Pathologic Quiz Case

A 69-Year-Old Asymptomatic Man With a Scrotal Mass

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A 69-year-old white man presented to his physician with complaints of a scrotal mass that he first noticed 5 to 6 years previously and that had remained stable in size during that period. A physical examination showed an irregular, nontender, fixed mass in the anterior scrotal wall. A scrotal ultrasound showed a bilobed, solid-appearing subcutaneous structure in the anterior portion of the scrotal wall (Figure 1, arrow); the testes were normal bilaterally. The radiologist's diagnosis was a sebaceous cyst. The mass was subsequently excised and then submitted to our laboratory, where it was processed routinely.

Grossly, the specimen consisted of a 3 × 3-cm ellipse of skin with an underlying 3 × 2.5-cm firm, well-delineated mass. The cut surface was tan-yellow and solid, with a mildly variegated appearance. At scanning magnification, the tumor was subcutaneous and unencapsulated, consisting of 2 unequal lobules separated by an irregular strip of collagenous tissue, and it showed well-circumscribed, noninfiltrating margins. At higher magnification, typical interlacing fascicles of spindle cells with predominantly cigar-shaped nuclei and abundant eosinophilic cytoplasm were present (Figures 2 and 3). Constituting approximately 30% of the tumoral nuclei were diffusely distributed, highly pleomorphic nuclei displaying nucleomegaly, hyperchromasia, and pseudoinclusions (Figure 4). Mitotic figures could not be identified, and necrosis was absent. Immunohistochemistry was performed on 4-μm-thick sections of the tumor with a Dako Corporation (Carpinteria, Calif) autostainer using a panel of monoclonal antibodies. The tumor displayed strong immunoreactivity for desmin (dilution 1:1000; Ventana, Tucson, Ariz), h-caldesmon (dilution 1:50; Dako), and smooth muscle actin (dilution 1:2; Sigma Chemical Company, St Louis, Mo) and was negative for HMB-45 (dilution 1:400; Dako) and keratin AE1/AE3 (dilution 1:1200; Chemicon International, Temecula, Calif).

What is your diagnosis?

Accepted for publication September 19, 2003.

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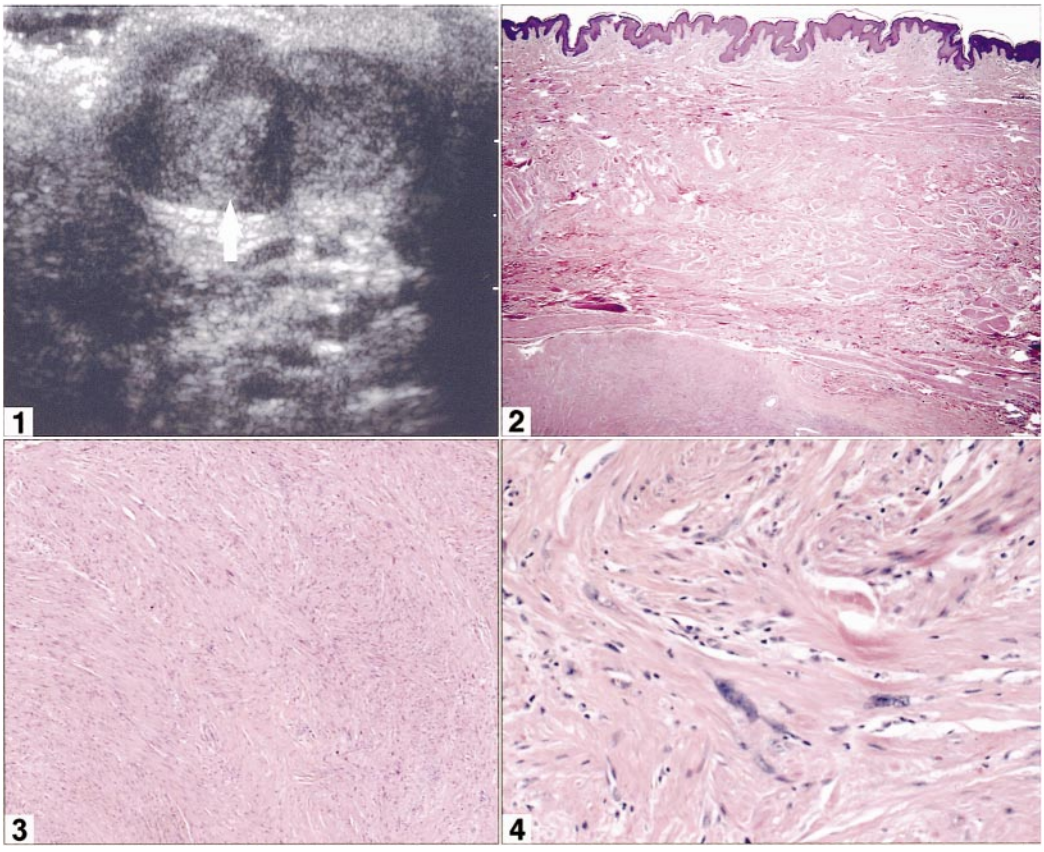

