CASE REPORT

Anal canal gastrointestinal stromal tumors - report of a rare case and review of the literature

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Abstract

Background: Gastrointestinal stromal tumors **(**GISTs) are considered as rare gastrointestinal tumors, and their location in the anal track is exceptionally unusual. We describe the case of a 28-year-old man with anal GIST, and a review of the cases that have been reported so far in the literature.

Case report: The patient was referred for treatment of a gradually enlarging perianal mass. Clinical examination and imaging including orthosigmoidoscopy, transanal ultrasound, and magnetic resonance imaging (MRI) revealed a mass sized 7.5 cm in greatest diameter, in relation with the sphincters, which was excised under general anesthesia. His post-operative course was uneventful and he was discharged on the fourth postoperative day. Pathologic examination revealed characteristics of anal GISTs and further treatment with tyrosine kinase inhibitors was planned.

Conclusion: Anal GISTs usually present with rectal bleeding and pain, and only sixteen cases have been reported in the literature. MRI is the radiologic examination of choice, while optimal treatment is considered surgery in combination with adjuvant therapy. Long-term follow-up is necessary. Hippokratia 2016, 20(4): 313-316

Keywords: Gastrointestinal stromal tumor, GIST, anal canal, surgery

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Introduction

Gastrointestinal Stromal Tumors (GISTs) are the most predominant mesenchymal tumors of the gastrointestinal (GI) tract. GISTs vary in size and location, arising from the lower esophagus to the anus. They are most commonly found in the stomach (60 %), followed by jejunum and ileum (30 %), duodenum (5 %), colorectum (<5 %), and esophagus (<1 %). Rarely, they can be found in extra-lumen sites including the mesentery, the omentum, and the retroperitoneum (<5 %)[1]. These tumors equally occur in both genders and, although they may present in any age group, their peak incidence is in the 5th and 6th decade of life[2].

Of foremost importance to GISTs' pathogenesis are two mutations: the mutation of the KIT gene (and its associated overexpression of the KIT receptor tyrosine kinase), and the mutation of the PDGFRA gene. Overall, 80-85 % of patients with GISTs are positive for mutations of either KIT or PDGFRA, while the remaining are usually described as "wild type" in reference to KIT and PDGFRA mutation status, even though recent molecular studies have tried to put a more defined label on them, as well[3].

GISTs are usually asymptomatic, and the diagnosis is often incidental, either during endoscopic procedures for other diseases or on computed tomography imaging, performed for unrelated abdominal conditions. Clinical manifestations are not specific of the occurrence of these tumors and include early satiety, anorexia, nausea, and vomiting, which are symptoms attributable to the location of the tumor along the GI tract. Rarely, acute gastrointestinal obstruction or bleeding may be the first symptom of GISTs[4]. Surgery is the first-line treatment and the only treatment option that may potentially lead to full remission in patients with a localized GIST larger than two cm in diameter[5]. Unlike carcinomas, GISTs exhibit a notable absence of metastases to locoregional lymph nodes. Due to this fact, extended lymph node dissection is not required for a complete gross (R0) resection[6]. On the contrary, the contemporary operative strategy is a limited wedge or segmental resection[7]. Herein, we report a case of an extremely rare location of GIST, namely the anal canal, and the treatment strategy that we employed. A literature review was carried out, due to the rarity of this lesion.

Case Report

A 28-year-old male patient was admitted to our department for surgical treatment of a sizeable perianal mass. His clinical history was unremarkable and he re-

ported a gradually increasing in size perianal mass, especially to the left side during the preceding six months with concomitant pain but no signs of bleeding (Figure 1A). His symptoms were initially attributed to hemorrhoids, and the patient was accordingly treated conservatively. Laboratory tests, included cancer markers, were within normal limits. Clinical examination and imaging including orthosigmoidoscopy and transanal ultrasound showed an anal mass on the fifth hour causing only minor intraluminal pressure, without any other abnormalities (Figure 2A). Magnetic resonance imaging (MRI) revealed a lobular tumor of heterogeneous signal, without central enhancement, with dimensions of 7 x 7.5 x 6 cm, in relation to the sphincters, as well as enlarged inguinal lymph nodes (Figure 2B). Based on his clinical condition and the imaging findings, surgical treatment was considered preferable. Under general anesthesia with the patient in lithotomy position, the mass was completely excised in clear surgical margins (Figure 1B, Figure 1C). Postoperative period was uneventful, and the patient was discharged four days later on good health condition.

