Protuberant, Pink, Irritated Growth on the Buttocks

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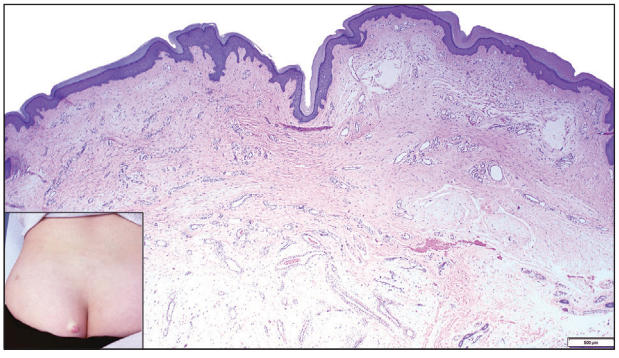
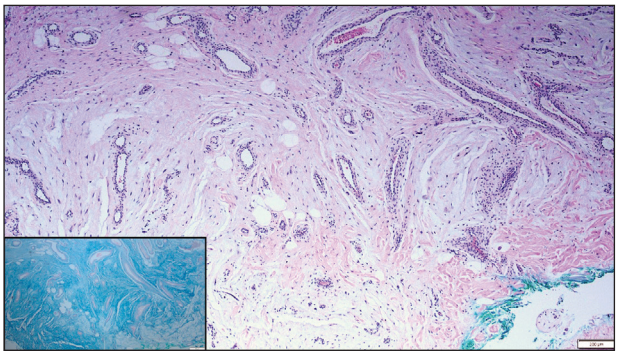


H&E, original magnification ×4. Reference bar indicates 500 μm.



H&E, original magnification ×10 (reference bar indicates 200 μm). Inset: colloidal iron stain, original magnification ×10 (reference bar indicates 50 μm).

A 25-year-old woman presented with an irritated growth on the left buttock of 6 months' duration. The lesion had grown slowly over time and became irritated because of the constant rubbing on her clothing due to its location. Physical examination revealed a 1-cm, pink, protuberant, soft, dome-shaped nodule on the left upper medial buttock (inset). A biopsy was performed for diagnostic purposes.

THE BEST **DIAGNOSIS IS:**

a. focal cutaneous mucinosis
b. myxofibrosarcoma
c. neurofibroma
d. spindle cell lipoma
e. superficial angiomyxoma

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The authors report no conflict of interest.
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THE **DIAGNOSIS:** Superficial Angiomyxoma

Superficial angiomyxoma is a rare, benign, cutaneous tumor of a myxoid matrix and blood vessels that was first described in association with Carney complex.[1] Tumors may be solitary or multiple. A recent review of cases in the literature revealed a roughly equal distribution of superficial angiomyxomas in males and females occurring most frequently on the head and neck, extremities, and trunk or back. The peak incidence is between the fourth and fifth decades of life.[2] Superficial angiomyxomas can occur sporadically or in association with Carney complex, an autosomal-dominant condition with germline inactivating mutations in protein kinase A, *PRKAR1A*. Interestingly, sporadic cases of superficial angiomyxoma also have shown loss of *PRKAR1A* expression on immunohistochemistry (IHC).[3]

Common histologic mimics of superficial angiomyxoma include aggressive angiomyxoma and angiomyofibroblastoma.[4] It is thought that these 3 distinct tumor entities may arise from a common pluripotent cell of origin located near connective tissue vasculature, which may contribute to the similarities observed between them.[5] For example, aggressive angiomyxomas and angiomyofibroblastomas also demonstrate a similar myxoid background and vascular proliferation that can closely mimic superficial angiomyxomas clinically. However, the vessels of superficial angiomyxomas tend to be long and thin walled, while aggressive angiomyxomas are characterized by large and thick-walled vessels and angiomyofibroblastomas by abundant smaller vessels. Additionally, unlike superficial angiomyxomas, both aggressive angiomyxomas and angiomyofibroblastomas typically occur in the genital tract of young to middle-aged women.[6]

