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Case Report

A rectal gastrointestinal stromal tumor case accompanied by elevated CEA mimicking rectal carcinoma on ^{18}F-FDG PET/CT

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Abstract: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasm arising from gastrointestinal tract and can be benign or malignant. Rectal GISTs are rare and have poor prognosis. We here reported an older male who presented with features of distending discomfort in the rectum and pain in the anus due to a large rectal tumor. Physical examinations detected a mass in the rectum without blood staining on the gloved finger. Carcinoembryonic antigen (CEA) was found to be slightly elevated and the prostate-specific antigen level was normal. ^{18}F-FDG PET/CT showed a soft tissue density mass at the bottom of the pelvic, with an unclear boundary to the surroundings with the significantly increased FDG uptake (SUVmax 17.5). Although a rectal carcinoma was suspected based on the finding of PET/CT and CEA, the histopathological examination confirmed the diagnosis of the malignant GIST of the rectum. The patient was then treated with imatinib and on follow-up regularly. In this case, ^{18}F-FDG PET/CT shows the advantage of visualizing both primary and metastatic lesions and provides valuable information for the diagnosis, staging, evaluation, and prognosis of GIST.

Keywords: Gastrointestinal stromal tumor, GIST, rectum, ^{18}F-FDG, PET/CT, case report

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasm arising from interstitial cells of Cajal in the gastrointestinal tract. GISTs most commonly occur in the stomach and the small intestine [1]. Rectal GISTs are rare and reported to account for only 5% of all GISTs [1, 2]. Tumors in the rectum present a challenge in diagnosis and treatment compared to other locations within the gastrointestinal tract, because of the complexity of pelvic anatomy and poor prognosis. The common clinical symptoms are abnormal bowel movement, rectal masses and rectal bleeding. 2-Deoxy-2-[fluorine-18]-fluoro-D-glucose (^{18}F-FDG) positron emission tomography computed tomography (PET/CT) is an important diagnostic and staging tool for the GISTs [3], which has also been found to be highly sensitive in assessment of response to Imatinib [4]. Here, we present a case of a gastrointestinal stromal tumor of rectum imaged by ^{18}F-FDG PET/CT.

Case presentation

A 68-year-old man presented with complaints of dysuria, distending discomfort in the rectum and pain in the anus for more than one year with a change in stool form. Physical examinations detected a mass at the 3 o'clock direction about 4 cm to the anus in the knee-chest position, which was found with firm texture, smooth surface, well-defined borders and good mobility on palpation. Blood staining was not detected on the gloved finger. Laboratory tests showed slightly increased carcinoembryonic antigen (CEA, 7.36 ng/ml) and carbohydrate antigen 242 (CA-242 20.71 U/ml). The prostate-specific antigen level was normal. The patient had a history of hyperplasia of prostate for more than 10 years and pulmonary tuberculosis for more than 20 years.

