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Case Report

^{18}F-FDG PET/CT imaging of primary malignant melanoma of rectum with liver metastases mimicking rectum cancer: case report and literature review

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Abstract: Malignant melanoma (MM) is an aggressive malignant tumor, which mostly occurs on the skin, uvea, etc. The mucosal MM accounts for a small proportion of all MM and can occur in the digestive tract. Primary MM of the digestive tract is rare and can be found in the middle and lower third of the esophagus and the rectum containing melanocytes. Primary rectal MM often occurs in middle-aged and elderly women, with rapid progress and strong invasion. We report a case of a 61-year-old man diagnosed with primary malignant melanoma of the rectum with liver metastases mimicking rectum cancer. ^{18}F-FDG PET/CT showed the rectal wall was markedly thickened with a high metabolic level (SUVmax 10.6) and the boundary between the lesions and the prostate was unclear. In addition, increased FDG uptake were found in multiple lymph nodes, lung, liver, and bones, suggesting metastasis. In this case, ^{18}F-FDG PET/CT shows the advantage of evaluating the whole-body situation and provides valuable information for the diagnosis, tumor stage, evaluation of treatment efficacy, and prognosis of MM.

Keywords: Malignant melanoma, primary, rectum, ^{18}F-FDG, PET/CT

Introduction

Malignant melanoma (MM) is an aggressive malignant tumor, which is prone to relapse and metastasis and has a poor prognosis. It mostly occurs on the skin, uvea, etc. The mucosal MM accounts for 0.8%-3.7% of all MM and can occur in the digestive tract [1, 2]. Primary anorectal MM is a rare type of MM, which accounts for only 0.5%-2% of all MM [3]. Rectal MM mostly occurs in middle-aged and elderly women, with rapid progress and strong invasion [4]. The common clinical symptoms are rectal bleeding, abnormal bowel movement, perianal or rectal masses, etc. [5, 6]. 2-Deoxy-2-[fluorine-18]-fluoro-D-glucose (^{18}F-FDG) positron emission tomography combined with computed tomography (PET/CT) has a high sensitivity in the diagnosis of metastatic lesions, which can help to find small or metastatic lesions and make an accurate tumor stage [7, 8]. As for the treatment of MM, ^{18}F-FDG PET/CT can be used to assess whether patients can have surgery or not and it plays a role in the early recognition of tumor response and detection of side effects of autoimmunity. It can also prospectively predict long-term efficacy and provide the best time window for treatment [8-10].

Case presentation

A 61-year-old man presented with no obvious predisposing cause of anal pain and discomfort, difficulty in defecation, and bloody stool for more than one month. Physical examinations found a normal appearance of the anus with bloody secretion. Laboratory tests showed increased white blood cell count (15.00 × 10^9/L), neutrophil count (10.90 × 10^9/L), interleukin 6 (39.71 pg/mL) and procalcitonin (0.07 ng/mL). The patient was previously in good health and had no melanoma or nevus of the skin or mucosa, no history of resection of body surface tumor, and no familial history of hereditary diseases.

Abdominal contrast-enhanced CT revealed a rectal mass and multiple soft tissue nodules around the rectum, suggesting lymph node