Histopathological examination showed a non-encapsulated lesion measuring 8.6 x 6.6 x 4.5 cm, and weighing 110 grams. The cut surface of the mass had a gray-white appearance. Conventional slides stained with hematoxylin and eosin revealed the presence of a spindle-cell tumor with high cellularity and with centrally located foci of hemorrhage and necrosis. Neoplastic cells were arranged in short fascicles and whorls and had elongated nuclei with mild to moderate atypia and perinuclear vacuolization. The mitotic index was high with up to 21 mitosis/50 high-power field (HPF). Between the neoplastic cells, thin bundles of collagen fibers were present. At the periphery of the neoplasm, striated muscle fibers were present. Immunohistochemical analysis revealed diffuse and dense immunoreactivity of the neoplastic cells to the antigens CD117 (Figure 3A) and CD34 (Figure 3B). Few scattered cells were positive for protein S-100. No immunoreactivity was observed for smooth muscle antigen (SMA), desmin, epithelial membrane antigen (EMA), and cytokeratin AE1/3. The final diagnosis was that of a GIST. Considering the maximum diameter of the tumor and its mitotic index, the tumor was classified in a prognostic group 6a. Following histopathology confirmation of GIST, the patient was referred to a tertiary oncology center to be further treated with tyrosine kinase inhibitors (TKIs).

Discussion

While both the rectum and anus are extremely rare locations of GISTs with an estimated incidence of 5 % of all GISTs, it has been reported that anal GIST is a rarity representing only approximately the 3 % (2-8 %) of all anorectal mesenchymal tumors[8,9]. Indeed, only 15 cases

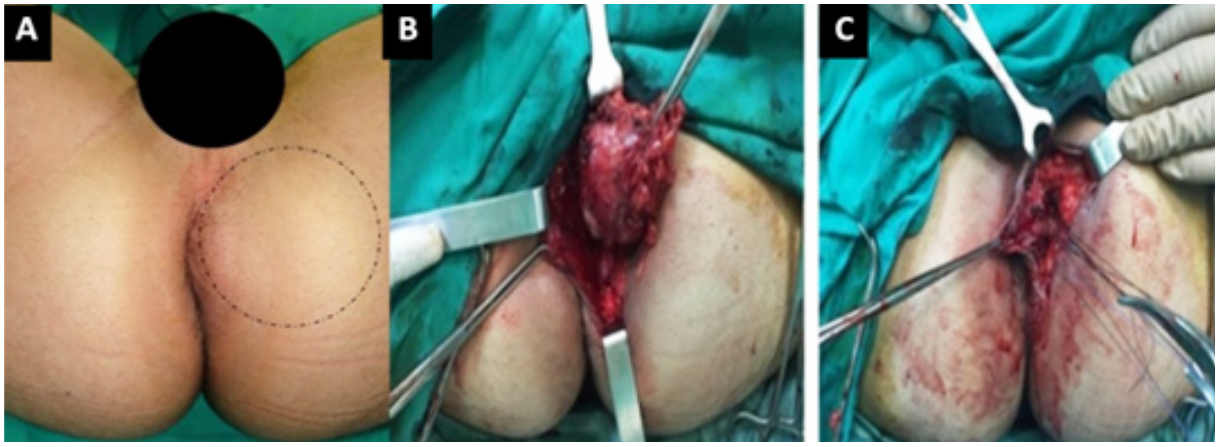

Figure 1: A) Clinical photo showing the presence of a sizeable left perianal mass, B and C) intraoperative photos demonstrating complete excision of the mass with clear surgical margins.

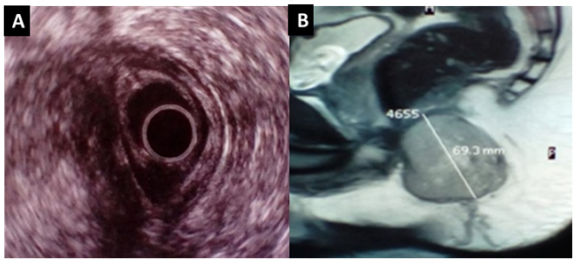

Figure 2: A) Transanal ultrasound showed an anal mass and B) sagittal magnetic resonance imaging showing a lobular tumor of heterogeneous signal, without central enhancement.

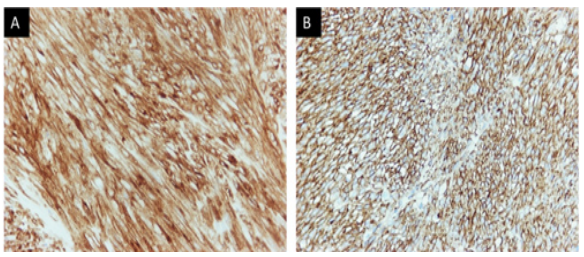

Figure 3: Dense and diffuse immunoreactivity of the neoplastic cells for antigens CD117 (A) and CD34 (B) (x400, immunoperoxidase with hematoxylin counterstain).

Table 1: Characteristics of patients reported in the literature as anal canal gastrointestinal stromal tumors.

