Stromal Tumors of Uncertain Malignant Potential (STUMPS) and Stromal Sarcomas

Prostatic stromal tumors arising from the specialized prostatic stroma are rare and distinct tumors with diverse histological patterns. In the past, these tumors have been reported under a variety of terms including atypical stromal (smooth muscle) hyperplasia, phyllodes type of atypical stromal hyperplasia, phyllodes tumor, and cystic epithelial-stromal tumors. As the phyllodes “leaf-like” pattern is only seen in a subset of both benign and malignant stromal tumors, we prefer to designate stromal tumors of the prostates in more general descriptive terms as STUMPs and stromal sarcomas, as has also been recommended by the 2004 World Health Organization Classification of Tumours of the Urinary System and Male Genital Organs. (4) To date, there have been three large studies on these lesions. (1,5,7) STUMPs have been reported to occur between the ages of 27 and 83 years, with a median age of 58 years and a peak incidence in the 6th and 7th decades. Patients present most commonly with lower urinary tract obstruction, followed by an abnormal digital rectal examination, hematuria, hematospermia, rectal fullness, a palpable rectal mass or elevated serum PSA levels. On gross examination, STUMPs appear white-tan and may demonstrate a solid or solid-cystic pattern with smooth-walled cysts filled with bloody, mucinous or clear fluid. These tumors may involve either the transition zone or the peripheral zone and may range in size from microscopic lesions (which are typically incidentally found) to large, cystic lesions up to 15 cm in size.

Microscopically, four patterns of STUMP have been described and include: (1) hypercellular stroma with scattered atypical, but degenerative appearing cells admixed with benign prostatic glands; (2) hypercellular stroma consisting of bland fusiform stromal cells with eosinophilic cytoplasm admixed with benign glands; (3) leaf-like hypocellular fibrous stroma covered by benign appearing prostatic epithelium similar in morphology to a benign phyllodes
tumor of the breast; and (4) myxoid stroma containing bland stromal cells and often lacking admixed glands. Most recently, we have noted a 5th pattern consisting of cellular epithelioid stroma. Cases can exhibit a mixture of the above patterns. Areas of BPH can have microscopic fibroadenoma-like foci which should not be designated as STUMP.

Approximately half of all reported cases of STUMP demonstrate the first pattern of hypercellular stroma containing atypical cells intermixed with, but not compressing, benign glands. The atypical stromal cells in these cases are pleomorphic and hyperchromatic, with a marked degenerative appearance. Mitotic figures are typically absent and atypical mitoses should not be seen. Cases of STUMP demonstrating hypercellular, elongated bland stromal cells with admixed glands may be occasionally misdiagnosed as a cellular stromal proliferation associated with BPH, although the extent of hypercellularity and often more eosinophilic nature of the cytoplasm is unique. The benign, phyllodes pattern of STUMP may also contain atypical, degenerative-appearing stromal cells and may be associated with a variety of benign epithelial proliferations, including basal cell hyperplasia, adenosis, and sclerosing adenosis. Finally, the myxoid pattern of STUMP may be confused with stromal nodules of BPH, although the myxoid pattern of STUMP consists of extensive sheets of myxoid stroma without the nodularity identified in BPH. Occasionally the extensive myxoid stroma is admixed with benign prostate glands.

STUMPS and stromal sarcomas, although the neoplastic cells are mesenchymal, often have associated epithelial proliferations. These include adenosis, glandular crowding and complexity, prostatic intraepithelial neoplasia (PIN), squamous metaplasia, urothelial metaplasia, basal cell hyperplasia, adenosis, and clear cell cribriform hyperplasia. (10) Within these tumors there is epithelial-mesenchymal crosstalk, as has been described in benign prostate and in
prostatic carcinogenesis. In unusual cases of STUMP, the epithelial proliferation may predominate to the extent that it can mask the diagnosis of STUMP.

Most cases of STUMP are positive for CD34 and vimentin and variably positive for smooth muscle actin, and desmin. Due to the derivation of these tumors from the prostatic stroma, progesterone receptor is frequently present on immunostaining, although estrogen receptor is less commonly positive. C-kit and S-100 have been negative in all cases examined. Most STUMPs carry chromosomal alterations consistent with a neoplastic process, disproving earlier proposals that STUMPs were BPH with degenerative atypia.

Although STUMPs are generally considered to represent a benign neoplastic stromal process, a subset of STUMPs has been associated with stromal sarcoma on concurrent biopsy material or has demonstrated stromal sarcoma on repeat biopsy, suggesting a malignant progression in at least some cases. (7) There appears to be no correlation between the pattern of STUMP and association with stromal sarcoma. As most STUMPs are confined to the prostate and rarely progress to sarcoma, STUMPs are in general associated with a good prognosis.

In contrast to STUMPs, stromal sarcomas tend to affect a slightly younger population, with a reported age range of 25 to 86 years. Approximately half of all reported cases of stromal sarcoma occur before the age of 50 years. Stromal sarcomas may arise de novo or may exist in association with either a pre-existent or concurrent STUMP.