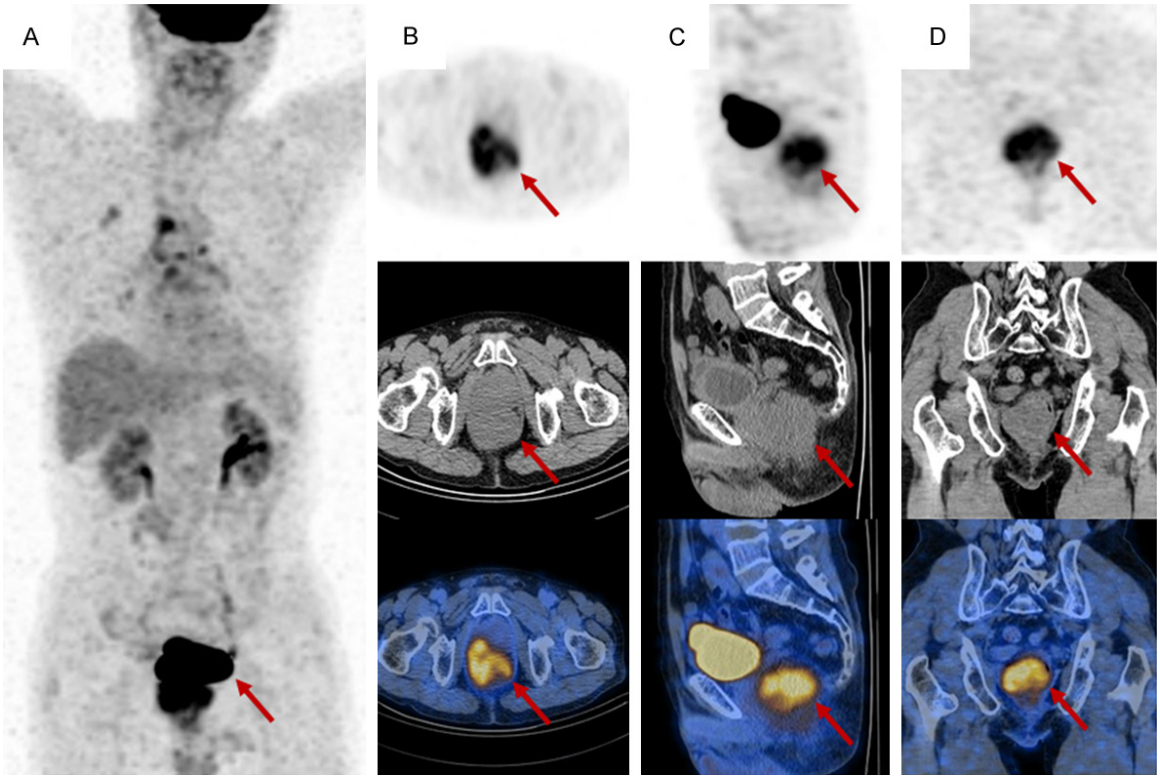

Figure 1. ^{18}F-FDG PET/CT images. (A) The whole-body maximum intensity projection showed the hypermetabolic lesion of the rectum. (B) Pelvic transverse, (C) Sagittal and (D) Coronal images showed a soft tissue density mass at the bottom of the pelvic, with an unclear boundary to the rectum and right seminal vesicle. Increased FDG uptake of the lesion was observed with SUVmax 17.5.

Contrast-enhanced computed tomography (CT) of the abdomen revealed an irregular soft-tissue mass in the mesorectum on the right with infiltration into rectal muscular and the right margin of prostate. The size of the lesion was 62 mm × 62 mm × 49 mm. To further evaluate the whole-body situation, ^{18}F-FDG PET/CT was performed. PET/CT showed a soft tissue density mass at the bottom of the pelvic, with an unclear boundary to the rectum and right seminal vesicle, measured 62 mm × 55 mm × 48 mm (**Figure 1**). FDG uptake of the lesions was significantly increased (SUVmax 17.5) and no enlarged lymph nodes with increased FDG uptake were found around the rectum in the pelvis, suggesting a rectal malignant tumor. Multiple high density lymph nodes with slightly increased FDG uptake (SUVmax 5.6) were found in hilum and mediastinum, however they were considered to be age-related non-specific because of high density.

Biopsy of the rectum was reported as spindle cell tumor arranged in fascicles and braided with mild to moderate atypia. Immunohistochemiscal staining showed positive for CD117, CD34, DOG-1, SMA and Ki-67 (8%), and negative for Desmin, S-100 and SDHB (**Figure 2**). A final diagnosis of malignant GIST of the rectum at high risk was then made according to the National Institutes of Health (NIH) staging system [5].

After considering the condition of the patient, Imatinib, which is a kind of specific tyrosine kinase receptor inhibitor, was used to treat the GISTs and transurethral resection of the prostate was performed for the treatment of benign prostatic hyperplasia. The patient was followed up regularly without any evidence of recurrence. After 2 months of treatment, magnetic resonance imaging (MRI) showed that the size of the tumor changed to 35 mm × 38 mm × 37 mm, and there were no enlarged lymph nodes around (**Figure 3**).

