

Stromal Tumor of Uncertain Malignant Potential of the Prostate

Lauren M. Murer, MD; Geoffrey A. Talmon, MD

• 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.


Prostatic stromal tumor of uncertain malignant potential (STUMP) is an exceedingly rare tumor of the specialized prostatic stroma that encompasses a broad spectrum of histologic patterns and clinical behavior. STUMP is considered by most to be a neoplastic lesion and is often morphologically similar to prostatic stromal sarcoma.1 The clinical course is unpredictable, ranging from a focal incidental finding on biopsy that never progresses, to an obstructing mass that recurs after resection, to a highly aggressive lesion leading to widespread metastases and death.

This entity has previously been classified under a variety of names including phyllodes tumor of the prostate, atypical stromal hyperplasia, cystosarcoma phylloides, and cystic epithelial-stromal tumor. Following a 1998 study by Gaudin et al,2 prostatic stromal lesions that were not obvious morphologically similar to prostatic stromal sarcoma.1 The clinical course is unpredictable, ranging from a focal incidental finding on biopsy that never progresses, to an obstructing mass that recurs after resection, to a highly aggressive lesion leading to widespread metastases and death.

This entity has previously been classified under a variety of names including phyllodes tumor of the prostate, atypical stromal hyperplasia, cystosarcoma phylloides, and cystic epithelial-stromal tumor. Following a 1998 study by Gaudin et al,2 prostatic stromal lesions that were not obvious morphologically similar to prostatic stromal sarcoma.1 The clinical course is unpredictable, ranging from a focal incidental finding on biopsy that never progresses, to an obstructing mass that recurs after resection, to a highly aggressive lesion leading to widespread metastases and death.

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.6 In a case report by Muglia et al,7 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,8 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.8 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.5

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.5,8 Gaudin et al15 classified STUMPs into 4 distinct histologic patterns by...
the degree of stromal cytologic atypia, and the presence and appearance of a nonneoplastic epithelial component, 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.

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.

Nagar and Epstein 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. No correlation with the histologic subtype of STUMP and the association with progression to sarcoma has yet been documented.
DIFFERENTIAL DIAGNOSIS AND ANCILLARY STUDIES

Given the variety of histologic appearances of STUMP, other proliferations of the specialized prostatic stroma must be considered in the differential diagnosis. Cases that exhibit hypercellular or myxoid stromal patterns with admixed benign epithelial components are often confused with the stromal proliferations present in BPH, and the distinction may prove difficult in small specimens. Indeed, this has led some experts to consider STUMP to be within the spectrum of BPH, although most agree that it is a distinct entity as it often rapidly recurs, is seen in younger men, occurs in the peripheral zone, may infiltrate locally, and may dedifferentiate to or coexist with stromal sarcoma. The presence of hypercellular stroma, eosinophilic cytoplasm, and lack of nodularity can assist in differentiating STUMP from BPH.

STUMP is often difficult to distinguish from low-grade prostatic stromal sarcoma by morphology, especially in cases with a preponderance of large, bizarre, degenerative nuclei. While primary prostatic stromal sarcomas are rare, their differentiation is critical as the long-term survival in patients with stromal sarcoma is poor, with a 5-year disease-free survival of 38%. The presence of necrosis, atypical mitotic figures, marked hypercellularity, and nuclear pleomorphism without degenerative features are features of sarcoma, rather than STUMP.

The atypical stromal cells of STUMP arise from the specialized, hormonally responsive mesenchymal cells of the prostate and as such express similar immunohistochemical properties to normal prostate and stromal sarcoma. STUMP, as well as prostatic stromal sarcoma, expresses progesterone receptor (Figure 2) but is negative for estrogen receptor. In addition, STUMP is positive for CD34 and vimentin, with variable staining for smooth muscle actin and desmin.

Sarcomatoid transformation of a high-grade prostatic adenocarcinoma may present with atypical spindle cells and may enter into consideration STUMPs with the common degenerative-atypia pattern. The presence of adjacent typical prostatic adenocarcinoma, combined with at least focal positivity for cytokeratins, may be helpful in separating the two.

Other spindle cell lesions that rarely involve the prostate may enter the differential diagnosis, including inflammatory myofibroblastic tumor, solitary fibrous tumor, rhabdomyosarcoma, smooth muscle tumors, and direct extension of gastrointestinal stromal tumor from adjacent colon. These entities tend to occur as expansile masses without entrapped benign epithelial components and as such present 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 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.

