

Expanding the Spectrum of Prostatic Mesenchymal Neoplasm: Clinicopathological Insights From Eight Cases

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Abstract

Mesenchymal neoplasms of prostate make up <1% of tumors occurring in this anatomical location. In this series we discuss 8 cases of prostatic (6) and periprostatic (2) mesenchymal tumors. 100% of the patients are adults with age ranging from 18–70 years. Most common presenting symptom was lower urinary tract obstructive symptoms. 3 out of 8 cases had frank hematuria. Serum PSA was normal in all cases. Radiology (CT scan and MRI) revealed intra-prostatic (6) and peri-prostatic (2) mass lesions. Diagnosis was offered in TRUS and in 4 cases we received radical cystoprostatectomy specimen. We came across 3 cases of prostatic leiomyosarcoma and 1 case each of prostatic rhabdomyosarcoma, undifferentiated pleomorphic sarcoma and clear cell sarcoma. This will be the first case report of primary prostatic clear cell sarcoma to the best of our knowledge. We got 1 case of GIST arising from the recto-vesical pouch and infiltrating into the prostate, and another case of solitary fibrous tumor arising from the periprostatic tissue. All cases in this case series were reported in TRUS biopsy, highlighting the pivotal role of TRUS biopsy in diagnosis, management and prognosis of prostatic and periprostatic lesions. In addition to that, in this case series we discuss a case of clear cell sarcoma of prostate which has not been reported in the English literature. Thus, this case series expands the spectrum of prostatic mesenchymal tumors.

Keywords: Mesenchymal tumors; TRUS biopsy; Clear cell sarcoma

Introduction

Mesenchymal neoplasms of the prostate are exceedingly rare, accounting for <1% of all malignant prostate neoplasms.[1] These neoplasms are usually sampled by Trans rectal ultra-sound guided (TRUS) biopsies. Pathologists often face significant diagnostic difficulties as the biopsy size is small and the availability of tissue is limited and many a times the diagnosis is a surprise.[2] The most frequently recognized mesenchymal neoplasms at this location includes Prostatic stromal tumors, Solitary Fibrous Tumors, Myofibroblastic proliferations, Smooth muscle neoplasms, Gastrointestinal stromal tumors, Schwannomas, Rhabdomyosarcomas and Post-radiation sarcomas.[1] Rhabdomyosarcoma is frequent during young age whereas leiomyosarcoma is more frequent in adults. This case series discusses eight cases of mesenchymal neoplasms,

including six arising from the prostate and two from the periprostatic region, highlighting the diagnostic complexities associated with these unusual and diverse neoplasms.

A total of 8 cases of prostatic (6) and peri prostatic (2) mesenchymal tumours were included in this study. The youngest patient was 18 years and oldest was 70 years old. All the patients presented with LUTS and their serum PSA was within normal limits. Diagnosis was offered on TRUS biopsies in 6 cases and subsequently we received cystoprostatectomy specimens in 3 patients. The other 2 cases, we received cystoprostatectomy specimen which were diagnosed as spindle cell tumor on TRUS from other hospitals.

Institutional ethical committee approval was obtained. The TRUS biopsy and the specimens were processed as per standard procedure. The following IHC markers were performed; SMA, Desmin, HMB 45, SOX 10, CD 99, CD 34, PAN CK and BCL 2. The antibodies used were ready to use monoclonal antibodies from Biogenex.

