Case Report

Gastrointestinal stromal tumor presenting with lower urinary tract symptoms – A series of five cases with unusual clinical presentation

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ABSTRACT

Spindle cell tumors of the prostate are very uncommon and the majority involve the prostate secondarily from adjacent organs. Gastrointestinal stromal tumors (GISTs) are specific C-kit (CD 117) expressing mesenchymal tumors occurring in the gastrointestinal tract, commonly in the stomach and intestine; however, it is seldom seen involving the prostate. Although primary prostatic GISTs have been described, majority of them are secondary involvement from rectal GIST. The patient usually presents with urinary tract symptoms or prostate enlargement simulating a prostatic neoplasm. GIST as a differential diagnosis for prostatic mass is never thought of. We present a series of five cases of GIST arising from/involving the prostate mimicking a primary prostatic malignancy and the challenges associated with them for diagnosis and treatment.

INTRODUCTION

Spindle cell lesions of the prostate are uncommon and their differential diagnosis may include varied entities with different treatment implications. A few of them are primary to the prostate, while others secondarily involve the prostate from the adjacent organs. Gastrointestinal stromal tumors (GISTs) are specific C-kit (CD 117) expressing mesenchymal tumors occurring in the gastrointestinal (GI) tract, with the majority being in the stomach (70%), followed by small intestine and rectum.[1,2] Extra-GISTs (EGISTs) are similar tumors which arise from soft tissues outside the GI tract. Around 10% of them involve the anorectal region and may present with lower urinary tract symptoms (LUTS) or prostate enlargement simulating a prostatic primary.[3] EGIST occurring in prostate or in relation to prostate is extremely rare with only a handful of cases reported.[3,4] Targeted TKI inhibitors such as imatinib and dasatinib therapy alone or prostatectomy in addition to TKI therapy are the preferred methods for the treatment of prostatic EGIST; thus, it is necessary to identify and diagnose this tumor accurately.[5] We hereby report a series of five cases of GIST of prostate or involving prostate presenting with LUTS.

CASE SUMMARIES

We retrieved and identified five cases of primary prostatic GIST from the records. The age of the patients was 58, 84, 69, 55, and 65 years with a mean age of 66.2 years. All the five patients had symptoms of LUTS which included dysuria and frequent micturition (n = 5) and obstructive symptoms (n = 3). The serum prostatic specific antigen (PSA) levels were within normal limits in all cases with a range of

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0.046–1.889 ng/mL. The tumor ranged in size from 6.5 cm to 12 cm in the largest dimension. Clinical features and radiology have been tabulated below [Table 1].[Figure 1]

Case 1 showed radiological recurrence in the sigmoid mesentery and the patient had been then switched to sunitinib chemotherapy. The patient showed complete radiological regression on sunitinib therapy on subsequent follow-up imaging and is alive with no recurrence/relapse for 4 years (48 months). Case 2 underwent transurethral resection of prostate chips which was reported as a smooth muscle tumor of uncertain malignant potential in view of focal H-caldesmon and CD34 positivity. However, the tumor progressed in size over the next 3 months and underwent CP which was confirmed to be a GIST using a broad panel of immunohistochemistry. The patient was then started on imatinib mesylate therapy; however, further follow-up was not available. Case 3 and Case 5 were referred cases for pathology diagnosis and were reported as GIST on prostate biopsy specimens with the help of ancillary immunohistochemical findings. Case 4 underwent a 12-core biopsy which was initially reported as low-grade leiomyosarcoma.(Figure 2 a-e) However, after the multidisciplinary meeting, a differential diagnosis of GIST was thought of which was then confirmed with the help of immunohistochemistry. The patient received neoadjuvant chemotherapy with imatinib mesylate and had complete metabolic resolution of the disease with marked regression in the size of the mass followed by cystoprostatectomy. Sequencing studies revealed exon 11 mutation in the tumor. (Figure 2f) Total follow-up duration following diagnosis is 47 months and disease-free survival following stopping of imatinib mesylate is 3 months [Table 2].

DISCUSSION

Till date, only 13 cases of primary prostatic GIST and <30 cases of EGIST involving the prostate have been reported in the literature,[1-9] with a mean age of 59.5 years similar to our patients.[7] The mean age of the patients in this review was 60 years with a wide age range of 31–92 years. Serum PSA levels ranged from 0.2 to 2.45 ng/ml.[4] The mean range of serum PSA in our series was 0.046–1.889 ng/mL. The tumor size varies and ranges from 1.5 cm to as large as 15 cm.[7,8] The largest tumor had a size of 12 cm in our series.