Author	Sex	Age	Symptoms
Azzaza et al	Female	70	Anal canal mass
Carvalho N et al	Male	73	Anal mass
Chak-Man Li et al	Female Male	73 67	Anal pain Rectal bleeding
Duarte et al	Male	75	Gluteal mass
Kumar et al	Male	60	Dark color stool
Lanteri R et al	Female	81	Rectal bleeding, abdominal colic pain
Nigri GR et al	Male	78	Incidental finding
Oluyemi et al	Male	61	Rectal bleeding
Paramythiotis et al	Male	27	Anal mass, pain
Ramzan et al	Male	65	Pain during defecation, Constipation
Singhal et al	Male	61	Pain during defecation, Rectal bleeding
Terada et al	Female	70	Anal mass
Wachter et al	Male	56	anemia
Current case	Male	28	Enlarging anal mass

(with the present) of anal canal GISTs have been reported in the literature. The majority of anorectal GISTs, and consequently of anal canal GISTs, present in males in their fifth to seventh decade of life[10]. Reported cases of anal canal GISTs mention rectal bleeding and pain during defecation as the most common presenting symptoms of the disease and the main reason for the evaluation of the patient. In one patient, the presence of anal canal GIST was an incidental finding during a routine physical exam, while in another reported case the presence of the anal mass was noted by the patient. In Table 1, the characteristics of the patients in literature reported cases with anal canal GISTs are summarized[8-11]. In most cases, anal GISTs were discovered during endoscopic procedures for other unrelated health issues or while investigating the presenting symptoms. The endoscopic features characteristical of GISTs include a smooth shape, a normal overlying mucosa, occasional mucosal ulceration, and firm consistency on compression[12]. The typical imaging algorithm for GISTs includes an initial staging evaluation with multiphasic computed tomography (CT). A CT scan, with intravenous contrast and image acquisition of both the arterial and portal phases, allows for identification of hypervascular lesions in the liver, which may signify the presence of metastatic disease, and furthermore, this modality may be used for the follow-up of patients, since these lesions become hypodense with treatment. In a CT scan, GISTs may also appear as well-circumscribed extra-luminal space-occupying masses that, after infusion of the contrast, exhibit heterogeneous enhancement, especially some larger GISTs, with necrotic-hemorrhagic areas or degenerative components[13]. In MRI imaging, these tumors may present as circumscribed, smooth solid masses that cause narrowing of the lumen. The submucosal location of GISTs makes endoscopy less useful for diagnosis. Some lesions might have central necrosis. Therefore, on MRI, they tend to have diffuse low signal on T1 and high signal on T2. Post-contrast enhancement is homogenous in the solid variety and ring pattern in case of a necrotic center. Signs of malignancy include a large size, lobulated contours, increase in size on follow-up imaging and presence of hematogenous metastases. Up to 50 % of all GISTs will have evidence of metastatic disease at the time of presentation, which significantly impacts prognosis[11]. Endoanal ultrasound is also a very useful imaging technique. Anal GISTs may be depicted as hypoechoic lesions in the intersphincetric plane without the presence of regional lymphadenopathy[9,10]. A preoperative biopsy is not necessary when a lesion is considered suspicious, resectable or operable. However, a preoperative specimen would be appropriate when treating patients with disseminated disease or in locally advanced GISTs, where neoadjuvant therapy is being considered[14]. The final diagnosis is established with both its unique microscopic features, which are distinctive of GISTs, and the immunochemical methods (CD-117, CD34, actin, desmin, S-100, and ki-67). The pathology report should include relevant features of the tumor such as its size (< or >5 cm), the number of mitoses per 50 HPF (10 mm^2; low grade ≤5/50 HPF; high grade >5/50 HPF) counted in the most active regions, and margins status[15,16].

GISTs are best treated by surgery, while radiotherapy or conventional chemotherapy are not efficient as adjuvant therapies. However, controversy exists regarding whether abdominoperineal resection (APR) or conservative surgery is the best alternative surgical option for anal canal GISTs[17]. Although the incidence of local recurrence is reported to be lower after APR, the distant metastasis and survival rates are not significantly different[9,10]. Therefore, it has been suggested that low-risk GISTs with size below two cm and mitosis less than five per 50 HPF may be considered suitable for local excision if sphincter-saving surgery is technically feasible, while more aggressive GISTs should be treated with radical excision[14]. Furthermore, the margin positivity (R1) may indicate the need of a more aggressive treatment, such as abdominoperineal resection, if a local resection has been employed, especially if the tumor belongs to high or very high-risk group (size >5 cm, >5 mitosis per 50 HPF)[9]. Regarding Tyrosine kinase inhibitors, such as imatinib, as adjuvant therapy, there is still some controversy, as the incidence of anal canal GISTs is very low, and they are still categorized in a larger group, namely the rectal GISTs. It has been proposed that imatinib may be administered for unresectable primary or recurrent GIST since it has shown efficiency in controlling the disease's pro-

gression. Furthermore, patients with high-risk tumors are good candidates for imatinib adjuvant therapy, to reduce the incidence of recurrence[17].

