Pathologic Quiz Case

Testicular Pain and Scrotal Swelling in a 25-Year-Old Man

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A 25-year-old man presented to his personal physician complaining of left scrotal swelling and pain. A clinical diagnosis of epididymitis was rendered, and the patient was started on ciprofloxacin and scheduled for scrotal ultrasonography in 3 days. Ultrasonography revealed a 0.5-cm right testicular mass. The patient was referred to a urologist for further workup; no palpable masses were identified in either testis. A computed tomographic scan revealed no evidence of metastatic neoplasm, and β-human chorionic gonadotropin and α-fetoprotein levels were not elevated. Three days later, the patient underwent a right radical orchiectomy. The radical orchiectomy specimen consisted of a 3.5 × 2.4 × 2.0-cm testis with a portion of attached spermatic cord. Serial sections of the testis revealed a 0.5-cm, white, well-circumscribed nodule within the otherwise unremarkable tan testicular parenchyma. The lesion was solid and homogeneous with no areas of cystic change, hemorrhage, or necrosis. Microscopically, the lesion consisted of a well-circumscribed collection of neoplastic cells rimmed by a dense cuff of lymphoid tissue with occasional germinal centers (Figure 1). The tumor cells had ample eosinophilic vesicular cytoplasm and eccentric nuclei containing single eccentric nucleoli (Figure 2). The cells formed solid and hollow tubules and were set in a collagenous stroma (Figure 3). Scattered neutrophils were present in the tissue between the neoplastic cells. Rare calcifications were seen predominantly at the periphery of the tumor, some within foci of intratubular tumor (Figure 4); these calcifications were small and resembled psammoma bodies. A discontinuous fibrous capsule containing thick-walled vessels surrounded the neoplasm.

The testicular parenchyma uninvolved by the tumor was unremarkable. A periodic acid–Schiff stain demonstrated no glycogen in the cytoplasm of the tumor cells. Tumor cells showed moderately strong positivity for inhibin and were negative for placental alkaline phosphatase and low-molecular-weight cytokeratin. Other than a small postoperative hematoma at the surgical site, the patient's recovery was unremarkable, and the left-sided epididymitis resolved following antibiotic therapy.

What is your diagnosis?

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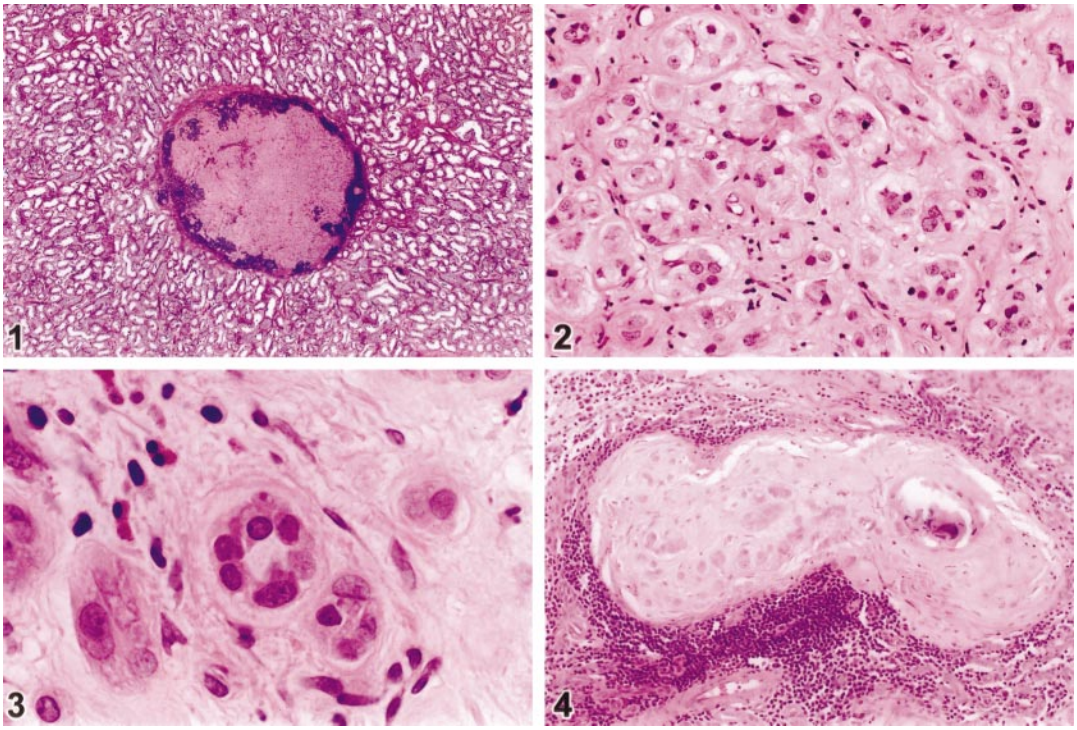