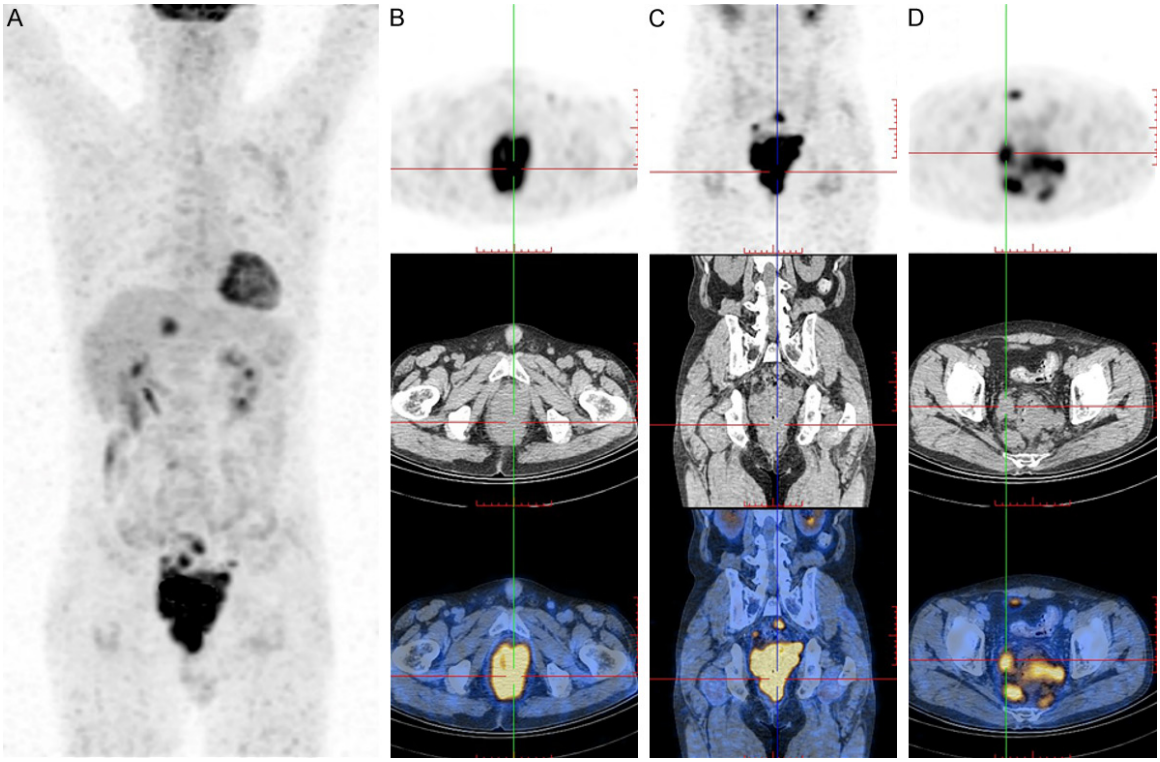

Figure 1. ^{18}F-FDG PET/CT images. (A) The whole-body maximum intensity projection showed the hypermetabolic lesion of the rectum. Pelvic transverse (B) and coronal (C) images showed that the rectal wall was thickened, the corresponding lumen was narrow, and the boundary between the lesion and the prostate was unclear. Increased FDG uptake of the lesion was observed with SUVmax 10.6. (D) Multiple lymph nodes in the pelvis with increased FDG uptake.

metastasis. There were low-density lesions in the caudate lobe of the liver, also suggesting metastasis. To further evaluate the whole-body situation, ^{18}F-FDG PET/CT was performed. The rectal wall was markedly thickened, with about 4.8 cm at its thickest part while intestinal stenosis occurred. The boundary between the lesions and the prostate was unclear and FDG uptake of the lesions was increased (SUVmax 10.6). Multiple enlarged lymph nodes with increased FDG uptake were found around the rectum in the pelvis (SUVmax 7.9) with the short diameter of the largest one at about 2.6 cm. Multiple lungs and subpleural nodules with soft tissue density less than 0.8 cm in diameter were found without FDG uptake. A patchy ground-glass lesion was found in the upper lobe of the right lung, with a mild increased FDG uptake and a SUVmax of 0.7. Also, a lesion with increased FDG uptake in the caudate lobe of the liver was found (SUVmax 7.2). There was a small low-density lesion with FDG uptake on the right side of the fourth lumbar vertebra (SUVmax 3.7), suggesting metastasis (**Figures 1**, **2**). Based on the imaging results, a rectal malignant tumor was considered with multiple metastases of lymph nodes, lung, liver, and bone.

To make the final diagnosis, a rectoscopy and biopsy were performed. The circumferential rectal mass was 2-12 cm away from the anal margin, occupying 1/3 of the lumen. The mass was hard and prone to bleeding, while multiple colonic polyps were also found. The biopsy showed diffuse proliferation of markedly heterotypic tumor cells in the intestinal mucosa with melanin granules in the cytoplasm (**Figure 3A**). Immunohistochemistry staining results demonstrated the positive expression of Vimentin, S-100, human melanoma black 45 (HMB-45), melanoma antigen A (Melan-A), micronuclear linker histone 1, melanocyte-stimulating hormone 2 (MSH2), MSH, postmeiotic segregation increased 2 (PMS2) and Ki-67 (80%+), whereas the negative expression of pan-cytokeratin 7 (CK7), CK20, cluster of differentiation 56 (CD56), CD20, CD3, chromo-