Conclusion

Anal canal GISTs are exceptionally rare tumors, and their symptoms can be misleading. Long-term follow-up of patients with anal canal GISTs should be employed since there have been recurrences that were described even ten years after the initial resection. Routine physical examination, as well as proctoscopy, should be offered at predetermined time points or when new symptoms arise. Close clinical examination, surgical treatment and careful pathologic examination of perianal masses are crucial for the best overall treatment of these conditions.

Conflict of interest

The Authors declare no conflict of interest

References

1. Pisters PW, Patel SR. Gastrointestinal stromal tumors: current management. J Surg Oncol. 2010; 102: 530-538.
2. D'Adamo D. Advances in the treatment of gastrointestinal stromal tumor. Adv Ther. 2009; 26: 826-837.
3. Valsangkar N, Sehdev A, Misra S, Zimmers TA, O'Neil BH, Koniaris LG. Current management of gastrointestinal stromal tumors: Surgery, current biomarkers, mutations, and therapy. Surgery. 2015; 158: 1149-1164.
4. Paramythiotis D, Panidis S, Panagiotou D, Vasileiadou K, Kalogera-Fountzila A, Kouskouras K, et al Surgical management of a giant metastatic Gastrointestinal Stromal Tumor without neoadjuvant therapy with TKI: Case Report. Surg Chron. 2012; 17: 278-281.
5. Paral J, Slaninka I, Kalabova H, Hadzi-Nikolov D. Gastrointestinal stromal tumors: review on morphology, molecular pathology, diagnostics, prognosis and treatment options. Acta Gastroenterol Belg. 2010; 73: 349-359.
6. Huang W, Goldberg RJ, Anderson FA, Kiefe CI, Spencer FA. Secular trends in occurrence of acute venous thromboembolism: the Worcester VTE study (1985-2009). Am J Med. 2014; 127: 829-839.e5.
7. Poškus E, Petrik P, Petrik E, Lipnickas V, Stanaitis J, Strupas K. Surgical management of gastrointestinal stromal tumors: a single center experience. Wideochir Inne Tech Maloinwazyjne. 2014; 9: 71-82.
8. Singhal S, Singhal A, Tugnait R, Varghese V, Tiwari B, Arora PK, et al. Anorectal gastrointestinal stromal tumor: a case report and literature review. Case Rep Gastrointest Med. 2013; 2013: 934875.
9. Nigri GR, Dente M, Valabrega S, Aurello P, D'Angelo F, Montrone G, et al. Gastrointestinal stromal tumor of the anal canal: an unusual presentation. World J Surg Oncol. 2007; 5: 20.
10. Carvalho N, Albergaria D, Lebre R, Giria J, Fernandes V, Vidal H, et al. Anal canal gastrointestinal stromal tumors: Case report and literature review. World J Gastroenterol. 2014; 20: 319-322.
11. Ramzan A, Sarfraz MD, Majeed H, Baig S, Inayat F. Recurrent anal canal gastrointestinal stromal tumor. Pakistan J Radiol. 2015; 25: 175-178.
12. Sepe PS, Brugge WR. A guide for the diagnosis and management of gastrointestinal stromal cell tumors. Nat Rev Gastroenterol Hepatol. 2009; 6: 363-371.
13. Lee CM, Chen HC, Leung TK, Chen YY. Gastrointestinal stromal tumor: Computed tomographic features. World J Gastroenterol. 2004; 10: 2417-2418.
14. Lamba G, Gupta R, Lee B, Ambrale S, Liu D. Current management and prognostic features for gastrointestinal stromal tumor (GIST). Exp Hematol Oncol. 2012; 1: 14.
15. Poveda A, del Muro XG, López-Guerrero JA, Martínez V, Romero I, Valverde C, et al. GEIS 2013 guidelines for gastrointestinal sarcomas (GIST). Cancer Chemother Pharmacol. 2014; 74: 883-898.
16. Changchien CR, Wu MC, Tasi WS, Tang R, Chiang JM, Chen JS, et al. Evaluation of prognosis for malignant rectal gastrointestinal stromal tumor by clinical parameters and immunohistochemical staining. Dis Colon Rectum. 2004; 47: 1922-1929.
17. Azzaza M, Ammar H, Abdessayed N, Gupta R, Nakhli MS, Chhaider A, et al. Wide local excision for anal GIST: A case report and review of literature. Int J Surg Case Rep. 2017; 30: 97-100.