Discussion

GISTs originate from the interstitial cells of Cajal, which arise from the muscularis propria

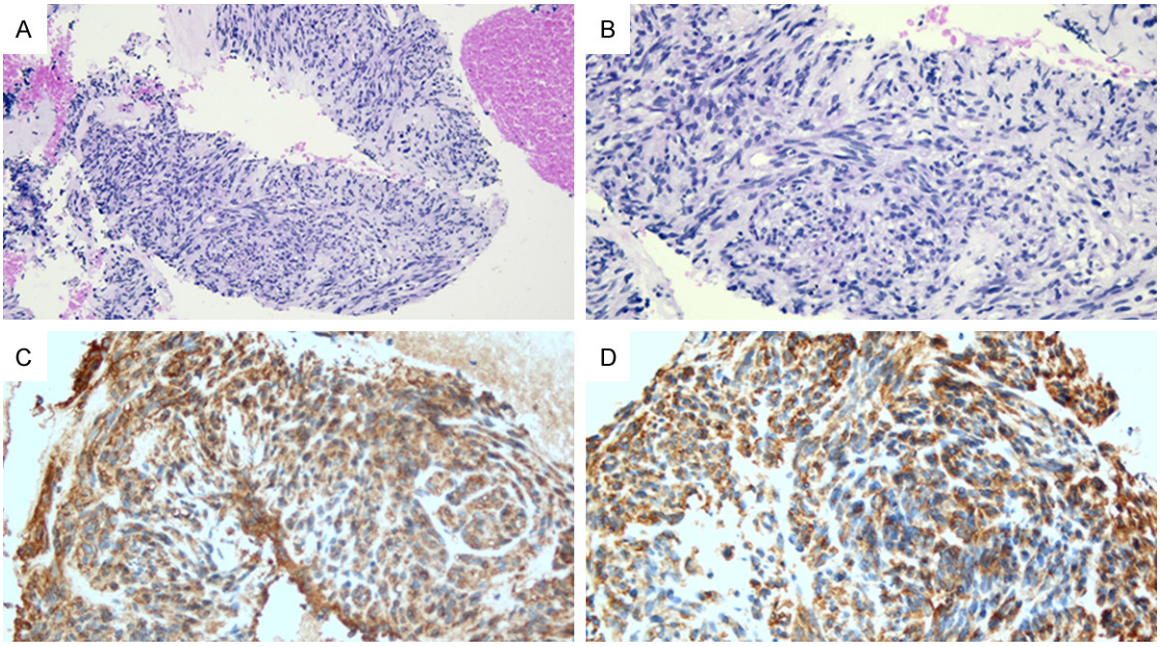

Figure 2. Histologic and immunohistochemical features. (A) × 200 and (B) × 400 Hematoxylin-eosin (HE) staining showed that pindle cell tumor were arranged in fascicles and braided with mild to moderate atypia (C) CD117 positive (D) DOG1 positive.

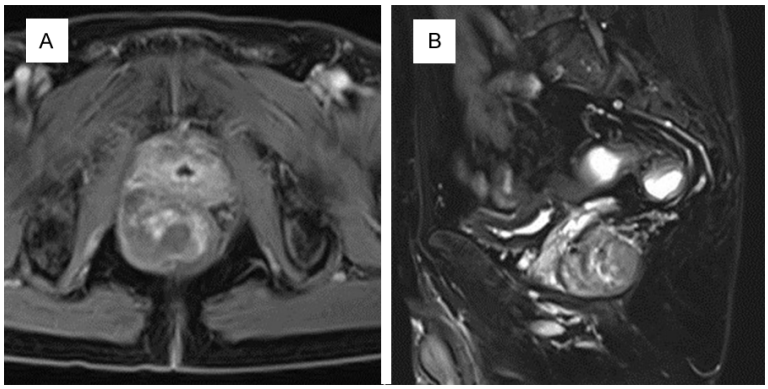

Figure 3. (A) Transverse and (B) sagittal sections of pelvis MRI imaging after 2 months of imatinib treatment. A significant reduction in the size of the rectal mass was shown.

of the gastrointestinal tract wall [6]. GISTs develop with the activating mutation of c-kit/platelet-derived growth factor receptor alpha (*PDGFRα*) in most cases. Majority of GISTs occur in the gastrointestinal tract. Stomach (50% to 60%) and the small intestine (25%) are common primary sites whereas primary rectal GISTs are rare (5%). The most common metastatic sites of GISTs are liver and peritoneal. Several rare distant metastatic sites, such as bones and lungs, have also been reported [2]. Bones metastases usually involve the mandible, spine and femur, whereas there was also a case of metastasis to the scapula [7]. Previous epidemiology evidence has shown that most rectal GISTs patients are aged 16 to 84 years old and are diagnosed at a median age of 54 years with a higher incidence in males [8]. There were no special clinical manifestations in the early stage of rectal GISTs, and many rectal GISTs were accidentally found during physical examination. With the development of GISTs, patients may have clinical manifestations such as hematochezia, difficulty in defecation or changes in defecation habits. In this case, the clinical manifestations were distending discomfort in the rectum, pain in the anus and a change in stool form. Dysuria was considered the result of benign prostatic hyperplasia.

