Stromal Tumor of Uncertain Malignant Potential of the Prostate

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- Stromal tumor of uncertain malignant potential (STUMP) of the prostate is a rare tumor with a variable and unpredictable clinical course. Many STUMPs are diagnosed incidentally and never progress, while others may invade locally and rapidly recur after surgical intervention, and yet others may lead to distant metastasis and death. A wide array of histologic patterns is encompassed by STUMP, and distinguishing these tumors from prostatic stromal sarcoma or other causes of stromal expansion often proves difficult. Owing to the rarity of this tumor, there is not yet a consensus on appropriate management. However, owing to the possibility of aggressive behavior, close management and consideration of definitive resection is warranted.

The clinical history of patients with STUMP is not well defined owing to the relative rarity of the tumor. Since 1998, there have been only a few published large case series that have summarized the major clinical features of patients with STUMP. Patients in these studies range in age from 25 to 86 years, with men in their sixth or seventh decade of life most commonly affected. In a study of 50 cases, only 17% of those with pure STUMP were younger than 50 years. The clinical, laboratory, and imaging abnormalities associated with STUMPs are generally nonspecific. The most common presenting signs and symptoms were chronic lower urinary tract obstructive symptoms, abnormal digital rectal examination findings, hematuria, hematospermia, rectal dysfunction and/or sensation of fullness, acute urinary retention, and elevated prostate specific antigen levels. On rectal examination, the prostate may be diffusely enlarged, nodular, or soft, spongy, and cystic. In a case report by Muglia et al., imaging findings for a patient with STUMP included enlargement and a heterogeneous appearance on ultrasonography, and diffuse heterogeneity and low enhancement on T2-weighted magnetic resonance imaging. Most STUMPs are diagnosed on needle biopsy or transurethral resection of the prostate, and less often by prostatectomy.

Pathologic Features

On gross examination, STUMP may be white, tan, or yellow and range from solid and firm to partially cystic and multiloculated. The lesions range in size from microscopic up to 15 cm with small or large smooth-walled cysts. The cyst contents may be serous, mucinous, or sanguinous. Both the peripheral and transitional zones of the prostate may be affected. In some cases, the tumor may extend out of the prostate and may be adherent to other organs of the pelvis. While STUMPs have a variety of histologic appearances, all cases are characterized by expansion of the specialized prostatic stroma. In all of the reported subtypes, mitotic activity is minimal and necrosis is not often seen.

The etiology and pathogenesis of STUMP is unknown, and no confirmed risk factors have been identified. A small number of cases are diagnosed in the setting of a concurrent prostatic adenocarcinoma. Owing to the rarity of these tumors, the classification, expected clinical course, and treatment recommendations are still a matter of debate.
the degree of stromal cytologic atypia, and the presence and appearance of a nonneoplastic epithelial component,2 and patterns may coexist in the same specimen.

The first pattern demonstrating marked cellular atypia akin to the so-called degenerative atypia seen in other spindle cell lesions is the most common and accounts for at least 50% of cases (Figure 1, A). It is composed of normal to slightly hypercellular stroma with scattered cytologically atypical cells interdigitating between benign prostatic glands (Figure 1, B). Stromal cells vary from plump to spindled with clear or lightly eosinophilic cytoplasm. Cytologic atypia is present and is manifested by degenerative-appearing cells with pronounced nuclear pleomorphism and enlargement; multinucleation; ground glass, vesicular, or smudged nuclei; prominent nucleoli; and occasional intranuclear inclusions. Squamous metaplasia is variably present.

The second, histologic pattern, “hypercellular,” consists of hypercellular stroma composed of bland, fusiform cells with eosinophilic cytoplasm, resembling benign prostatic hyperplasia (BPH) but with more hypercellular stroma. The cytologic atypia characteristic of the first pattern is absent. The associated epithelial elements are nonneoplastic and look similar to those present in the first pattern.

The third is composed of an expanded stroma and proliferating benign glandular elements reminiscent of the phyllodes tumor of the breast. The stroma is hypocellular, fibrotic, leaflike in configuration, and devoid of mitotic figures. Cytologically atypical, degenerative-appearing stromal cells, similar to those seen in the first pattern, are variably present. The stroma is covered by benign glands arranged in long, epithelial-lined clefts in a frondlike configuration, similar to those found in mammary phyllodes tumors. Metaplastic and/or proliferative changes in the glands are often present, including basal cell hyperplasia, adenosis, sclerosing adenosis, and squamous metaplasia.2

The fourth pattern, “myxoid,” is composed of expansive overgrowth of bland stromal cells within a myxoid background. This pattern often lacks glandular epithelium and may also resemble the stromal nodules of benign prostatic hyperplasia; however, myxoid STUMP consists of sheets of stromal cells and lacks the nodularity of BPH.8

Nagar and Epstein9 reviewed the epithelial component of a large cohort of STUMPs. The most common abnormality was glandular crowding (50%), followed by basal cell layer prominence (46%) and papillary infolding (19%). Less commonly observed were cystic glands, basal cell hyperplasia, urothelial metaplasia, squamous metaplasia, cribriform hyperplasia, adenosis, high- or low-grade prostatic intraepithelial neoplasia, and atrophy.

Some cases of STUMP have progressed to prostatic stromal sarcoma on subsequent biopsy, and some sarcomas are present in association with a concurrent STUMP, a feature that lends credibility to the hypothesis that STUMP has the ability to undergo malignant transformation.5 No correlation with the histologic subtype of STUMP and the association with progression to sarcoma has yet been documented.

**Figure 1.** Stromal tumor of uncertain malignant potential of the prostate in a 76-year-old man who has received conservative management for 9 years. This biopsy specimen consists of benign acini admixed with areas of plump, stromal cells with degenerative-type nuclear atypia, manifested by large, smudged nuclei with occasional multinucleation. Mitotic figures and necrosis are absent (hematoxylin-eosin, original magnifications ×10 [A] and ×20 [B]).

**Figure 2.** The stromal cells demonstrate nuclear positivity for progesterone receptor (Dako, Carpinteria, California) (original magnification ×20).
STUMP presents a significant challenge for patient management. While many will prove to be indolent in nature, their behavior is unpredictable. In cases where STUMP has behaved aggressively, dedifferentiated, or coexisted with sarcoma, no correlation with a specific histologic subtype or other risk factor has been identified. As such, close follow-up and consideration of surgical management, especially in younger patients, is warranted. The size and extent of the lesion, as well as patient age, comorbidities, and preferences, should be considered when determining a treatment plan.

The prognosis of STUMP is equally variable. One retrospective study found that in patients who did not undergo definitive resection, the tumor recurred in 46% of cases. In some cases, the tumor recurs several times, requiring multiple procedures over time. Several case reports have been published documenting patients diagnosed with STUMP who present with or develop distant metastasis, most commonly to the lung and lymph nodes. Two of the 3 patients in these reports died of their illness.

CONCLUSION

STUMP is a very rare tumor of the specialized prostatic stroma with an unpredictable clinical behavior. STUMP is considered by most a neoplasm with 4 distinct histologic patterns, and more than 1 may be present within the same tumor. These lesions may locally invade surrounding tissues or recur after surgical intervention and be a potential precursor to prostatic stromal sarcoma. Owing to the rarity of this entity, the classification, clinical course, and recommended treatments are still under debate.

References


Stromal Tumor of Uncertain Malignant Potential—Murer & Talmon