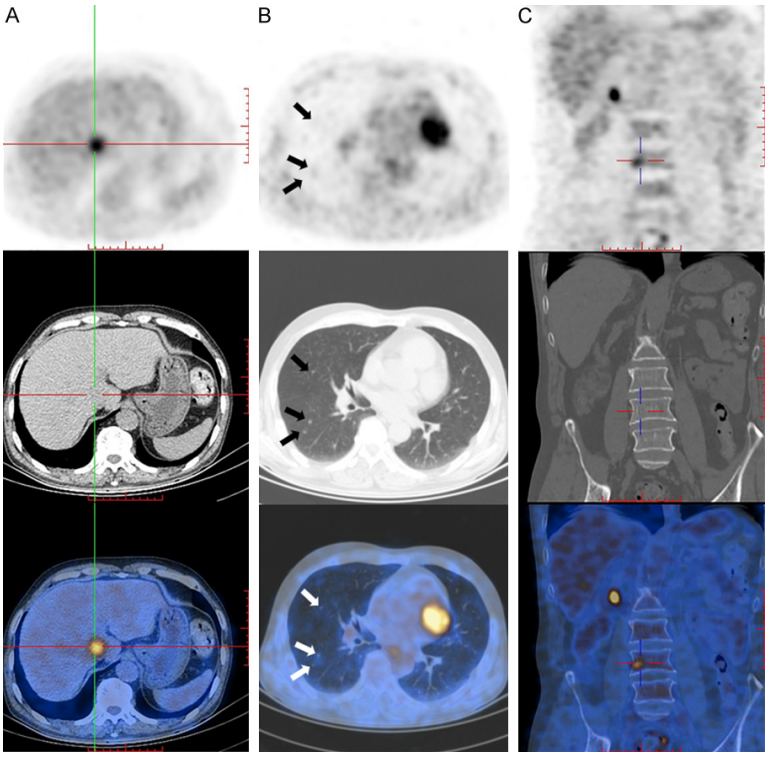

Figure 2. ^{18}F-FDG PET/CT images. (A) The lesion in the caudate lobe of the liver with increased FDG uptake. (B) Several nodules in the upper lobe of the right lung with increased FDG uptake partially. (C) The lesion on the right side of the fourth lumbar vertebra with increased FDG uptake.

granin A (CgA), Villin, caudal homeobox 2 (**Figure 3B-D**). Based on the pathology and immunohistochemistry, the final diagnosis of malignant melanoma (MM) was made.

After a multidisciplinary discussion, we considered that the patient had multiple metastases throughout the body and the clinical stage was stage IV. Medical treatment as the main treatment was recommended and emergency surgery should be performed in case of intestinal obstruction. Although the patient was treated with 240 mg Toripalimab in combination with 5 mg Axitinib for four cycles, he died five months after the diagnosis.

Discussion

Malignant melanoma (MM) is an aggressive malignant tumor derived from melanocytes or precursor cells, which is prone to relapse and metastasis and has a poor prognosis. Its incidence has been increasing worldwide. It mostly occurs on the skin, uvea, etc. The mucosal MM accounts for 0.8%-3.7% of all MM and often occurs in the mucosa tissues adjacent to the skin, such as the nasopharynx, laryngopharynx, pleura, trachea, bronchi, digestive tract, and genitourinary tract [1, 2]. Primary MM of the digestive tract is rare and can be found in the middle and lower third of the esophagus and the rectum containing melanocytes. Primary anorectal MM accounts for 0.5%-2% of all MM and accounts for 0.05%-4.6% of anorectal malignancies [3]. The etiology of rectal MM is currently unknown and has been reported to be related to a history of benign nevus of the anus and human papillomavirus (HPV) infection [11]. The patient in our case had no melanoma or nevus of the skin or mucosa and had no previous history of resection of a body surface tumor. The final diagnosis was primary rectal MM. Rectal MM mostly occurs in middle-aged and elderly women with rapid progress and strong invasion. It is prone to hematogenous and lymphogenous metastasis and can metastasize to the liver, lung, and brain [4]. The common clinical symptoms are rectal bleeding, change of bowel movement, perianal or rectal masses, etc. [5, 6]. Progressive severe abdominal pain or vomiting caused by liver metastasis has also been reported as the first manifestation [12]. Because of the lack of characteristic symptoms and signs, MM could be misdiagnosed as hemorrhoids, rectal polyps, or rectal cancer, resulting in delayed treatment and affecting the prognosis. The clinical symptoms of the patient, in this case, included anal pain, and difficult defecation with blood in the stool, which progressed rapidly. The time from symptom onset to diagnosis was only two months whereas lymph nodes, lung, liver, and bone metastasis occurred at the time of the diagnosis.