Histopathologic examination is imperative for differentiating between superficial angiomyxoma and more aggressive histologic mimics. Superficial angiomyxomas typically consist of a rich myxoid stroma, thin-walled or arborizing blood vessels, and spindled to stellate fibroblastlike cells (quiz image 2).[3] Although not prominent in our case, superficial angiomyxomas also frequently present with stromal neutrophils and epithelial components, including keratinous cysts, basaloid buds, and strands of squamous epithelium.[7] Minimal cellular atypia, mitotic activity, and nuclear pleomorphism often are seen, with IHC negative for desmin, estrogen receptor, and progesterone receptor; positive for CD34 and smooth muscle actin; and variable for S-100 and muscle-specific actin. Although IHC has limited utility in the diagnosis of superficial angiomyxomas, it may be useful to rule out other differential diagnoses.[2,3] Superficial angiomyxomas usually show fibroblastic stromal cells, proteoglycan matrix, and collagen fibers on electron microscopy.[8] Importantly, histopathologic examination of aggressive angiomyxoma will comparatively present with more invasive, infiltrative, and less well-circumscribed tumors.[9] Other differential diagnoses on histology may include neurofibroma, focal cutaneous mucinosis, spindle cell lipoma, and myxofibrosarcoma. Additional considerations include fibroepithelial polyp, nevus lipomatosis, angiomyxolipoma, and anetoderma.

An important differential diagnosis in the evaluation of superficial angiomyxoma is neurofibroma, a benign peripheral nerve sheath tumor that presents as a smooth, flesh-colored, and painless papule or nodule commonly associated with the buttonhole sign. Histopathology of neurofibroma features elongated spindle cells with comma-shaped or buckled wavy nuclei and variably sized collagen bundles described as "shredded carrots" (Figure 1).[10] Occasional mast cells also can be seen. Immunohistochemistry targeting elements of peripheral nerve sheaths may assist in the diagnosis of neurofibromas, including positive S-100 and SOX10 in Schwann cells, epithelial membrane antigen in perineural cells, and fingerprint positivity for CD34 in fibroblasts.[10]

Cutaneous mucinoses encompass a diverse group of connective tissue disorders characterized by accumulation of mucin in the skin. Solitary focal cutaneous mucinoses (FCMs) are individual isolated lesions of mucin deposits that are unassociated with systemic conditions.[11] Conversely, multiple FCMs presenting with multiple cutaneous lesions also have been described in association with systemic diseases such as scleroderma, systemic lupus erythematosus, and thyroid disease.[12] Solitary FCM typically presents as an asymptomatic, flesh-colored papule or nodule on the extremities. It often arises in mid to late adulthood with a slightly increased frequency among males.[12] Histopathology of solitary FCM commonly

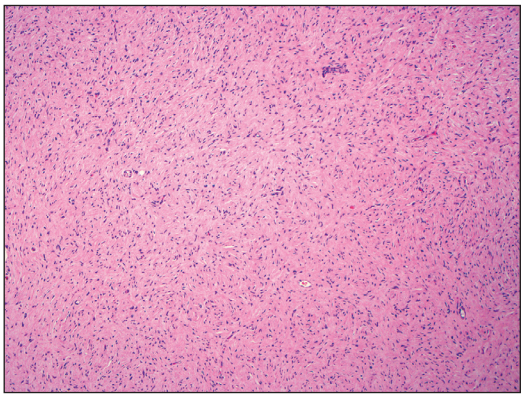

FIGURE 1. Neurofibroma. Interlacing bundles of elongated cells with comma-shaped nuclei are seen on a background of variably sized collagen bundles where the stroma contains mucin and interspersed mast cells (H&E, original magnification ×10).

demonstrates a dome-shaped pool of basophilic mucin in the upper dermis sparing involvement of the underlying subcutaneous tissue (Figure 2).[13] Notably, FCM often lacks the vascularity as well as stromal neutrophils and epithelial elements that are seen in superficial angiomyxomas. Although hematoxylin and eosin stains can be sufficient for diagnosis of solitary FCM, additional stains for mucin such as Alcian blue, colloidal iron, or toluidine blue also may be considered to support the diagnosis.[12]

Spindle cell lipomas (SCLs) are rare, benign, subcutaneous, adipocytic tumors that arise on the upper back, posterior neck, or shoulders of middle-aged or elderly adult males.[14] The clinical presentation often is an asymptomatic, well-circumscribed, mobile subcutaneous mass that is firmer than a common lipoma. Histologically, SCLs are characterized by mature adipocytes, spindle cells, and wire or ropelike collagen fibers in a myxoid background (Figure 3). The spindle cells usually are bland with a notable bipolar shape and blunted ends. Infiltrative growth patterns or mitotic figures are uncommon. Diagnosis can be supported by IHC, as SCLs stain diffusely positive for CD34 with loss of the retinoblastoma protein.[7]