Case Report

In the first case, tumor was well defined, isointense on T1, and hyperintense on T2 weighted MRI imaging (Fig 1A). We received a TRUS biopsy on which a diagnostic possibility of stromal tumor-Spindle cell sarcoma was offered. This was followed by a radical cysto-prostatectomy specimen measuring 11.5x10x6.5cm and on cut section showed a greyish-white mass measuring 3x2.5x2.5cm. (Fig 1B). Microscopy revealed a tumor with interlacing fascicles of spindle cells with moderate nuclear pleomorphism and mitotic activity. (Fig 1C) along with few epithelioid clear cells with vesicular nuclei and prominent nucleoli. Differential diagnosis of LMS, Prostatic stromal sarcoma, STUMP and monomorphic synovial sarcoma were considered on H & E. However, SMA, CD 34, CD 99, Desmin and Pan CK were negative. In view of the clear cells, melanocytic markers were done and the tumor showed positivity for HMB 45, SOX 10 and S 100. A provisional diagnosis of clear cell sarcoma was made. Since clear cell sarcoma is not reported in prostate we proceeded with NGS next generation sequencing (NGS). Paired end sequencing was performed on illumina platform (NovaSeq 6000/ NextSeq2000) with oncocept solid panel which detects 206 solid tumor genes. The tumor was Positive for *EWSR1::ATF1* fusion gene while no pathogenic fusion identified in *PAX3*, *ETV6*, *FUS*, *STAT6*, *ALK* and *SS18* (Fig 1D). Patient had received radiotherapy and is doing well.

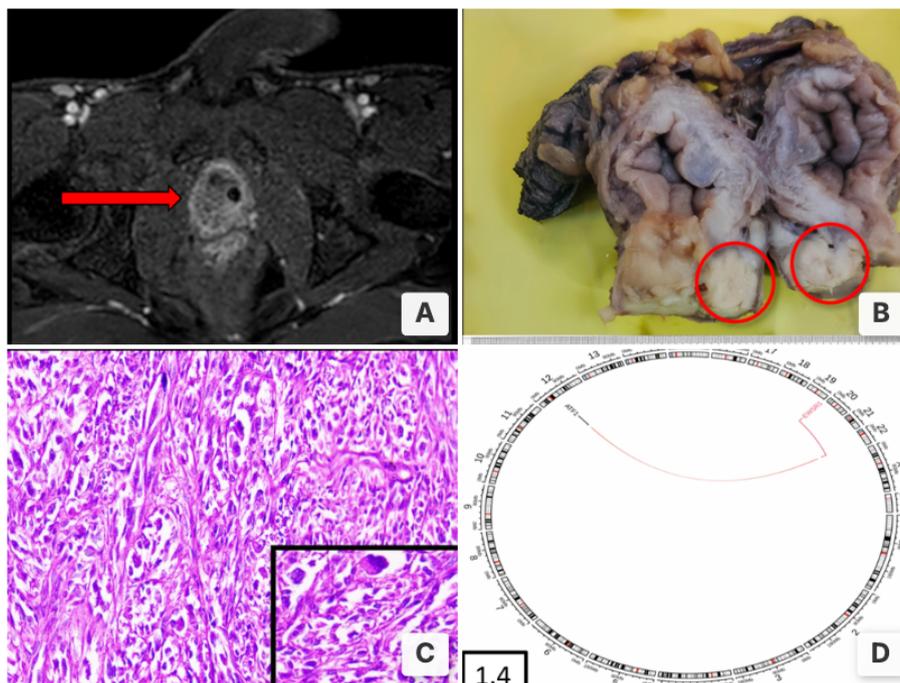


Figure 1: A. MRI-T2WI: Well defined, lobulated, encapsulated hyperintense lesion seen on right side of prostate (red arrow). B. Cysto-prostatectomy specimen shows a grey white tumor (red circle) involving prostate with adjacent unremarkable bladder. C. Shows tumor with interlacing fascicles of spindle cells with moderate nuclear pleomorphism admixed with clear cells; inset shows mitotic activity. D. Next generation sequencing positive for *EWSR1::ATF1* fusion gene.

