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Case Report

A young man with primary prostatic extra-gastrointestinal stromal tumor: a rare case report and review of the literature

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Abstract: Mounting evidence demonstrates the presence of extragastrointestinal stromal tumor (EGIST) which originates from tissues outside the gastrointestinal (GI) tract and shares overlapping immunohistological features with gastrointestinal stromal tumor (GIST). GIST emanating from prostate is extremely rare. To our knowledge, there are only 3 definitely reported cases of primary prostatic EGIST. Herein, we report a case of prostatic EGIST in 31-year-old man with low urinary tract symptoms who was initially misdiagnosed as sarcoma of prostate. Imaging studies assist in determining the origin and location of EGIST. Immunohistochemical assessment (DOG-1, CD117, and CD34) helps in differentiating such lesion from other stromal tumors and in addressing an appropriate and optimal therapeutic strategy.

Keywords: Extragastrointestinal stromal tumor (EGIST), prostate, differential diagnosis, imatinib

Introduction

Extragastrointestinal stromal tumor (EGIST) is defined as mesenchymal neoplasms arsing from soft tissues outside the gastrointestinal (GI) tract, which is morphologically, histologically, and immunophenotypically similar to its gastrointestinal counterpart (i.e. gastrointestinal stromal tumor, GIST) [1]. The diagnosis of EGIST relies on the combination of tumor location, histopathologic appearance, and immunohistochemical analysis. Immunohistochemistry study plays a major role in GIST diagnosis. Most of these tumors express KIT (CD117) tyrosine kinase and show the presence of activating mutations in KIT or PDGFRα. Recently, a novel antibody, DOG1, has been identified to be sensitive and specific, in particular, for KIT-mutation-negative ones. Imatinib mesylate with activity against KIT and PDGFRA is the primary therapeutic candidate. To our best knowledge, there are rare definitive reports on EGIST arising from prostate [2-4]. In this report, we present our unique case and discuss the clinical presentation, differential diagnosis, pathologic characteristics, and therapeutic strategies for primary prostatic EGIST.

Case report

A 31-year-old man was admitted to our hospital with dysuria. He had frequency, urgency for 4 months and intermittent gross hematuria for 2 weeks. Digital rectal examination revealed an enlarged prostate with hard consistency but without bump, tenderness, or bleeding. The surface of prostate was not smooth. Serum level of prostate specific antigen (PSA) was 0.37 ng/ml. Pelvic B-mode ultrasound examination showed an expanded prostate (6.0 × 6.1 × 6.5 cm) with irregular internal structure and dark area of fluid. Ultrasonic inspection displayed a 1.4 cm protrusion with moderate echo at vesical neck, which showed no clear boundary with the prostate. Pelvic magnetic resonance imaging (MRI) examination (**Figure 1**) demonstrated 1) abnormal shape of prostate and seminal vesicles with mixed signal (generally, moderate signal was mainly detected), 2) an enlarged prostate with expansive growth and compression of the rectum and bladder. The whole-body bone scan revealed no bone involvement. Besides, no tumor dwelling inside or outside of the rectal wall was detected by enteroscopy and transrectal ultrasound (TRUS)