Imaging manifestations of rectal MM include local masses or annular thickened bowel, which can break through the serosal layer and invade adjacent organs, accompanied by lymph node metastasis and distant metastasis. Contrast enhancement CT scan showed that the lesions

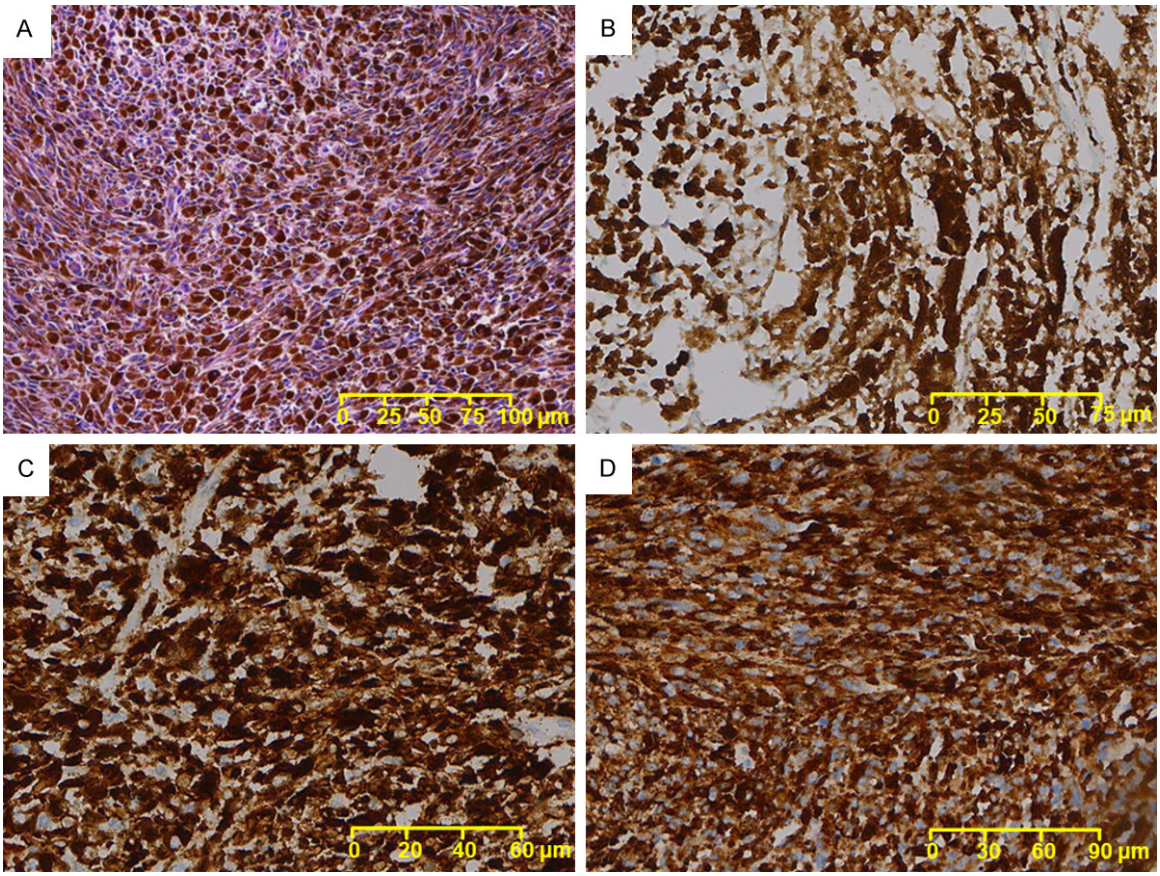

Figure 3. Histologic and immunohistochemical features. (A) Hematoxylin-eosin (HE) staining showed that heterotypic tumor cells proliferated in the intestinal mucosa, and melanin granules were found in the cytoplasm. In immunohistochemical staining (Envision × 200), the highly specific markers of malignant melanoma S-100++ (B), Melan-A+ (C), HMB45++ (D).

were mainly moderately enhanced in the arterial phase and continuously enhanced in the venous phase or the delayed phase. As melanin is a paramagnetic medium on MRI, the T1 and T2 relaxation times can be shortened, which is characterized by hyperintensity on T1WI and hypointensity on T2WI. However, CT and MRI imaging are limited in detecting metastasis of MM.

