ACTA SCIENTIFIC CANCER BIOLOGY

Volume 3 Issue 10 October 2019

Case Review

A Confusing Recto-Prostatic Mass Finally Diagnosed as Rectal Gist by Immunohistochemistry: Response Elicited by Imatinib

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Received: September 04, 2019; **Published:** September 30, 2019

Abstract

Rectal GIST (Gastrointestinal Stromal Tumours) constituting 5% of all GISTs and 0.1% of all tumours originating in the rectum is a rare disease. Advanced imaging, histopathological examination and above all immunohistochemistry positivity for CD117, DOG1 and CD34 are mandatory not only for clinching the diagnosis, but also to distinguish between a primary prostatic EGIST (Extragastrointestinal Stromal Tumours) and a primary rectal gist invading prostate.

We report this case of a recto-prostatic mass finally diagnosed as a primary rectal GIST with prostatic invasion taking place in a 60 years old gentleman, clinical feature of which mimicked the symptoms of a primary prostate cancer. While, imaging techniques like Ultrasonography (USG), Contrast Enhanced Magnetic Resonance Imaging and finally Positron Emitting Tomography Scan did not suffice to point out the primary site of the GIST, diagnosis was finally achieved by HPE and IHC from prostatic tissue showing evidence of invasion of disease from rectal origin.

Chemotherapeutic intervention with Imatinib remains successful to bring out favorable response. To the best of our knowledge, probably we are reporting the first case of rectal GIST with prostatic invasion from our country.

Keywords: Rectal Gist; Immunohistochemistry; Imatinib

Introduction

While in one hand, rectal GIST is a rare entity which constitutes 5% of all GISTs and 0.1% of all tumours originating in the rectum, on the other hand only five cases of EGIST with prostatic origin have been reported in literature till date. We dealt with this case of GIST diagnosed from prostatic specimen and utterly confusing images suggestive of a recto- prostatic lesion. Finally diagnosed as a rectal GIST with extensive prostatic invasion, this case is extremely interesting for its location, involvements and overall the dilemma in detecting the origin.

Case Report

A 60 years old, euglycemic normotensive gentleman with average built (weight - 61 kg; height - 163 cm) first attended in our out-patient department on with complaints of anal pain and burning sensation for last 3 months and altered bowel habit for last 15 days. Present history of illness included gradually aggravating symptoms of urinary retention for last 4 months. Patient's treatment history started when he received symptomatic medications and was advised an ultrasonography of whole abdomen by a local general physician. The USG revealed hugely enlarged prostate (measurement- 8.18 cm x 7.83 cm x 7.45 cm; weight - 249.8 gm) with heterogeneous parenchyma which evoked the need to perform a serum Prostate Specific Antigen (PSA) test which was 1.53 ng/ml i.e. within normal limit. Further, Magnetic Resonance Imaging (MRI Plain and Contrast) showed evidence of a large, lobulated-margined, mixed-intensity lesion, seen in pelvic cavity between posterior wall of bladder, seminal vesicles and prostate anteriorly and anterior wall of rectum posteriorly. The lesion was predominantly iso to mildly hypointense in T1 and heterogeneously hyperintense in T2 with marked T2 hyperintensity in its upper part. On CEMR the lesion showed heterogeneous enhancement except non-enhancing area of cystic/ necrotic change in its upper part. The solid part of the lesion showed mildly restricted diffusion. The lesion had contiguously infiltrated posterior aspect of prostate and had displaced seminal vesicles antero- superiorly. In its posterior aspect, the lesion was seen to involve anterior rectal wall and showing polypoid projection within rectal lumen. The lesion approximately measured about 85 mm anteroposteriorly, 63 mm mediolaterally and 102 mm superoinferiorly (Figure 1 and 2) This imaging first suspected and suggested the possibility of a Rectal GIST.

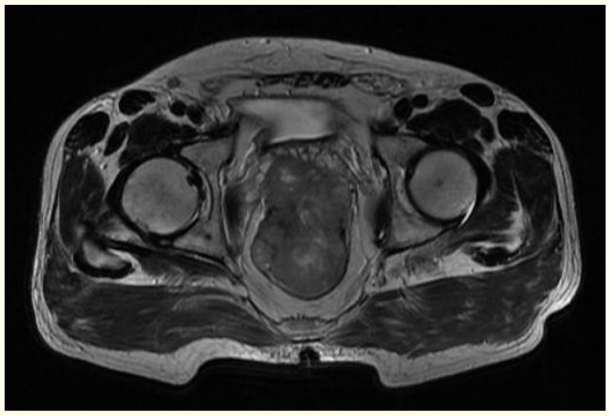

Figure 1: MRI Axial T2 view showing the recto-prostatic mass distorting the pelvic anatomy.