In the second case, TRUS biopsy showed stellate to spindle tumor cells with scant eosinophilic cytoplasm arranged in sheets admixed with occasional bizarre cells. The tumor was infiltrating into the muscle. Based on histomorphology and Immunohistochemistry profile (Desmin- Positive, CK, CD 15, CD 99 and CD 45 Negative) a diagnosis of Embryonal rhabdomyosarcoma was made. Embryonal RMS is the most common sarcoma in young adults and patients generally presents with LUTS and peri anal pain as in our 21 year old patient. The clinical history and IHC markers confirm the diagnosis of the entity.

In the cystoprostatectomy specimen of 3rd case, the prostate was measuring 3x2x2 cm with 3 attached masses measuring

10x7.5x7cm, 7x7x3cm and 6x4x5 cm. The cut surfaces were greyish white with areas of hemorrhage and necrosis (Fig 2A). Microscopy (Fig 3A) showed spindle and plump cells arranged in sheets and intersecting with marked pleomorphism and mitotic activity which was consistent with features of undifferentiated pleomorphic sarcoma. The tumor showed strong and diffuse positivity for vimentin, focal positivity for BCL2, while Caldesmon, CD99, CD34, CD117, SMA, PR, SOX 10, SS18-SSx were negative. Since all the above markers were negative, UPS was offered as a diagnosis of exclusion and advised for further workup. But unfortunately, patient expired within days of the surgery.

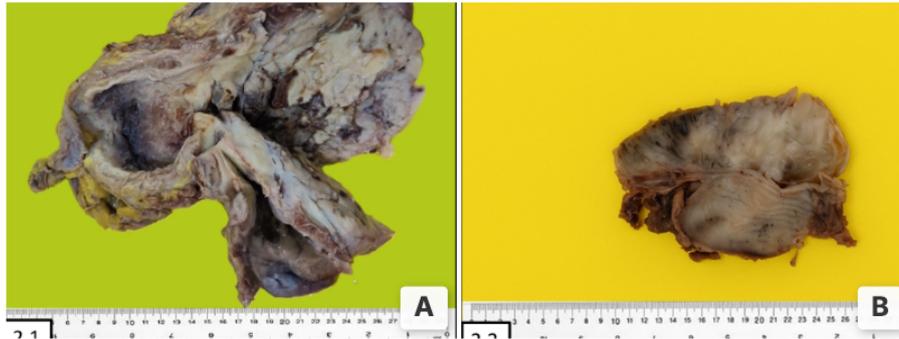


Figure 2: A. Cystoprostatectomy specimen showing prostate (red arrow head) with adjacent greyish white tumor with areas of hemorrhage and necrosis. B. Cystoprostatectomy specimen showing prostate measuring (red arrow head) along with a solid, grey white, variegated periprostatic tumor.

Cystoprostatectomy specimen of Case 4 showed prostate measuring 5x3.5x3cm and a solid, grey white, variegated periprostatic tumor with hemorrhage, cystic change and calcification measuring 12x6x5cm (Fig 2B). Histopathology revealed ovoid-spindled cells with indistinct cell borders arranged in ill-defined small fascicles along with hemangiopericytoma like vasculature and hyalinized stroma (Fig 3B). With the above histology differential diagnosis of GIST and Synovial sarcoma were considered. *STAT6* positivity confirmed the diagnosis of Solitary Fibrous Tumor (SFT).

The TRUS biopsy of fifth case revealed a cellular tumor composed of spindle cells arranged in intersecting fascicles (Fig 3C). LMS and GIST were the possibilities considered for the spindle cell tumor in the recto vesical space infiltrating the prostate. SMA negative and focal CD 34 positive confirmed the diagnosis of GIST. Patient is currently on Tyrosine kinase inhibitors.

We came across 3 cases of leiomyosarcoma of prostate. TRUS revealed high grade prostatic leiomyosarcoma in the first case. The radical cystoprostatectomy confirmed the diagnosis which was positive for SMA, Desmin, and Vimentin. The patient is currently on radiotherapy. In the second case, the tumor was SMA positive with Ki-67 (15–20%), confirming diagnosis of low-grade leiomyosarcoma. Third case was initially diagnosed as STUMP on TRUS, later revealed pleomorphic nuclei and necrosis (Fig 3D) with desmin positivity and variable Ki-67 (2–10%) on TURP specimen and was reported as high-grade leiomyosarcoma.