^{18}F-FDG PET/CT examination combined with morphological and metabolic information can be used as a favorable examination [13]. A literature search was performed on the PubMed database from 2007 to 2022, using the keyword “rectal malignant melanoma” and “PET/CT”. There were eight cases of rectal MM with PET/CT findings. The basic information and PET/CT manifestations of rectal MM are summarized in **Table 1** [14-21]. Of the above eight patients, elderly men constitute the majority and the age of onset is 40-76. Patients with rectal MM usually present with rectal bleeding, pain, and tenesmus, which is consistent with previous literature reports. It should be noted that in our case, the lesion was large (thickening at about 4.8 cm), but no symptoms of acute intestinal obstruction occurred, which might be related to the soft texture of rectal MM and its growth along the longitudinal axis of the intestinal lumen. It has been reported that the SUVmax of anorectal MM could reach is a maximum of 20.7. All the lesions of the above eight patients showed hypermetabolism, while SUVmax in our case is 10.6. Rectal MM is easy to invade blood vessels and lymph nodes, with a high incidence of metastasis. Of the above eight patients, only one patient showed no tumor metastasis, while others had local lymph node metastasis or distant metastasis, including lung, liver, bone, and muscle. Because of the advantage of ^{18}F-FDG PET/CT in

Table 1. Literature review of rectal MM cases with basic information and ^{18}F-FDG PET/CT manifestations

No.	References	Age (years)	Sex	Clinical symptoms	Location	Metabolism of the primary tumor	Sites of metastases	Metabolism of the metastases
1	Joshi et al. [14]	60	M	Weight loss	Rectum	Hypermetabolism	Liver and muscle	Hypermetabolism (SUVmax of 2.7 and 4.5)
2	Bulut et al. [15]	72	M	Rectal bleeding and generalized weakness	Lower rectum	Hypermetabolism	Lymph nodes	Hypometabolism
3	Li et al. [16]	76	M	Rectal bleeding, pain and tenesmus	Lower rectum	Hypermetabolism	Bones, lung, liver, and lymph nodes	Hypermetabolism
4	Yen et al. [17]	60	F	Bloody stool	Rectum	Hypermetabolism (SUVmax 15.3)	None	/
5	Wang et al. [18]	56	M	Severe pain in the lower right limb, nausea, and vomiting	Upper rectum	Hypermetabolism	Bone	Hypermetabolism
6	Kuka et al. [19]	58	F	Lower abdominal pain and rectal bleeding	Rectum	Hypermetabolism	Lymph nodes	Not mentioned
7	Pirenne et al. [20]	66	M	Rectal bleeding. pain, and tenesmus	Rectum	Hypermetabolism	Lymph nodes	Not mentioned
8	Tai et al. [21]	40	F	Anal bleeding	Rectum	Hypermetabolism (SUVmax 5.9)	Lymph nodes and bone	Hypermetabolism

evaluating tumor metastasis in the whole body, ^{18}F-FDG PET/CT should be considered more for rectal cancer patients in the clinical application. PET/CT has high sensitivity in the diagnosis of metastatic lesions, which can help to find small or concealed metastatic lesions [7]. Also, it is helpful to accurately stage the tumor by knowing the number and metastasis of lesions in the whole body by PET/CT [8].