Accurate diagnosis of the rectal GISTs is established by biopsy and immunohistochemistry. According to tumor cell morphology, majorities of GISTs can be divided into three subtypes:

spindle cell type, epithelioid type, and mixed spindle cell-epithelial type [9]. The best immunostaining method to identify gastrointestinal stromal tumors is the detection of expression of KIT, also known as CD117, a transmembrane tyrosine kinase receptor that has been immunolocalized in various tumors. About 5% of gastrointestinal stromal tumors do not stain positive for KIT. Other immunohistochemical markers commonly observed in GISTs are CD34 (60%-70%) and smooth muscle actin (SMA) (30%-40%). A small number of gastrointestinal stromal tumors can be positive for desmin or S-100. Molecular testing revealed that most cases had activating mutations in the KIT or PDGFRA genes, and some cases involved other molecular changes, including mutations in the succinate dehydrogenase (SDH) subunit, BRAF, NF1, K/NRAS, and PIK3CA, as well as gene rearrangements, such as FGFR1, NTRK3 and BRAF, etc [9].

CT and MRI play considerable role in evaluation of rectal GISTs size, morphology, depth of infiltration and metastasis for diagnosis, prognosis and recurrence. Contrast enhancement CT scan shows solid nodule or mass in the rectum with enhancement by intravenous contrast medium. GISTs are hyper-vascular, most of which are inhomogeneous medium to high enhancement. MRI is performed when patients cannot tolerate intravenous contrast media or GISTs occur in the untypical sites such as rectum which need to evaluate the range of surgical anatomy. In this case, CT was used to assess the size and extent of tumor. However, CT and MRI imaging are limited in detecting whole body metastasis of GISTs.

^{18}F-FDG PET/CT imaging, combining the advantages of both anatomic information from CT and functional information from PET, will be helpful for clinical decision-making, response evaluation and prognosis, etc. There were several previous cases of rectal GISTs imaged by PET/CT reported. Kramp et al [10] found a large metabolically active distal rectal tumor with macroscopic invasion of the surroundings, and observed decrease in tumor size and complete metabolic evaluation within 3 months after treatment. Selcukbiricik et al [7] showed a rectal GIST with a large metabolically active lesion in scapula, which revealed metastasis in scapula. Li et al [11] reported a rectal GIST without metastasis and SUVmax of the tumor was 8.8. In our case, the SUVmax was significantly high (17.5). All the lesions of the reported patients showed hypermetabolism.

Because GISTs often lack specific clinical manifestations at the early stage, many patients might have metastatic disease when GIST is diagnosis. In previous literature reports, the metastasis rate at the time of diagnosis was as high as 61% [12]. CT and MRI have limitations in detecting metastatic lesions, whereas PET/CT imaging plays an important role in GISTs staging because it visualizes both primary and metastatic lesions. PET/CT is also helpful in identifying unknown primary lesions or clarifying ambiguous CT findings when CT findings are inconclusive or inconsistent with clinical findings [13]. The sensitivity of PET to detect GISTs, including metastases, ranges from 86% to 100% [14, 15]. PET/CT accurately delineates the primary tumor and metastases, and is used to guide the clinical treatment. Lesions that have little impact on adjacent major organs can be directly surgically resected. For inoperable lesions, targeted treatment can be used to reduce the size of the tumor and monitor changes in the condition. If adjuvant therapy is effective, PET/CT can also be used to determine the surgical field [16].