The histomorphologic features of EGIST are similar to conventional GIST and are composed of cellular spindle cells with perinuclear vacuolations, arranged in long intersecting fascicles mimicking a smooth muscle tumor. Nuclear palisading in a myxoid stroma may be a reminiscent of nerve sheath origin. Mitosis is variable. The risk stratification of GIST is based on tumor size and mitotic activity.[5] On risk stratification of GIST, 3 out of 5 cases in our series were categorized as GIST of high malignant potential or aggressive tumor based on either their large size (case 2 and case 4) and/or high mitotic activity (>5/50 hpf) and necrosis (case 1). The

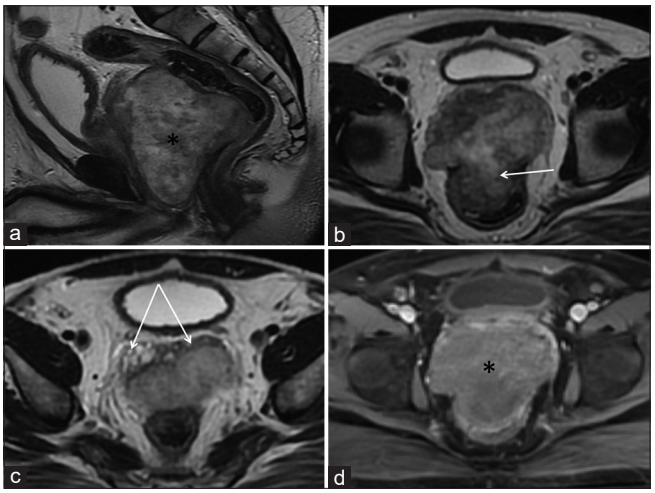

Figure 1: Magnetic resonance imaging of the pelvis showing a large heterogeneously hyperintense mass (* in a and d) with heterogeneous enhancement replacing the entire prostate gland. It invades the rectum posteriorly (arrow in b) and the seminal vesicles (arrows in c). Note that the bulk of the tumor is in the prostate

Table 1: Clinical profile of the patients

Age (years)	PSA (ng/mL)	Tumor site	Tumor size (cm)	Radiology	Surgery	Risk potential	Recurrence	Metastases
58	0.8	Prostatic mass attached to rectum	6.5	A large mass 6.5 cm involving the prostate with diffuse wall thickening of the rectosigmoid colon	CP + resection of anterior rectal wall	High risk	Occurred after 1 year on imatinib sigmoid mesentery deposit	None
84	0.046	Prostate mass	12	A heterogeneously enhancing mass completely replacing the prostate and measured 12 cm in the largest dimension	CP	High risk	Occurred after initial TURP	None
69	0.7	Prostate mass	-	NA	TURP	Low risk	Not known	Not known
55	1.889	Prostatic mass infiltrating rectum	11	A hypermetabolic mass in the pelvis posterior to the urinary bladder and anterior to the rectum with epicenter in the prostate and infiltration in the anterior rectal wall	CP+AR	High risk	None	None
65	1.1	Prostate mass	-	NA	TURP	Low risk	Not known	Not known

CP=Cystoprostatectomy, AR=Anterior resection, PSA=Prostate specific antigen, TURP=Transurethral resection of the prostate, NA=Not applicable

Table 2: Microscopy and immunohistochemical features

Features	Case 1	Case 2	Case 3	Case 4	Case 5
Cellularity	Yes	Yes	Yes	Yes	Yes
Nuclear pleomorphism	Present	Present	Absent	Present	Absent
Mitosis/50 hpf	>5	>5	<5	>5	<5
Necrosis	Present	Absent	Absent	Absent	Absent
Initial immunoprofile	C-kit	Focal H-caldesmon	C-kit	SMA, h-caldesmon	C-kit
Diagnosis	GIST	STUMP	GIST	Leiomyosarcoma	GIST
Additional immunohistochemistry	-	Ckit	-	Ckit, DOG1 and CD34	-
Revised diagnosis	-	GIST	-	GIST	-

STUMP=Smooth muscle tumor of uncertain malignant potential, GIST=Gastrointestinal stromal tumor, DOG-1=Discovered on GIST-1, SMA=Smooth muscle antigen, hpf=High-power field

