Misdiagnosis of esophageal leiomyoma combined with adrenal cortical adenoma as esophageal cancer with adrenal metastasis by fluorine-18-fluorodeoxyglucose positron emission tomography: A case report

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Abstract. Leiomyoma is a benign muscular abnormality that commonly occurs in the middle and distal third of the esophagus, leading to thickening of the esophageal wall and subsequent esophageal luminal narrowing. Notably, esophageal leiomyoma often does not show increased 18F-fluorodeoxyglucose (FDG) uptake on positron emission tomography (PET). The present study described a case of esophageal leiomyoma combined with adrenal adenoma. Results of the PET-computed tomography analysis revealed that FDG metabolism was increased in the lower segment of the esophagus and the left adrenal gland, with maximum standardized uptake values of 6.5 and 4.1, respectively. Therefore, initially, the patient was diagnosed with an esophageal malignant tumor with left adrenal metastasis. Open surgery was performed for complete removal of the lesions, and results of a routine pathological analysis revealed esophageal leiomyoma combined with adrenal cortical adenoma. The present study indicates that to avoid unnecessary surgeries, esophageal leiomyoma and adrenal cortical adenoma should be diagnosed through a comprehensive assessment with endoscopy, endoscopic ultrasound, computed tomography, magnetic resonance imaging and tissue sample pathology, not just PET.

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Introduction

Benign esophageal tumors are uncommon, accounting for <10% of all esophageal tumors. Esophageal leiomyoma is considered the most common benign tumor of the esophagus, and its incidence ranges from 0.005 to 5.1% (1). Histological analysis is required for a definitive diagnosis; however, numerous diagnostic tools, such as endoscopy, computed tomography (CT) and 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) are also used for differentiation from other malignant tumors, such as esophageal cancer (2). Notably, 18F-FDG-PET is used to determine whether a mass is benign or malignant, as benign masses may also form lesions in the esophagus and extra-esophageal organs and may be misdiagnosed as malignant tumors. Notably, few previous studies report on the use of 18F-FDG-PET in cases of esophageal leiomyoma involving lesions in other organs (3). The present study describes a patient who was considered to have esophageal cancer with adrenal metastasis based on PET-CT findings. The esophageal lesion tissue was surgically resected, and the results showed that it was esophageal leiomyoma combined with adrenal adenoma. If a correct diagnosis could have been made preoperatively, unnecessary surgical treatment could have been avoided.

Case report

Patient. A 57-year-old male patient was referred to Jinan Central Hospital (Jinan, China) in March 2024. During a routine health examination, a thoracoabdominal CT scan showed a mass with a size of ~5.1x2.8 cm in the lower segment of the esophagus. Pathological analysis of a gastroscopic biopsy revealed chronic mucosal inflammation, squamous epithelial papillary hyperplasia and localized granulation tissue hyperplasia in the lamina propria (Fig. 1A), indicating a benign result. Due to the potential for misdiagnosis using endoscopic sampling, malignancy could not be confirmed. Thus, 18F-FDG-PET was performed to determine whether the lower esophageal mass was benign or malignant. PET/CT

imaging revealed irregular thickening of the esophageal wall at the T8-T10 vertebral level, with an intraluminal soft-tissue mass of ~5.6x2.7x6.6 cm and a maximum standardized uptake value (SUV) of 6.5. A nodular lesion was also observed in the left adrenal gland, with heterogeneous density and FDG uptake. The lesion exhibited a maximum SUV value of 4.1 (delayed maximum SUV, 5; Fig. 2A-C). Based on the results obtained using PET/CT analysis, the lesion was diagnosed as a malignant esophageal tumor with adrenal metastasis. Thus, the results obtained during the initial gastroscopic biopsy were considered a false-negative. A repeat gastroscopy revealed a 2.0x2.5-cm submucosal tumor-like elevation in the lower esophagus. Results of the pathological analysis revealed mild acute and chronic inflammation of the mucosa, focal atypical squamous epithelial hyperplasia and smooth muscle hyperplasia in the submucosa, with no tumor cells (Fig. 1B); thus, the mass was considered benign. In addition, the mass exhibited a clear outline and was localized, with no definitive histological diagnosis of malignancy. As the patient was willing to undergo surgery, esophageal mass resection was considered feasible.