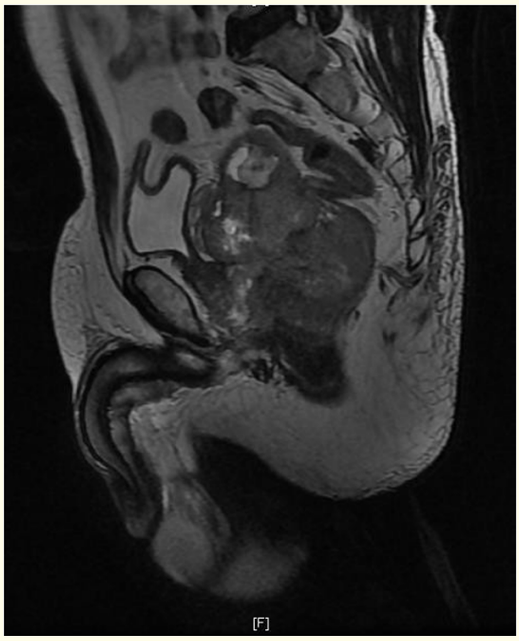

Figure 2: MRI Sagittal T2 view showing the SOL with its involvements and necrosis in upper part.

Colonoscopy showed one large globular mass with normal overlying mucosa seen extending from just proximal to anal verge for 8 cm proximally in rectum. Tru-Cut Biopsy of Prostate Gland showed a lesion composed of spindle shaped cells with enlarged nuclei with no nuclear pleomorphism and scanty mitotic figures. Smooth muscle bundles and rectal glands were also present (Figure 3 and 4).

For proper categorization of this spindle cell lesion Immunohistochemistry (IHC) was done. The lesional cells were positive for CD 34, CD117, DOG1 and negative for SMA and S100.Thus, the final diagnosis of Rectal GIST was achieved extent of which was further evaluated with a PET CT scan which revealed FDG avid heterogeneously enhancing irregular soft tissue mass with area of necrosis

Figure 3: Low power view showing one core of tumour tissue and other core showing colonic glands (HandE 200X).

Figure 4: High power view showing fascicles of malignant spindle cells with moderate nuclear atypia (HandE 400X).

noted arising from the rectum infiltrating the prostate gland, abutting the bilateral seminal vesicles and posterior wall of urinary bladder with an exophytic component extending up to and abutting the recto sigmoid junction cranially (9.0cm x 6.6cm x 12.0cm ; SUVmax 47.6). No distal or nodal metastases was depicted. Treatment was planned with Imatinib for this locally advanced rectal GIST with contiguous prostatic invasion. After one year of continuous administration of Imatinib now on patient's follow up imaging was further evaluated with RECIST (v1.1) which spoke for partial response of the disease.

Discussion

In retrospect, the term "GIST" was coined in 1983 by Mazur and Clark to describe intra-abdominal non-epithelial neoplasms without features of smooth muscle cells and immunohistochemical characteristics of Schwann cells [1].

Gastrointestinal stromal tumors (GISTs) are rare neoplasms which represent only 0.1 - 3% of all gastrointestinal malignancies [2]. The most common GIST sites are the stomach (60% - 70%) followed by the small intestine (20% - 25%). Rectal GIST constitutes

5% of all GISTs and 0.1% of all tumors originating in the rectum [3]. Common sites of metastasis for GIST include liver, peritoneum and omentum; lymph node and extra- abdominal metastases are rare [4]. GISTs that arise primarily outside the GI tract are termed extragastrointestinal stromal tumours (EGISTs).

EGISTs are known to arise from various anatomic sites, such as the momentum, mesentery, retroperitoneum and gall bladder. However, large, typical, completely differentiated GISTs are rare in the extra GI tract [5]. To the best of our knowledge, there have been only five cases of primary prostatic GISTs. Previously, Hansel., *et al.* showed that EGISTs may involve the prostate via a direct extension from the abdominal wall.

[6] In addition, Ghobadi., *et al.* concluded that anorectal GISTs mimic the presentation of prostate cancer [7].