Gross examination of stromal sarcomas demonstrates predominantly tan-white, solid, fleshy lesions ranging in size from 2 to 18 cm. Occasionally, areas of edema, hemorrhage, or small cysts may be identified. Microscopically, stromal sarcomas demonstrate either a solid growth of neoplastic stromal cells, which may have storiform, epithelioid, fibrosarcomatous, or patternless patterns, or may infiltrate between benign prostatic glands. Less commonly stromal
sarcomas may demonstrate leaf-like glands with underlying hypercellular stroma, which are also termed malignant phyllodes tumors. Stromal sarcomas have one or more of the following features within the spindle cell component: hypercellularity, cytological atypia, mitotic figures, and necrosis. Stromal sarcomas may additionally be subclassified into low and high grades with high grade tumors defined by moderate-marked pleomorphism and hypercellularity often with increased mitotic activity and occasional necrosis. Rarely, adenocarcinomas of the prostate can involve a stromal sarcoma.

Immunohistochemical findings are similar to those of STUMPs, with strong vimentin reactivity and positivity for CD34 and progesterone receptor. In a subset of cases studied, pancytokeratin and CAM5.2 stains were negative. One case of stromal sarcoma was reported to demonstrate nuclear reactivity for beta-catenin, although the significance of this finding is unclear. Stromal sarcomas can extend out of the prostate and metastasize to distant sites, such as bone, lung, abdomen and retroperitoneum.

The variability in behavior of STUMPs and stromal sarcomas, and their occasional co-existence, lead to challenges in patient management. Although many STUMPs may behave in an indolent fashion, their unpredictability in a minority of cases and the lack of correlation between different histological patterns of STUMPs and sarcomatous dedifferentiation, warrant close follow-up and consideration of definitive resection in younger individuals. Factors to consider in deciding whether to proceed with definitive resection for STUMPs diagnosed on biopsy include patient age and treatment preference, presence and size of the lesion on rectal exam or imaging studies, and extent of the lesion on tissue sampling. Expectant management with close clinical follow-up could be considered in an older individual with a limited lesion on biopsy where there is no lesion identified on digital rectal exam or on imaging studies.
Leiomyoma/Leiomyosarcoma

It is difficult to diagnosis a leiomyoma of the prostate, mainly because it is difficult to distinguish from a stromal nodule of benign hyperplasia. (9) Both entities may contain abundant smooth muscle, although leiomyomas typically demonstrate well-organized fascicles and may have other degenerative features such as a hyalinization and calcification that are not commonly seen in stromal nodules. Large single leiomyomas that are symptomatic are rare. The largest reported leiomyoma of the prostate measured 12cm. (11) Leiomyomas demonstrate virtually no mitotic activity and minimal to no nuclear atypia, with the exception of occasional scattered degenerative nuclei in a normocellular background.

Sarcomas of the prostate account for 0.1% to 0.2% of all malignant prostatic tumors. (12) Leiomyosarcoma is the most common sarcoma involving the prostate in adults, yet is still rare, affecting men between the ages of 40 to 78 years. It most frequently presents with urinary obstruction, as well as perineal/pelvic pain, urinary frequency, hematuria, constipation, rectal pain, and pain or burning on ejaculation. (3,12). Tumors vary from 1 to 25 cm, with the majority of reports of lesions between 5 and 10 cm. (14) Microscopically, these hypercellular lesions are composed of intersecting bundles of spindled cells with moderate to severe atypia. The vast majority of leiomyosarcomas in the literature have been high grade with frequent mitoses and necrosis, although we have also seen rare cases of low grade prostatic leiomyosarcoma. (13) Epithelioid leiomyosarcomas have been reported in the prostate. (3,6) Low grade leiomyosarcomas are distinguished from leiomyomas by moderate amount of atypia, focal areas of increased cellularity, scattered mitotic figures, and or a focally infiltrative growth pattern around benign prostate glands at the perimeter. Symplastic leiomyomas have, in contrast,
scattered atypia of a degenerative nature with an overall low cellularity. As opposed to some stromal sarcomas, leiomyosarcomas lack admixed normal glands, except entrapped glands at the periphery.

Leiomyosarcomas commonly express vimentin, actin, and desmin. Cytokeratin expression is observed in about one-quarter of cases. (3). In addition, some leiomyosarcomas have been reported to express the progesterone receptor, similar to STUMPs and stromal sarcomas. (8)

Patients with leiomyosarcoma commonly have a poor outcome, with the clinical course characterized by multiple recurrences. The majority (50-75%) of patients die from disease within 2-5 years with metastatic spread most commonly to the lungs, often several years following initial diagnosis. In the study by Sexton et al., the prognosis for leiomyosarcoma of the prostate, as for sarcomas of the prostate in general, was not dependent on stage, with the exception of a better prognosis for those men who presented without distant metastases. (12). The only other variable that these authors found to be predictive of a favorable prognosis was complete surgical resection with microscopically negative margins. Optimal treatment requires a multimodal approach rather than surgery alone. They also noted that survival of patients with isolated local recurrences could be prolonged with salvage surgery. In a report of dedifferentiated leiomyosarcomas from all sites, there was one prostate leiomyosarcoma metastatic to the lungs with 36 months survival with disease. (2)

References