During surgery, a 5.0x3.0-cm tumor was observed in the esophagus, and rapid intra-operative pathology was used to confirm the presence of a leiomyoma. Based on this, no further esophageal tissue resection procedures were performed, and the left adrenal mass was resected with the assistance of the Department of Urology (Fig. 3A and B). Post-operative pathological analysis was also used for confirmation of an esophageal leiomyoma. The results of the immunohistochemical analysis revealed the positive expression of desmin, smooth muscle actin (SMA) and Ki-67 (~1%) (Fig. 3C-E). The patient was also diagnosed with an adrenocortical adenoma with positive expression of inhibin-a, synaptophysin and Ki-67 (~5%; Fig. 3F-H). The present case demonstrated that esophageal leiomyoma may be accompanied by primary adrenal cortical adenoma, which was initially misdiagnosed as esophageal malignancy with adrenal metastasis using results of the PET analysis. The patient did not undergo other treatment after surgery, but recovered well and was followed up after 1 month.

Pathological assessment

Histopathology. Following proper tissue sampling, the tumor tissue blocks were immersed in a solution composed of 10% formaldehyde in 0.01 M phosphate-buffered saline (PBS) and fixed at room temperature for 2 h. Next, the tissue blocks were transferred to the Tissue-Tek VIP® 6 AI Tissue Processor (Sakura Finetek USA, Inc.) and then embedded in paraffin. The paraffin blocks were sliced into 5-μm thick sections. These sections were first dewaxed using xylene and then rehydrated in a series of ethanol solutions with decreasing concentrations (95, 90, 80 and 75%) and finally in water. The sections were then put into Harris hematoxylin staining solution and stained at room temperature for 5 min. Subsequently, the sections were differentiated with 0.3% acidic ethanol. Next, the sections were treated with 0.6% ammonia water at room temperature for 5 sec, and then the samples were incubated with eosin staining solution at room temperature for 1 to 3 min. The sections were dehydrated using ethanol and xylene at room temperature. Finally, the slides were mounted with neutral gum and observed under a Pathology Slide Scanner (Pannoramic SCAN II; 3DHISTECH Ltd.).

Immunohistochemistry. Tumor sections (5-μm thick) were sliced from the paraffin block, dewaxed and rehydrated. Subsequently, the slides were rinsed three times with 0.01 M PBS. Next, the slides were placed in a pressure cooker and treated with an antigen retrieval reagent (0.01 M citrate buffer solution, pH 6.0) for 10 min. The slides were washed again three times with 0.01 M PBS (pH 7.4, with each wash lasting 5 min) at room temperature. To inhibit the activity of endogenous peroxidase, a peroxidase blocking agent (kit cat. no. PV-9000; Beijing Zhongshan Jinqiao Biotechnology Co., Ltd., Beijing, China) was added and incubated for 30 min at room temperature in the dark. Permeabilization with 0.5% Triton (cat. no. T8200; Beijing Solarbio Science & Technology Co., Ltd.) was performed for 10 min. Next, 5% goat serum (cat. no. G1208; Wuhan Servicebio Technology Co., Ltd.) was used to block the slides at room temperature for 30 min to avoid non-specific binding. The sections were washed again three times with 0.01 M PBS (Ph 7.4, 5 min per wash), and then incubated with monoclonal primary antibodies, including anti-desmin (diluted at 1:400; cat. no. ab32362; Abcam), anti-inhibin-a (diluted at 1:250; cat. no. ab203824; Abcam), anti-synaptophysin (diluted at 1:2,000; cat. no. 17785-1-AP; Proteintech Group, Inc.), anti-Ki-67 (diluted at 1:8,000; cat. no. 27309-1-AP; Proteintech Group, Inc.) and anti-α-SMA (diluted at 1:3,000; cat. no. ab7817; Abcam) at 4˚C for 12 h. The primary antibodies were diluted with PBS. The slides were washed three times with 0.01 M PBS (5 min per wash) and then incubated with Enhanced Enzyme-labeled Goat Anti-Mouse/Rabbit IgG Polymer (undiluted; kit cat. no. PV-9000; Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.) at 37˚C for 30 min. Diaminobenzidine was used as the chromogen, and the sections were counterstained with Mayer's hematoxylin for 2 min at room temperature. Subsequently, the slides were sealed with neutral gum, and observed and captured under a Pathology Slide Scanner (Pannoramic SCAN II; 3DHISTECH Ltd.).