The final diagnosis of rectal MM requires pathological examination. The gross pathology mostly shows a polyp-like appearance with erosion and ulcer on the surface, and in the intestinal lumen, tumor cells infiltrate into the submucosa. The anatomical position is close to the comb line with or without pigmentation. Under the microscope, most of the tumor cells were diffuse, flaky, and diverse in morphology. Some tumor cells have no obvious heterotypy and melanin content is different. The blood vessels in mesenchyme were abundant and hemorrhage and necrosis were observed, with unclear or small nucleoli [22]. Immunohistochemistry is important for the diagnosis of MM, especially when the pathological type is amelanotic MM. The commonly used markers include S-100, HMB-45, Melan-A, and Vimentin [23]. HMB-45 and Melan-A have a high specificity, and S-100 is highly sensitive. The expression rate of Vimentin is the highest, but it lacks specificity. The above combination can improve diagnosis accuracy and decrease the misdiagnosis rate. In addition, MM cells express none or few CK. In our case, tumor cells were positive for S-100, HMB-45, Vimentin, and Melan-A, which were consistent with the previous literature reports and the diagnosis of MM could be confirmed. There are no effective staging guidelines for MM that originate in the digestive tract, and the TNM staging system of the American Joint Committee on Cancer (AJCC 8th ed.) is not completely applicable to MM of the digestive tract. Falch et al. created a 4-stage classification system [3]. When the local tumor spreads without infiltration of the muscular layer, the stage is I. When the local tumor spreads with infiltration of the muscular layer, the stage is II. When the regional tumors spread and/or have positive lymph-node metastasis, the stage is III. When it progresses to disseminated tumor spread, the stage is IV. In this case, ^{18}F-FDG PET/CT imaging showed that the patient had primary rectal metastasis with pelvic lymph node, lung, liver, and bone metastasis, resulting in stage IV.

In this case, rectal MM needs to be distinguished from lymphoma and adenocarcinoma. Lymphoma occurs mainly in the right colon and rarely occurs in the rectum. Patients often present with hepatosplenomegaly and enlarged lymph nodes in other parts of the body, accompanied by irregular fever. The lesions mostly grow infiltratively along the intestinal wall, with diffuse thickening and wider distribution. The PET/CT findings of lymphoma show abnormally hypermetabolism. The lesions of

adenocarcinoma are mostly soft tissue masses with endogenic growth. Hemorrhage and necrosis are more common. Infiltration into adjacent tissues and organs can be found in advanced tumors. Adenocarcinoma shows hypermetabolism on PET/CT, and distant metastasis is more common in the liver, presenting as multiple liver lesions. It should be noted that this case showed the findings of ^{18}F-FDG which is similar to adenocarcinoma, reminding the differential diagnosis of rectal MM for nuclear medicine patients. The findings of ^{18}F-FDG PET/CT can be used to assess whether patients can have surgery or not. With the development of immune checkpoint inhibitors and molecular targeted therapy, ^{18}F-FDG PET/CT also plays a role in the early recognition of tumor response and detection of life-threatening side effects of autoimmunity. It can also prospectively predict the long-term efficacy and the best time of discontinuing treatment, which is significant for treatment planning [8-10].

Rectal MM has an insidious onset and it is easy to invade blood vessels and lymph nodes, with high recurrence and metastasis rate. Most of the patients are in the advanced stage as they are diagnosed. The 5-year survival rate of MM patients in stage IV is only 15-20% according to AJCC [24]. Therefore, early detection, diagnosis, and treatment can improve the overall survival rate of MM patients. Surgical treatments include abdominal-perineal resection and extensional resection. At present, advanced MM is mainly treated by immunotherapy and targeted therapy, especially the immunotherapy of inhibiting oncogenic signaling pathways and enhancing anti-tumor activities [25]. In addition, programmed cell death protein 1 (PD-1) monoclonal antibody and cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) monoclonal antibody can be used for patients with advanced MM [26]. According to National comprehensive cancer network (NCCN) guidelines, it is recommended to choose anti-angiogenic drugs combined with chemotherapy or PD-1 monoclonal antibody combined with Axitinib as the first-line treatment. In this case, surgery is unsuitable, so PD-1 monoclonal antibody combined with tyrosine kinase inhibitor (TKI) was used for treatment, which can avoid the risk of bleeding and perforation caused by anti-angiogenic drugs. Multidisciplinary cooperation mode and combination treatment will be the development direction of the diagnosis and treatment of MM.

Conclusion

Rectal MM is an aggressive malignant tumor with a poor prognosis. MM should be taken into account in the differential diagnosis of middle-aged or elderly rectal tumor patients with blood in the stool. Although ^{18}F-FDG PET/CT is difficult to distinguish rectal MM from rectal adenocarcinoma, it still has the advantage of evaluating the whole-body situation by providing valuable information for the diagnosis, tumor stage, evaluation of treatment efficacy and prognosis of MM, while the definite diagnosis of MM still requires a combination of pathological and immunohistochemical examination.

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Disclosure of conflict of interest

None.

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