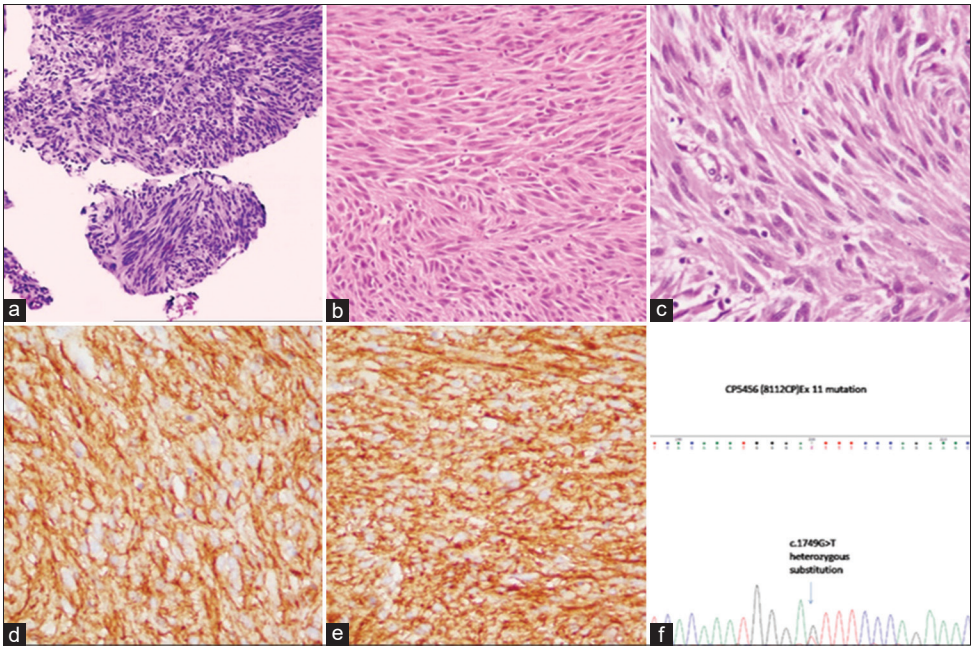

Figure 2: Hematoxylin and eosin stained sections (a-c) show a cellular spindle cell tumor with moderate nuclear pleomorphism and eosinophilic cytoplasm. Immunohistochemistry showed strong and diffuse positivity for C-kit (d) and DOG-1 (e). KIT sequencing revealed 1 bp heterozygous substitution in exon 11: C.1749G > T (f)

mitotic activity was <5/50 hpf in case 3; however, the tumor size information was not available for risk stratification. Most EGISTs of prostate are of large size involving the pelvis and rectum, and hence, it is difficult to accurately suggest their organ of origin.[3,6]

The immunoprofile of EGIST is similar to intestinal GIST with 90%–100% of the tumor showing strong and diffuse immunoreactivity to CD117/c-kit and DOG-1. SMA and CD34 positivity is reported in 30%–40% of cases. C-kit can be negative in approximately 20%–30% of the cases.[5,8]

With the discovery of KIT gain-of-function mutation in GIST, targeted therapies were studied upon and imatinib was used for the treatment of GIST in the year 2000.[10] Platelet-derived growth factor receptor alpha (PDGFR-A) and BRAF are other mutations associated with GIST.[2] One of our patients (case 4) underwent sequencing for KIT mutation and showed exon 11 mutation. Molecular studies were not performed in rest of the patients due to financial constraints and referral nature of the sample.

There is no consensus regarding the treatment of EGIST, and the patients are treated as per the risk stratification.[11] The choice of surgery depends on the tumor size, location, and extent of infiltration. Complete resection in EGIST of prostate/involving prostate would entail a radical prostatectomy. RP for low- and medium-risk resectable tumors and RP + adjuvant/neoadjuvant chemotherapy for medium- and high-risk tumors are the recommended lines of management.[11,12] Imatinib and sunitinib are the tyrosine kinase inhibitors recommended for treatment, especially for EGIST showing expression of CD117.[11,12]

Rectal GIST due to its anatomical location can sometimes present with symptoms simulating as prostate primary and histologically may resemble a prostatic stromal tumor. Hence, identifying these tumors is important due to their treatment implications. Due to a handful of cases of EGIST

reported till now, long-term prognosis following therapy is still not fully established.

CONCLUSION

EGIST may present with LUTS arising from or in relation to prostate. The accurate diagnosis depends on the imaging studies, pathological examination, and immunohistochemical results and has clinical implications with targeted TKI-based therapy.

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