Discussion

It is crucial that esophageal leiomyoma is differentiated from malignant esophageal cancer, cysts or esophageal strictures. The prognosis of esophageal leiomyoma is generally good. After complete resection, patients are usually cured and have a normal life expectancy. By contrast, esophageal cancer is a malignant tumor with a relatively poor prognosis. Leiomyoma is a benign muscular abnormality that commonly occurs in the middle and distal third of the esophagus, leading to thickening of the esophageal wall and subsequent esophageal luminal narrowing. Common clinical symptoms include difficulty in swallowing, vomiting, and retrosternal pain due to luminal narrowing and esophageal dysmotility (4). In the present study, the patient presented with none of the aforementioned clinical symptoms. Submucosal tumors (SMTs) are protrusive lesions originating from the muscularis mucosae, submucosa or muscularis propria, and these may also be extraluminal lesions. Notably, SMTs that are <2 cm in size are often asymptomatic and are incidentally found during endoscopic examination. SMTs exhibit differing levels of incidence in different parts of the gastrointestinal (GI) tract, with the majority of SMTs affecting the upper GI

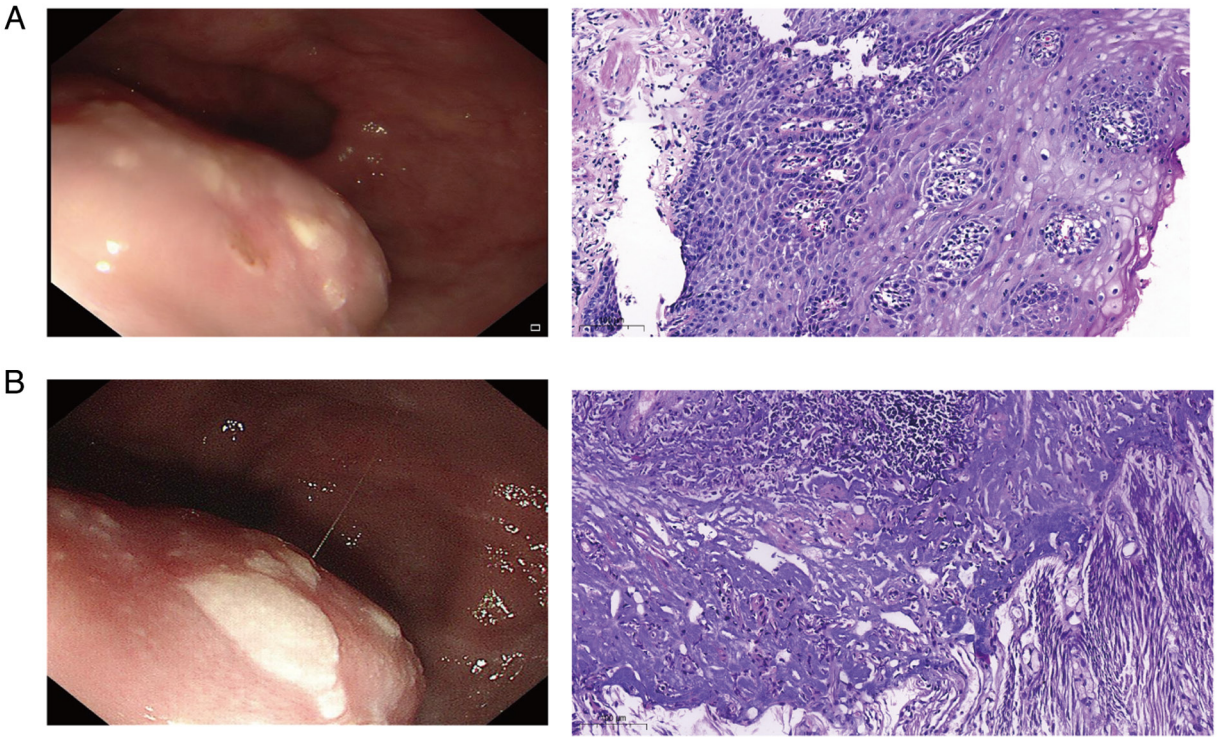

Figure 1. Esophagogastroduodenoscopy imaging and biopsy pathology. (A) Initial endoscopic findings and H&E staining of the biopsy sample (x200 magnification). (B) Repeat endoscopic findings and H&E staining of the biopsy sample (x200 magnification). H&E, hematoxylin and eosin.