Another important differential diagnosis to consider is myxofibrosarcoma, a rare and malignant myxoid cutaneous tumor. Clinically, it presents asymptomatically as an indolent, slow-growing nodule on the limbs and limb girdles.[7] Histopathologic features demonstrate a multilobular tumor composed of a mixture of hypocellular and hypercellular regions with incomplete fibrous septae (Figure 4). The presence of curvilinear vasculature is characteristic. Multinucleated giant cells and cellular atypia with nuclear pleomorphism also can be seen. Although IHC findings generally are not specific, they can be used to rule out other potential diagnoses. Myxofibrosarcomas stain positive for vimentin and occasionally smooth muscle actin, muscle-specific actin, and CD34.[7]

Superficial angiomyxomas are benign; however, excision is recommended to distinguish between mimics. Local recurrence after excision is common in 30% to 40% of patients.[15] Mohs micrographic surgery has been considered, especially if the following are present: tumor characteristics (eg, poorly circumscribed), location (eg, head and neck or other cosmetically or functionally sensitive areas), and likelihood of recurrence (high for superficial angiomyxomas).[16] This case otherwise highlights a rare example of superficial angiomyxomas involving the buttocks.

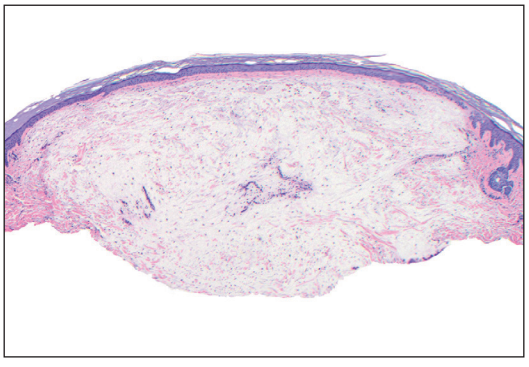

FIGURE 2. Focal cutaneous mucinosis. An isolated dome-shaped lesion with a focal, circumscribed, dermal pool of mucin and surrounding dermis with slightly increased fibroblasts (H&E, original magnification ×4).

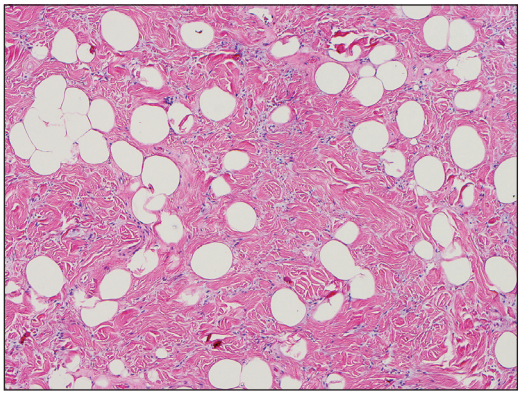

FIGURE 3. Spindle cell lipoma. A well-circumscribed subcutaneous tumor of mature adipocytes, spindle cells, and ropey collagen fibers with no infiltrative growth pattern or mitotic figures (H&E, original magnification ×10).

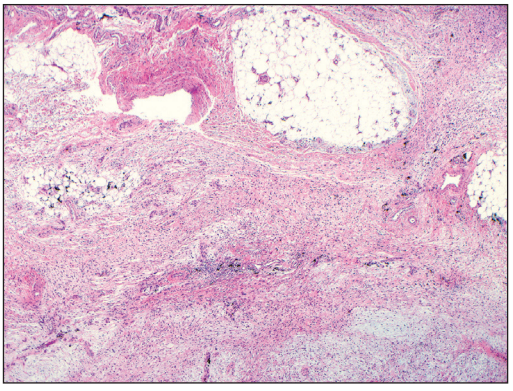

FIGURE 4. Myxofibrosarcoma. A lobulated tumor with a mixture of hypocellular and hypercellular areas with incomplete fibrous septae. Cells with atypical nuclei and pleomorphism with occasional multinucleated giant cells also are seen (H&E, original magnification ×10).

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