Pathologic Diagnosis: Atypical (Symplastic or Bizarre) Leiomyoma of the Scrotum

In most organ systems, there are well-defined pathologic parameters that help delineate malignant smooth muscle tumors from their benign counterparts. Among these, the presence or absence of cytologic atypia, coagulative necrosis, and increased mitotic activity are generally the most important, although specific criteria for malignancy differ from organ to organ. For lesions at either extreme, the presence or absence of all 3 features helps the physician predict with a reasonable degree of certainty, purely from pathologic features, the malignant potential of any given smooth muscle proliferation. Difficulties in predicting biologic behavior result when one or more of the pathologic features that have been outlined are absent in a specific tumor. In the uterine corpus, which is the most common anatomic site for smooth muscle neoplasia, elaborate algorithms and specific designations have long been used to deal with tumors at various points along the spectrum.[1] One such tumor is the *symplastic, atypical, bizarre, or pleomorphic leiomyoma.* In the uterine corpus and elsewhere, these benign smooth muscle tumors display bizarre, pleomorphic tumor cell nuclei, are mitotically inactive, and show no coagulative necrosis. Furthermore, they serve as an embodiment of the principle that nuclear pleomorphism does not necessarily equate to malignancy.

Smooth muscle tumors of the scrotum, presumably arising from the dartos muscle in that region, are distinctly uncommon, with less than 70 cases in the medical literature. Even less common are symplastic leiomyomas. To our knowledge, this is only the 10th case reported in this region. The 9 previous cases[2–8] occurred in men in their fourth to seventh decades of life, and their tumors were generally painless, solitary, and well circumscribed. None have recurred or metastasized. The series of 3 cases by Slone and O'Connor[3] represents the largest in the literature. The clinical impression in all 3 of their cases, similar to ours, was a cyst.

The differential diagnosis for this case includes piloleiomyomas (which presumably arise from the arrectores pilorum muscles), angioleiomyomas (which presumably arise from the musculature of vessels), and leiomyosarcomas. Angioleiomyomas are frequently encapsulated and, as the name suggests, are highly vascularized. Piloleiomyomas are usually poorly delineated and are more dermal than subcutaneous. Neither piloleiomyomas nor angioleiomyomas should show significant cytologic atypia. In addition, both lesions are generally painful. In the distinction of atypical leiomyomas from leiomyosarcomas of the scrotum, Newman and Fletcher[8] emphasized that the presence of mitotic figures in the latter tumors is the most important distinguishing criterion. Despite the high degree of nuclear atypia in our case, the absence of mitotic activity and necrosis warrants the diagnosis of atypical leiomyoma.

The high degree of nuclear atypia in atypical leiomyomas is believed to represent a degenerative phenomenon, similar to the ''ancient'' change observed in some nerve sheath tumors.[8] Indeed, the low Ki-67 proliferative index as well as the infrequency of aneuploidy in uterine atypical leiomyomas[9] would seem to support this contention. Some preliminary but valuable insights into the molecular mechanisms underlying these lesions have recently been elucidated by Ernst et al.[10] These investigators showed that uterine atypical leiomyomas have significantly increased global DNA methylation compared to typical leiomyomas or normal myometrial tissue. Since DNA methylation is associated with DNA inactivation, it was suggested that the morphologically observed nuclear atypia represent excessive heterochromatin material, which has a known association with inactivated DNA. While these findings are certainly intriguing, further investigations are required. In addition, it is unclear if the fundamental pathobiology of morphologically similar tumors is identical across organ systems.

In summary, we have documented an example of an atypical leiomyoma of the scrotum, only the 10th such reported case, to our knowledge.

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