Previous studies have shown that SUVmax can help predict the malignant potential of GISTs, because FDG-PET reflects the functional activity of lesions. Park et al [17] reported that SUVmax was significantly associated with NIH risk score. The optimal cut-off value for low risk (NIH very low, low risk) and high risk (NIH medium and high risk) was 3.94. In this case, the SUVmax of tumor is 18.4. Finally, it also carries a high risk, which is consistent with previous research.

PET/CT also allows timely assessment of treatment response to imatinib therapy. Imatinib is recommended for preoperative drug therapy to reduce tumor volume, reduce clinical stage, avoid joint organ resection, and is also recommended for unresectable and metastatic tumors. In previous studies, CT had been used to assess the effect of treatment on volumetric changes in solid tumors, but not all tumors that respond to imatinib treatment shrunk immediately after treatment due to cystic degeneration or hemorrhage. The conditions of some patients progressed after treatment, but there

might be no significant change on CT, and even the volume shrunk due to the increase of nodules and density in the tumor [18]. However, there are short-term changes in tumor metabolism, mainly manifested by decreased ^{18}F-FDG uptake in responsive patients, which is faster and more accurate than volumetric measurements [19, 20]. Studies have shown that the shortest changes in ^{18}F-FDG uptake can be observed after 24 hours of treatment [21]. PET/CT can also play a role in prognostic assessment, Choi [22] found that patients whose SUVmax of tumor decreased significantly after treatment had a longer tumor progression-free survival.

In this case, the patient presented with a rectal mass with high FDG uptake (SUVmax 17.5), requiring differential diagnosis from rectal adenocarcinoma and lymphoma. Rectal adenocarcinoma lesions are mostly soft tissue masses with endophytic growth. Patients with rectal adenocarcinoma often present with abdominal pain, changes in bowel habits, hematochezia, with increased tumor biomarkers such as CEA. Advanced tumors could invade adjacent tissues, and distant multiple liver metastases are common. Patients with lymphoma often have enlarged livers and spleens, as well as enlarged lymph nodes in other parts of the body. Most of the lesions grow infiltrative along the intestinal wall, with diffuse thickening and wide distribution. Rectal adenocarcinoma and lymphoma also showed hypermetabolism on PET/CT. Previous evidence showed that the SUVmax of primary gastrointestinal lymphoma is higher than GISTs [23]. In other cases, inflammatory lesions and physiological uptake can also lead to false-positive on PET/CT, while necrosis and myxoid degeneration can also lead to false-negative results.

For patients diagnosed as GISTs, clinical evaluation should be performed first to determine the location, size, location, and metastasis of the tumor to select the treatment options. The middle and lower part of the rectum is located in the pelvic cavity, and has a complex relationship with surrounding organs, nerves, and blood vessels. Once this part of GIST grows, there is a risk of resection of the rectum and anus or even joint resection of the pelvic organs. In addition, complex pelvic surgery also has the risk of pelvic nerve damage, which may affect the patient's postoperative defecation function and sexual function. Therefore, more aggressive treatment should be taken for rectal GISTs. The basic principles of GISTs surgical treatment include: complete tumor resection confirmed negative resection margins (R0), not recommending routine lymph node dissection, avoiding intraoperative tumor rupture, and protecting the integrity of the tumor pseudocapsule. Imatinib mesylate (IM), a kind of specific tyrosine kinase receptor inhibitor, should be used when the tumor is unresectable or is expected to have a high risk of complications after resection, and surgery should be performed after tumor shrinkage. Tumor size, mitotic index, R0 resection, and c-kit positivity are important prognostic factors. Previous evidence showed that even if the tumor was completely resected, the recurrence rate of malignant GISTs that invaded and metastasized was as high as 41% [24], and the 5-year survival rate of patients was less than 45% [2], which required long-term follow-up.

Conclusion

Gastrointestinal stromal tumors of the rectum are rarely reported tumors, and this primary location site is more likely to have worse outcomes. Rectal GISTs should be taken in to account when patients present with hematochezia, difficulty in defecation or changes in defecation habits. Diagnosis is established by biopsy and immunohistochemistry. ^{18}F-FDG PET/CT takes the advantage of evaluating the whole-body situation by combining anatomic and functional information, providing guidance for diagnosis, staging, clinical decision-making, prognosis and recurrence detection of rectal GISTs.

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Disclosure of conflict of interest

None.

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