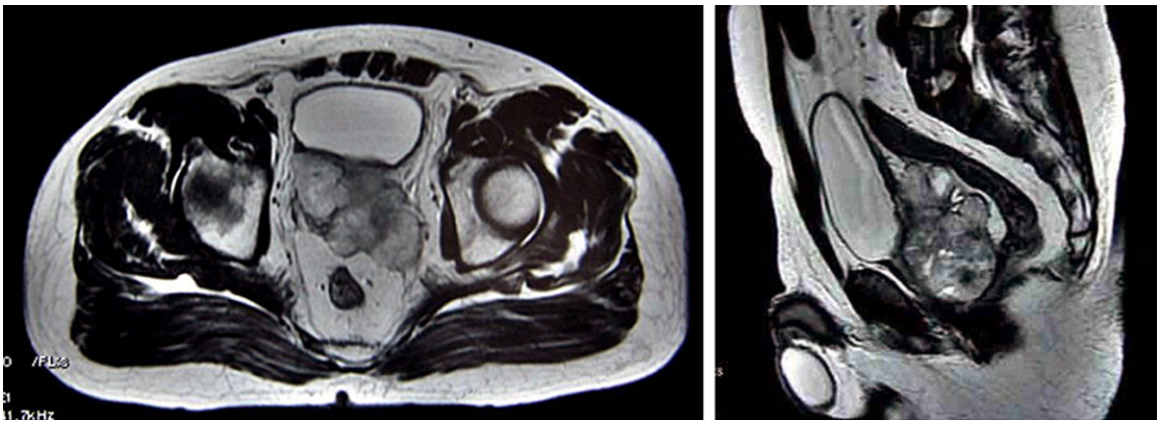

Figure 1. Magnetic resonance imaging showing 1) abnormal morphological appearance of prostate and seminal vesicles with mixed signal, 2) an enlarged prostate with expansive growth and compression of the rectum and bladder.

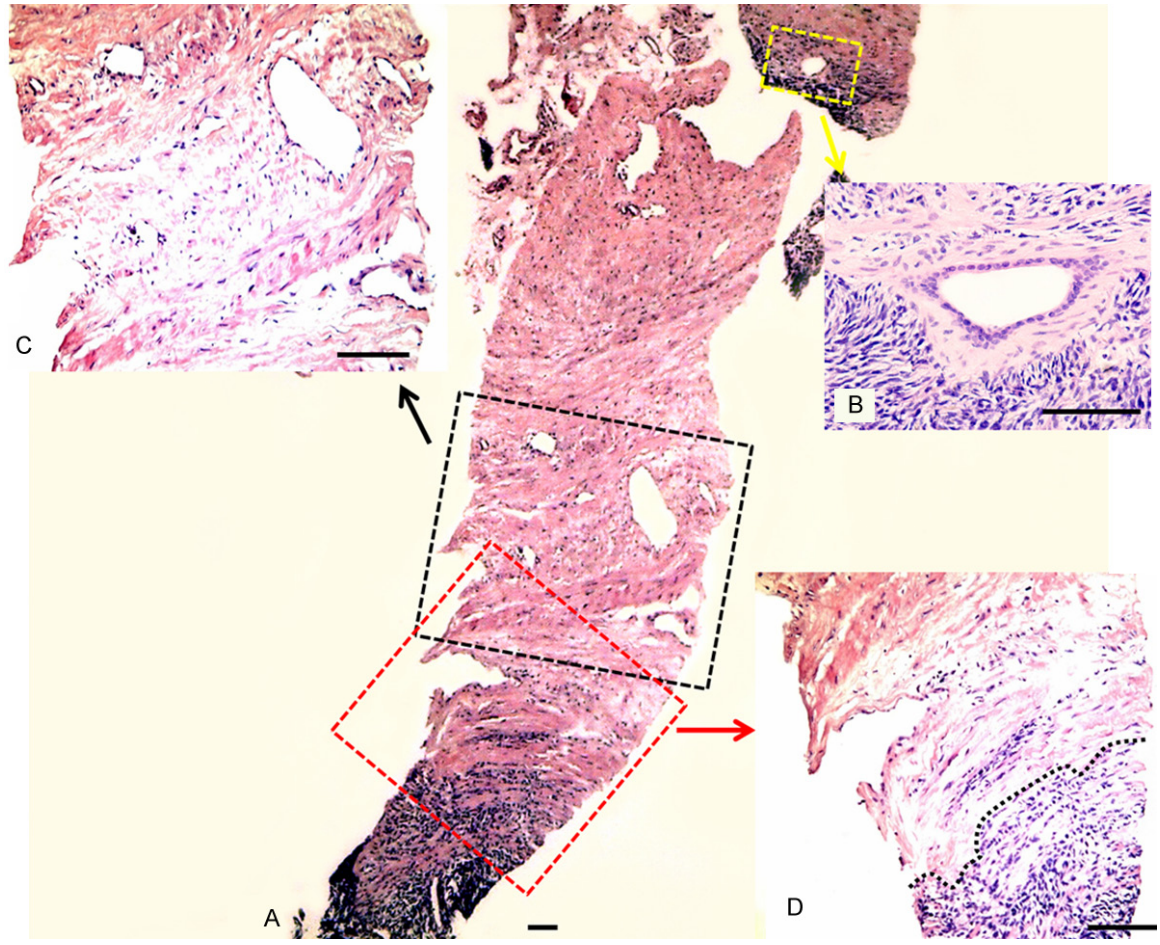

Figure 2. Histopathology of the tumor. H & E staining of tissue section from biopsy showed irregular dense arrangement of tumor cells (A) and the cytological pleomorphism of tumor tissue, composed of spindle-shape (B) and epithelioid cells (C). A boundary (dashed line) between regions of epithelioid or mixed epithelioid/spindle cell was observed (D). (magnification: A, × 100; B, × 400; C and D, × 200; Scale bars = 100 μm).