Pathologic Diagnosis: Large Cell Calcifying Sertoli Cell Tumor of the Testis

Sertoli cell tumors of the testis are uncommon neoplasms, accounting for a reported 1% of all testicular tumors.[1] Rare subtypes of this tumor have been designated as sclerosing and large cell calcifying types. First described by Proppe and Scully in 1980,[2] slightly more than 50 cases of large cell calcifying Sertoli cell tumor have been reported worldwide in the subsequent 20 years. These tumors have been described in the setting of Peutz-Jeghers syndrome[2] and as one of the findings in Carney complex.[3] Benign and malignant forms of large cell calcifying Sertoli cell tumors have been reported. Grossly well-circumscribed, light tan, and homogeneous, benign large cell calcifying Sertoli cell tumors are generally less than 4.0 cm in diameter and demonstrate low mitotic activity and no necrosis. Malignant forms of the tumor are larger, exhibit significant cellular atypia with necrosis, and show extratesticular spread or lymphovascular invasion[4]; mitotic activity greater than 3 mitoses per high-power field has also been associated with malignant behavior.[5] Only 1 case of large cell calcifying Sertoli cell tumor with distant metastasis has been documented to date.[6]

Histologically, large cell calcifying Sertoli cell tumors consist of nests and cords of eosinophilic cells set in a connective tissue background. Rarely, spindle cell morphology has been noted in these lesions.[7] The amount of calcification in these neoplasms is variable and ranges from large, readily identifiable calcifications to scattered psammoma-like microcalcifications. Neutrophilic infiltrates have also been observed in these lesions. Ultrastructurally, structures reminiscent of Charcot-Bottcher crystals have been seen in only a minority of cases.[8]

Based on the histologic morphology we have described, the differential diagnosis of these lesions is wide. Before the establishment of a large cell calcifying Sertoli cell tumor category, many of these tumors appear to have been misclassified as Leydig cell tumors. Currently, immunohistochemistry is of limited help in distinguishing these entities; both tumors may show varying degrees of expression of cytokeratin and inhibin. Tanaka et al,[9] however, have suggested some utility in differentiating these lesions by S100 protein subunit expression, with S100 β expression seen in tumors of Sertoli cell origin, but not of Leydig cell origin. Tubular formation should be seen only in Sertoli cell tumors, and any true tubular formation should exclude the diagnosis of Leydig cell tumor. Also, any degree of intratumoral calcification favors a large cell calcifying Sertoli cell tumor. Based on the general histologic features of the tumor in the current case, Leydig cell tumor was originally included in the differential diagnosis. The presence of true tubular formation in areas of the tumor as well as foci of intratubular growth, however, supported the diagnosis of a tumor of Sertoli cell origin.

The treatment for unilateral large cell calcifying Sertoli cell tumors has traditionally been radical orchiectomy, but in patients with bilateral tumors, such as those seen frequently in association with Carney complex, fertility and hormonal replacement become issues of greater concern. Given the potential risk of malignancy in these tumors, orchiectomy remains an option that must be presented to the patient. With no long-term follow-up reported on most cases, the efficacy of testis-sparing surgery versus radical orchiectomy remains an unsettled issue.

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