Discussion

Primary sarcoma of the prostate is an uncommon malignant tumor with an unfavorable prognosis. It arises from the mesodermal component of the genital tract.[3]

This series highlights the spectrum of these rare tumors, including a primary prostatic Clear Cell Sarcoma (CCS), Embryonal Rhabdomyosarcoma (ERMS), Leiomyosarcomas (LMS), Gastrointestinal Stromal Tumor (GIST), Solitary Fibrous Tumor (SFT) and Undifferentiated Pleomorphic Sarcoma (UPS). The reliance on immunohistochemistry (IHC) and molecular studies is crucial, especially since Prostate-Specific Antigen (PSA) is normal.

The diagnosis of CCS with the characteristic *EWSR1::ATF1* fusion gene is significant, as CCS is a rare, aggressive malignancy. CCS of the prostate is exceedingly rare with no prior case involving prostate reported in the literature to the best of our knowledge. The distinctive IHC profile and molecular confirmation demonstrates the multi-modality approach necessary for definitive diagnosis.

ERMS of the prostate is predominantly a pediatric tumor, very few cases are reported in adults.[4] It is characterized by rapid growth, with formation of large pelvic masses and wide dissemination.[5] Similar to our study Sow et al also reported embryonal RMS of prostate in a young adult, presented with LUTS. They emphasized the importance of concurrent chemoradiation post operatively. However, our patient was lost to follow up.

Leiomyosarcoma is the most common sarcoma in adults. The cases in the series and comparative literature illustrate the aggressive course of high-grade LMS, with median survival of months to few years.[6]

The rectovesical GIST exemplifies the challenge of distinguishing primary prostatic tumors from secondary involvement from adjacent organs. Definitive diagnosis of primary prostatic GIST requires strong radiological and pathological evidence