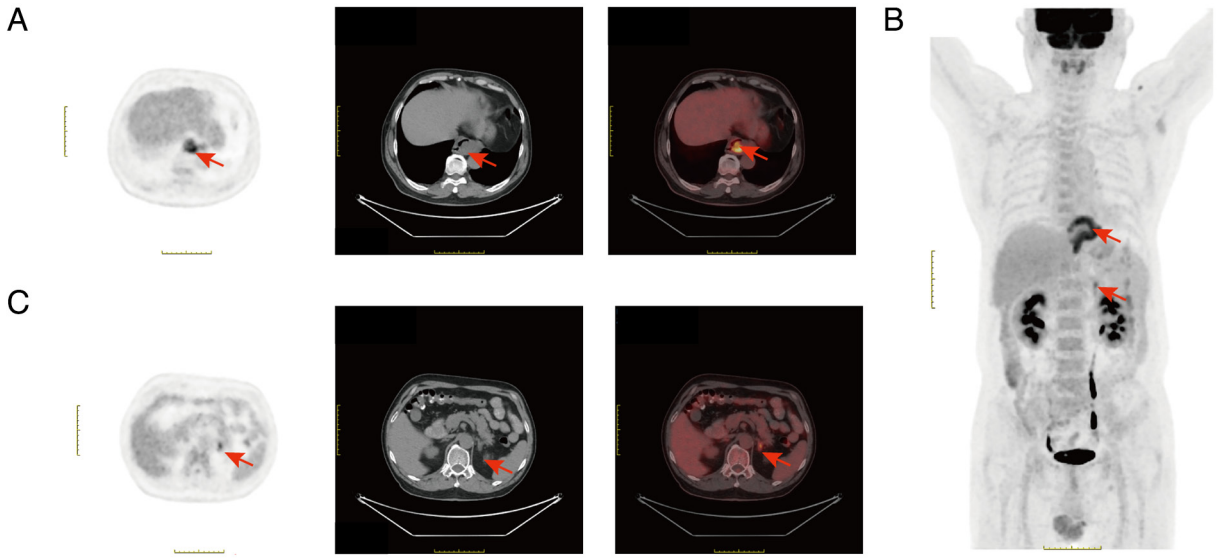

Figure 2. PET/CT imaging of esophageal leiomyoma and adrenal cortical adenoma. (A) The PET/CT images show a large, intensely 18F-fluorodeoxyglucose avid lesion in the esophagus (arrow), with a maximum standardized update value of 6.5. The corresponding CT images depict the abnormal mass in each organ. (B) Arrows point to the hypermetabolic lesions on the PET image. (C) A markedly hypermetabolic lesion can be observed in the adrenal region (arrows). PET/CT, positron emission tomography/computed tomography.

tract (5). In total, ~66% of SMTs occur in the stomach, and the remaining cases affect the esophagus, duodenum and colon (6). The predilection site of different types of SMTs is associated with their histopathological characteristics; thus the location of SMTs is of clinical diagnostic significance. Leiomyoma is a common pathological type of esophageal SMT, accounting for 60-80% of all esophageal SMTs. Furthermore, leiomyoma is more common in the middle and lower third of the esophagus (7,8), and the present case is reflective of a typical SMT presentation.

Esophageal leiomyomas are often PET-negative (FDG uptake is not increased and SUV is generally <2.5); however, results obtained using PET analysis in the present study demonstrated that esophageal leiomyomas may exhibit increased 18F-FDG uptake. In addition, the results of the post-operative histological examination confirmed the diagnosis of esophageal