Pathologic features that would favour a diagnosis of GIST include cells with spindled and/or epithelioid morphology, perinuclear cytoplasmic vacuolization, and positive immunostaining for CD117, DOG1 and CD34. [8,9] These tumours often show mutations of the KIT or platelet derived growth factor receptor alpha (PDGFRA) genes [10]. In addition, BRAF mutations have been reported to occur [10,11]. DOG1 immunohistochemical studies may be especially useful, as expression does not appear to be affected by the KIT or PDGFR gene mutation type, and it may be positive in KIT-negative GISTs [10,12].

The pathologic differential diagnosis of spindled neoplasms in the prostate includes schwannoma, melanoma, smooth muscle tumours, solitary fibrous tumour, and prostatic stromal sarcoma. The distinction between GIST and schwannoma can be difficult, as occasional GISTs may show areas suggestive of Verocay bodies. Diffusely and strong immunostaining for S -100 would be typical for schwannoma, while CD117 and smooth muscle markers would be negative. Cytoplasmic clearing and epithelioid cells are typically lacking in schwannoma. While some melanomas may have CD117 positivity, these tumors are DOG1 and CD34 negative, and should stain positively for melanoma tumour markers S100, MART - 1, HMB45, and SOX10. Leiomyoma and leiomyosarcoma typically are positive for smooth muscle actin and desmin, and negative for CD117 and CD34. Solitary fibrous tumors are usually CD34 positive, but they should also be BCL-2 positive and CD117 negative. Prostatic stromal sarcoma may be positive for CD34 and progesterone receptor, but has been negative for CD117 in the three reported cases that analysed this immunostain [8,13,14].

Before diagnosing a primary prostatic GIST, the possibility of a rectal GIST invading and secondarily involving the prostate should be considered [15]. Rectal GISTs may be seen as minute intramural nodules ranging to complex pelvic masses with pelvic extension [4,12]. They may be connected to the prostate, and may mimic a prostate tumour clinically and on imaging studies [4]. Though, primary prostatic GIST is also a true entity, GISTs diagnosed at the time of pathologic examination of prostatic specimens should also be considered to be of rectal origin, and it is somewhat controversial [16].

Miettinen., *et al* [4]. found that CD34 expression in rectal GIST is 92%, but only 50% in small intestinal GIST. Smooth muscle antigen (SMA) is most frequently seen in the small intestinal GISTs (47%), whereas it has been observed in only 14% of rectal GISTs. The reason for these variations has not yet been explained. Digital examination of the rectum, colonoscopy and transrectal ultrasound are essential for its diagnosis, together with preoperative biopsy, which plays a key role in the diagnosis of GIST, since it provides information on the immunohistochemical features and mitotic count. GIST typically expresses CD117, often CD34 and sometimes SMA and S-100, but its expressions vary depending on different sites.

The most important and easily applicable histological criteria for prediction of GIST are its size and mitotic rate [17-20]. A rate of ≤ 5 mitoses per 50 HPF is commonly used as a limit for a tumour with expected benign behaviour, and according to a large study, this can discriminate between benign and malignant tumours, especially gastric GISTs [17]. Tumours of 2 cm in diameter are generally expected to behave in a benign fashion. Tumours of < 5 cm in diameter are associated with a better survival rate than those of 5 cm -10 cm in diameter, which in turn have a better prognosis than those of > 10 cm in diameter. Degrees of cellularity and atypia have also been suggested as useful criteria, but their reproducibility is more problematic. The epithelioid phenotype, which seems to lead to a worse outcome, together with symptoms lasting for at least a year, might be considered as further prognostic factors.

For rectal GIST, various surgical procedures may be considered, including local excision, anterior resection of the rectum and abdomino- perineal resection. The choice of procedure depends on tumour size and location. [21] Imatinib is reserved for the treatment of patients with advanced GIST, in the adjuvant postoperative treatment of high risk tumors, or in cases of incomplete surgical resection [22].

Conclusion

It should be an open approach to diagnose and treat such complicated entity of locally advanced rectal GIST involving other structures to evoke confusion with a diagnosis of EGIST. However, Imatinib played the leading role in treatment of this inoperable case and the final outcome was favourable.

Consent

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

Ethical Approval

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have

therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Competing Interests

Authors have declared that no competing interests exist.

Authors' contributions

This whole work was carried out in collaboration with all authors. CR first examined and documented the detailed history of the patient and monitored the treatment planning and follow up. Histopathology and immunohistochemistry was the result of the effort of TKD. ID planned and supervised the entire study, did the literature search and wrote the manuscript. TKD was the leader of the study group and finalised the manuscript. All authors read and approved the final manuscript.

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