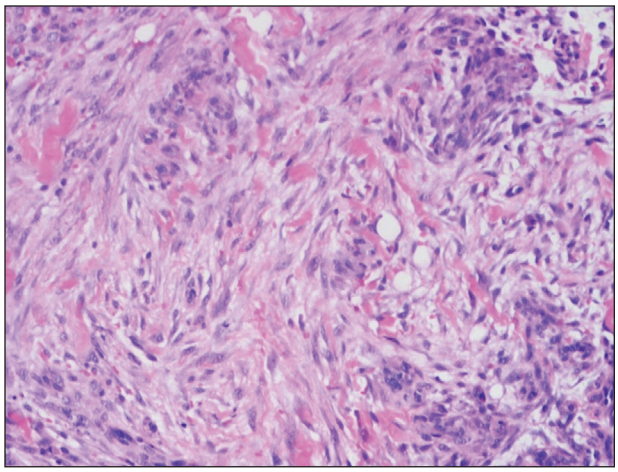

FIGURE 3. Nodular fasciitis. Zonal proliferation of spindle and stellate fibroblasts and myofibroblasts with extravasated erythrocytes (H&E, original magnification ×40).

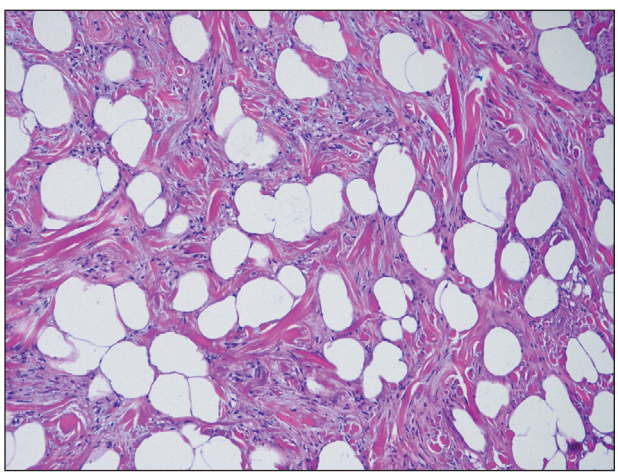

FIGURE 4. Spindle cell lipoma. Proliferation of adipocytes, aggregates of bland spindle cells associated with a mucinous matrix and collagen (H&E, original magnification ×40).

positive family history, neurofibromas are associated with neurofibromatosis type 1, which is linked to a defect in a tumor suppressor gene that codes for neurofibromin.[7]

Nodular fasciitis is a self-limited myofibroblastic neoplasm that contains fusion genes, with the most common being myosin-9–ubiquitin specific peptidase 6, *MYH9-USP6*, which leads to overexpression of *USP6*. Nodular fasciitis presents as a solitary, rapidly enlarging nodule affecting the subcutaneous tissue, muscles, or fascia.[8,9] It usually presents in the third or fourth decades of life.[8] The arms are the most common location in adults, while the most commonly affected site in children is the head or neck. Histopathology reveals a characteristic tissue culture pattern with a proliferation of plump spindle and stellate fibroblasts as well as myofibroblasts (Figure 3). Early lesions have haphazard spindle cells with a proliferation of small blood vessels and extravasated erythrocytes. Despite increased mitotic figures, cellular atypia is rare. The fibroblasts and myofibroblasts react positively for vimentin and muscle-specific actin.[8] This lesion is highly cellular comparatively and notably lacks the perivascular neutrophils and epithelial structures that would be expected in a cutaneous myxoma.[4,8]

Spindle cell lipomas, solitary subcutaneous masses commonly presenting on the upper back in middle-aged men, also can mimic cutaneous myxomas.[4] Histologically, these lesions may contain short bundles of spindle cells arranged in a school of fish–like pattern, mature adipocytes, or myxoid stroma and characteristic CD34 positivity (Figure 4). Spindle cell lipomas often will present with ropey collagen, which can easily distinguish them from cutaneous myxomas.[4]

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