examination. According to above indications, the initial diagnosis was sarcoma of the prostate. TRUS guided prostate biopsy was performed for pathologic diagnosis. Histologically,

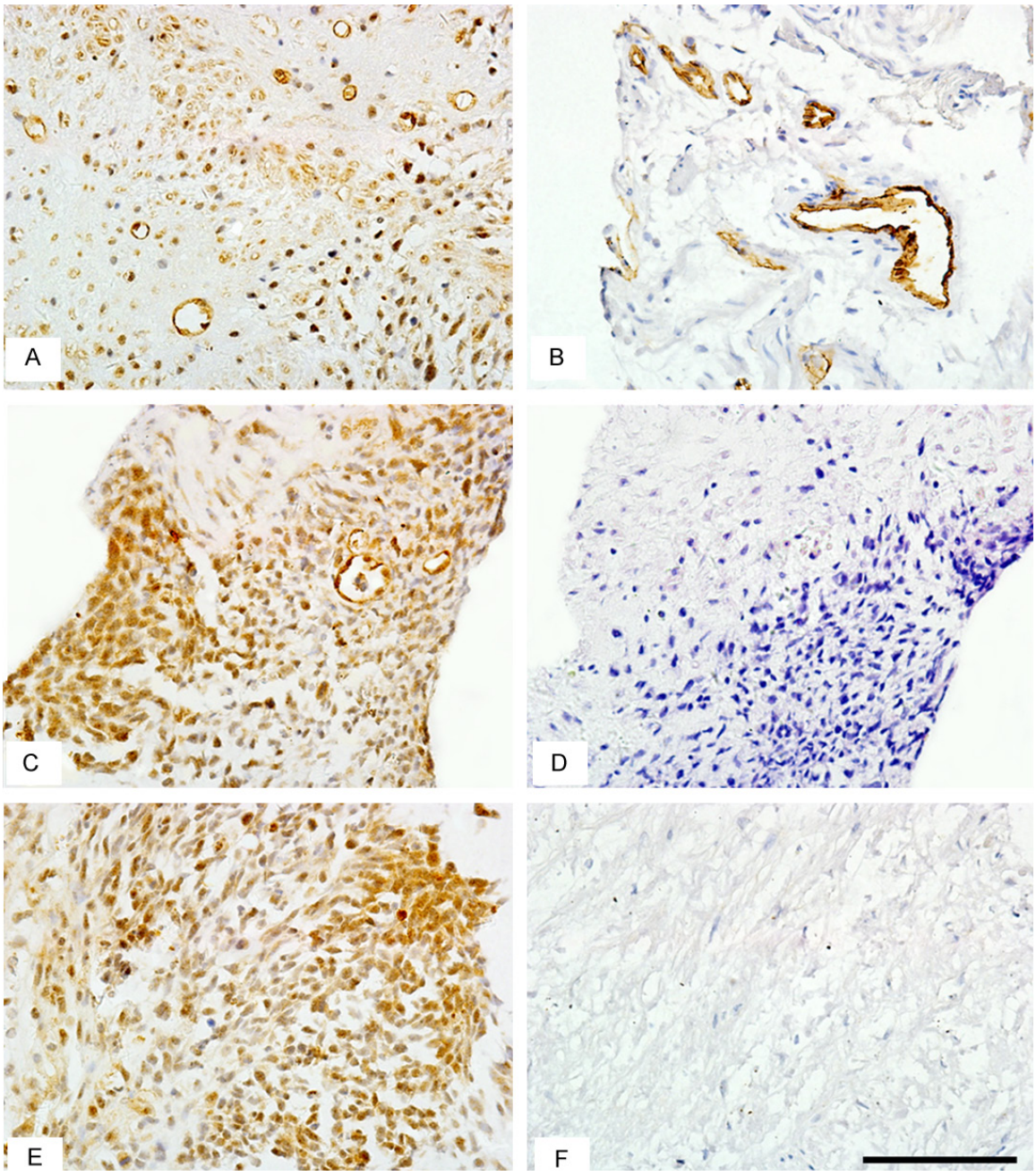

Figure 3. Immunohistochemical staining of the tumor cells. Immunostaining of the lesion displayed strong reactivity for CD34 (A) and diffuse positivity for CD117 (C) and DOG-1 (E). (B) is a positive control for CD34 staining illustrating the vessels, while (D) and (F) are blank controls for CD117 and DOG-1, respectively. (magnification: × 400; Scale bars = 100 μm).