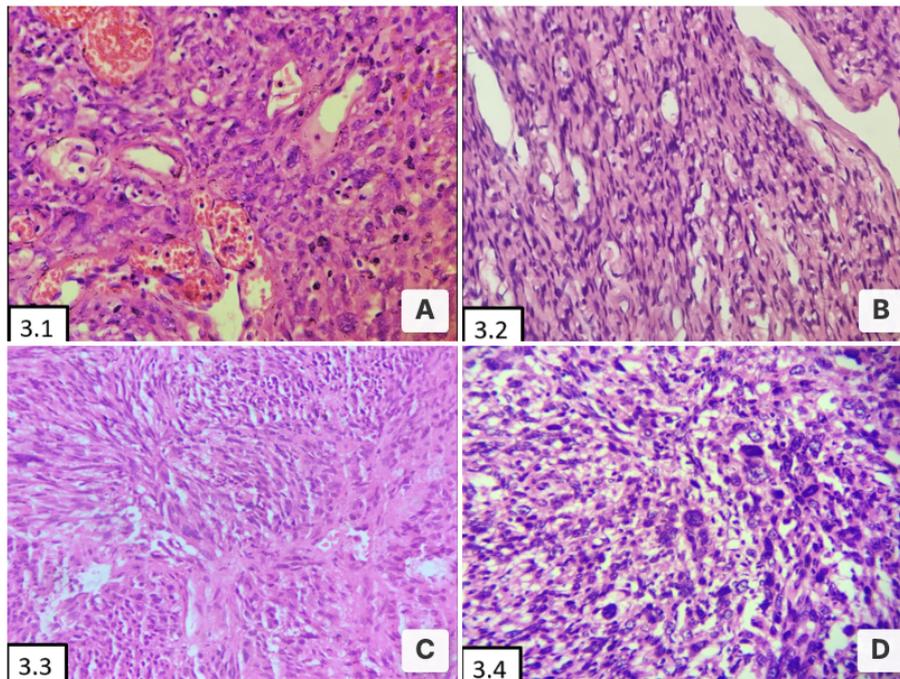


Figure 3: A. UPS: Polygonal and spindle cells with marked nuclear pleomorphism arranged in storiform pattern with high mitotic index. B. SFT: Tumor composed of haphazardly arranged ovoid spindle cells admixed with staghorn-like vasculature. C. GIST: Tumor composed of bland spindle cells with eosinophilic cytoplasm, elongated nuclei arranged in fascicles. D. LMS: Cellular tumor composed of intersecting fascicles of spindle cells, with marked cytologic atypia and increased mitotic count.

Table 1: Details of all 8 cases.

Sr No	Age	Complaints	PSA (ng/dl)	Radiology	TRUS (Trans Rectal Ultrasound) Biopsy
1	18	AUR, LUTS	0.09	MRI-Well defined, lobulated and encapsulated mass on right side of prostate	Spindle cell sarcoma with few clear cells
2	21	LUTS, Pain in peri anal region	5.4	CT- Markedly enlarged prostate with moderate sized ill defined irregular mass along inferior aspect of prostate extending up to urogenital diaphragm- s/o Soft tissue sarcoma	Embryonal Rhabdomyosarcoma
3	51	LUTS	0.83	MRI- Heterogenous signal intensity in peripheral part of gland in T2WI	Spindle cell neoplasm
4	68	LUTS		MRI- Circumscribed solid cystic lesion noted in rectovesical space extending from coccyx to L5, showing variegated appearance with intra lesional hemorrhage and calcification.	Solitary fibrous tumor
5	32	LUTS	0.5	MRI- Mass involving rectovesical and pre sacral spaces infiltrating prostate (Prostate not seen separately)	Gastro intestinal stromal tumor
6	70	LUTS	4	CT- Prostatic mass measuring 10x9.5x9 cm	High grade prostatic leiomyosarcoma
7	35	LUTS	0.82	MRI- 8.3x7x9.3 cm exophytic lesion on left lateral aspect of prostate and involving the base of the bladder	Low grade leiomyosarcoma
8	53	Hematuria, LUTS	3.60	CT - 4.5x4x3 cm soft tissue lesion involving the right lateral wall of bladder with loss of fat planes with prostate.	smooth muscle tumor of uncertain malignant potential (STUMP)

as secondary involvement from adjacent organs is common.[7] This underscores the need to include CD117 and DOG1 in the workup in such cases of given the therapeutic implications of tyrosine kinase inhibitors.

The poor outcome of our patient with UPS is consistent with the general aggressive nature associated with UPS.[8]

The SFT case is another rare entity that must be distinguished from prostatic stromal lesions. Prostatic SFTs have been reported in literature, while in our case it was arising from rectovesical pouch, which is a rare anatomical location.[9]

Primary prostatic sarcomas are aggressive tumors. While complete surgical resection with negative margins is generally the most favorable prognostic factor, multimodality treatment is often required.

Conclusion

In conclusion, this case series effectively expands the documented spectrum of mesenchymal neoplasms beyond commonly encountered entities with inclusion of first ever documented case of Clear cell sarcoma of Prostate in the literature.

The take home message from present study is that pathologists should think of prostatic mesenchymal tumors while reporting TRUS biopsy or prostatic resection specimens with normal PSA.

This case series reports first ever documented case of clear cell sarcoma of prostate in English literature to the best of our knowledge which can be included reference book/literature.

The future direction lies in documentation of similar cases by practicing pathologists which may justify its inclusion in future text books and reference articles and will aid in refining the diagnostic framework for rare prostatic sarcomas.

Abbreviations: LUTS- Lower urinary tract obstructive symptoms, AUR- Acute urinary retention

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