the tumor consisted of spindle-shape, oval, and epithelioid cells (**Figure 2**). Tumor cells were very big in size, with abundant eosinophilic cytoplasm and spherical/oval nuclei. The nuclei had a varying size, and some of them stained light. The mitotic count was more than 10 per 50 high-power fields (HPF). Tumor hemorrhage or necrosis were frequently seen. Tumor cells showed strong and diffuse immunoreactivity for DOG-1, CD117, and CD34 (**Figure 3**) and were negative for S-100 and smooth muscle actin (SMA) (not shown). The pathologic diagnosis was GIST of the prostate based on histological and immunostaining results. Considering extension of the mass and increased risk of rectal injury, no surgical treatment was per-

Table 1. Review of the Literature on Primary Prostatic EGIST

Ref.	Age (yrs)	Tumor Size (cm)	Clinical presentation	Immunoreactivity	Treatment	Follow-up Interval (Months)	Outcomes	Metastasis
[2]	49	8	Perineal pain	CD117, CD34, Desmin	RP	14	No recurrence	None
[3]	75	6.7	Dysturia, frequency, hesitancy	CD117, CD34, Desmin	TURP + RP	6	Good condition	None
[4]	49	14.2	Acute urinary retention, body weight loss	CD117, α-SMA	Imatinib	24	Reduced mass volume and liver nodules	Liver (when diagnosed)

Abbreviations: TURP, transurethral prostatectomy; RP, radical prostatectomy.

formed. Instead, the patient was administered imatinib (400 mg per day). He took imatinib intermittently due to financial reasons, resulting in a poor response during a 3-month drug treatment. As the mass volume increased apparently (6.5 × 7.2 × 9.0 cm), leading to urinary retention, he then received indwelling catheter for a 3-month follow-up. The patient ultimately developed intestinal obstruction and died for electrolyte disturbances and multiple organ failure. Due to no informed consented obtained, autopsy was not performed.

Discussion

GISTs may arise anywhere in the gastrointestinal tract, from the esophagus to the rectum. Recent studies have disclosed identical lesions (EGIST) occurring in various locations outside the alimentary tract. As a very rare tumor, EGIST constitutes only 5%-10% of GIST [5]. The mean patient age at diagnosis is 58 years (range: from 31 to 82). The majority of reports on EGIST that is histologically similar to GIST are derived from the mesentery, omentum, and retroperitoneum [6, 7]. However, a significant number of individual cases have also been demonstrated in other sites, encompassing pancreas [8, 9], female genital organs [10, 11], urinary bladder [12, 13] and seminal vesicles [14]. To our knowledge, only a few cases of EGIST presenting as prostatic mass have been reported previously, among which primary prostatic EGIST is less commonly [2-4].

Due to heterogeneous clinical presentation and unusual anatomic locations of prostatic EGIST, it is difficult to differentiate such tumor from other prostatic occupying lesions and to identify the origin of the mass. A variety of symptoms have been demonstrated in the previous reports (**Table 1**). As for our case, occasional hematuria was presented as well apart from low urinary tract symptoms, suggesting diverse manifestation of such disease as a pitfall for differential diagnosis. Although TRUS guided prostate biopsy is widely performed for the purpose of establishing pathologic diagnosis, it plays poorly in determining the location of tumors. Accordingly, prostatic mass diagnosed as EGIST by biopsy may originate from either prostate or rectum. In this context, other approaches including assistant imaging examinations as well as enteroscopy are required to help identifying between such two origins.

Apart from the reported cases of prostatic EGIST, it has been recently shown that some cases of GIST arising from the rectum present clinically as prostatic masses [15]. Herawi and coworkers reported 4 resected tumors (in an 8-case study) following initial diagnosis by needle biopsy [16]. Based on their data, two cases originated from rectum (one is shown to be primary in the rectum without prostatic involvement, the other one extensively involving the prostate), while the origins of the other two were not well defined (one was separated from the prostate, the other one a perirectal mass). More recently, a literature review has been carried by Anagnostou and his group to reveal 20 cases of EGIST occurring in the prostate, diagnosed as either primary EGIST or rectal neoplasms extending to this organ [17]. They recapitulated the previous reports diagnosed as primary prostatic GIST and doubted the existence of such neoplasm. They put a premium on the exclusion of rectal involvement before such diagnosis is made. In our case, the prostatic origin was addressed mainly based on imaging results. What is note, there is no evidence supporting the existence of other GIST inside or outside the GI. Thus, we consider this prostate lesion to be a primary prostatic GIST. Theoretically, as suggested by Loeb, an ideal diagnosis can be drawn when the prostatic tumor is surgically resected with intact capsule, revealing no connection to the rectal wall [18].

Histopathology represents the gold standard in GIST diagnosis and a number of antibodies have been used in the routine practice. CD34

may aid, but it is positive in many other types of soft tumors [19]. Most GIST stain positively for CD117 (C-kit) and harbor a kinase-activating mutation in either KIT or PDGFRα [20, 21]. Because the distribution and strong expression of CD117 is quite limited in sarcoma other than GIST [22], CD117 is a relatively specific marker for GIST. However, approximately ~4% to 15% of GIST fail to stain for CD117 [23, 24]. A large percentage of these tumors possess PDGFRα mutations and respond to tyrosine kinase inhibitors [25, 26]. In this regard, the traditional panel of immunohistochemical stains is not sufficient to address accurate diagnosis of GIST. Recently, DOG-1 has been shown to be a promising antibody used in GIST diagnosis [27, 28]. As the most specific and sensitive marker of GIST [29], DOG-1 can reliably stain cases that are CD117-weak/negative [30]. Moreover, the combination of positivity for both antibodies (CD117 and DOG-1) were demonstrated to be reassuring in histological diagnosis [31]. Mutation screening of KIT or PDGFRα assists in confirming the diagnosis [3] and predicting the likelihood of imatinib response [18], but this technique adds to the time and cost of diagnosis. Screening is required in tumors that are negative for both CD117 and DOG-1 [30].

Due to emerging adjuvant treatment strategies, the need for precise risk stratification and classification is increasingly emphasized to attain an optimal individualized therapy. A decade ago, Flecher et al. suggested that some effective prognostic parameters (e.g. tumor size and the mitotic rate) should be taken into significant consideration in risk assessment and that the definitions for the risk categories (as very low, low, intermediate, or high) should be proved to be clinically useful [32]. According to Flecher's study with combination to a recent work [33] assessing the reliability of the staging system for GIST in the new revision of the AJCC, our case had a high risk of aggressive behavior. Similar to that of GIST, the most effective treatment for EGIST is aggressive surgical intervention associated with the use of imatinib [34]. In patients with localized tumors (whose lesions are very small, even < 2 cm, and lesions with very low mitotic rates, even < 5 per 50 HPF), surgery remains the elective treatment, due to the insensitivity of tumor cells to radiotherapy or chemotherapy. They are considered low risk and have small chance to reoccur with surgery and may not require adjuvant targeted therapy. For advanced tumors, the role of surgery is very limited and the patients may benefit from imatinib therapy. Although imatinib therapy represents standard treatment, showing continuous improvements in progressive-free and overall survival, the therapeutic efficacy in metastatic cases remains disputed. Surgical intervention was not considered in current patient because the lesion compressed and extended toward bladder and rectum. Instead, we preferred imatinib to surgical treatment in terms of his dismal prognosis. However, the young patient took imatinib only intermittently due to financial reasons, leading to a poor response to the targeted therapy and rapid exacerbation.

In conclusion, we reported an extremely rare case of primary GIST arising from the prostate. The diagnosis depended on imaging studies, pathologic results as well as immunohistochemical findings. Imaging examinations combined with enteroscopy contribute to identifying tumor origin. A broader immunohistochemical panel including DOG-1, CD117, as well as CD34 allows the confirmatory diagnosis of GIST. Because of its rarity, clinicians involved in the assessment of a mass arising in the prostate are suggested to be alert of EGIST in differential diagnosis, even in a young man.

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Disclosure of conflict of interest

All authors have no conflicts of interest.

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