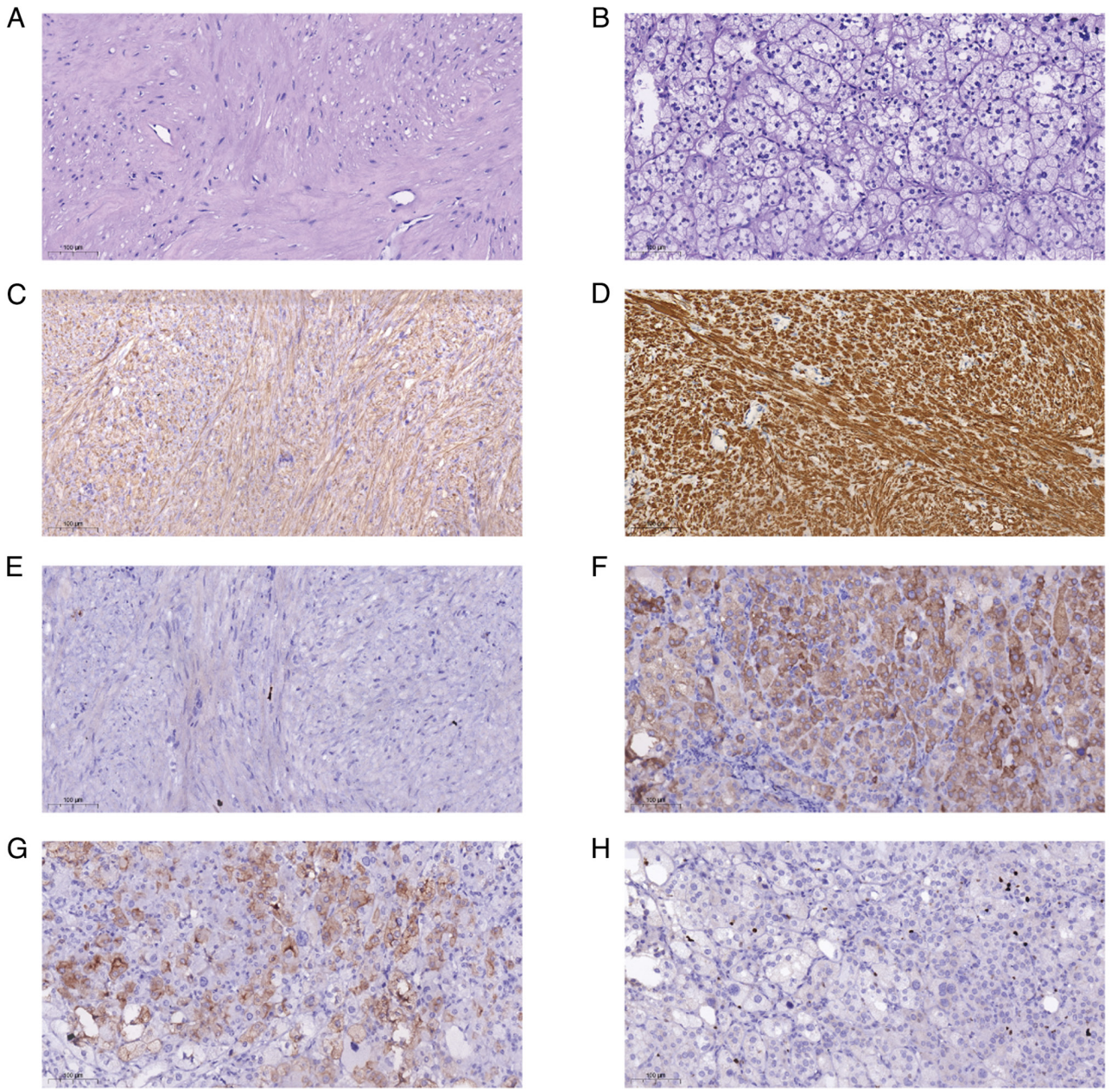

Figure 3. Pathology of the esophageal leiomyoma and adrenal adenoma. (A) Histopathology of the esophageal mass showing a leiomyoma on H&E staining (x200 magnification). (B) Histopathology of the adrenal mass, confirming an adrenocortical adenoma on H&E staining (x200 magnification). (C-E) Immunohistochemical staining for (C) smooth muscle actin, (D) desmin and (E) Ki-67 in the esophageal leiomyoma (x200 magnification). (F-H) Immunohistochemical staining for (F) inhibin-a, (G) synaptophysin and (H) Ki-67 in the adrenal adenoma (x200 magnification).

leiomyoma. False-positive PET/CT results for esophageal leiomyoma are rare, with few previous reports describing esophageal leiomyomas with increased FDG uptake (9,10). In the present case, the results of the PET/CT analyses demonstrated elevated FDG uptake in both the esophageal mass and the adrenal mass. Thus, the patient in the present case was initially diagnosed with an esophageal malignancy with adrenal metastasis. By contrast, post-operative pathological results revealed esophageal leiomyoma with a left adrenal adenoma. To the best of our knowledge, the present study is the first to report the case of a patient with this diagnosis. Thus, we hypothesized that the misdiagnosis may be a result of similarities with esophageal cancer observed during imaging, as this often presents as thickening of the esophageal wall and the formation of soft-tissue masses during CT analysis. In the present study, the results of the CT analysis highlighted key characteristics of esophageal cancer, leading to a misdiagnosis. Moreover, the misdiagnosis may be a result of increased FDG uptake. Notably, FDG is a glucose analog, and due to high levels of metabolism, tumor cells often absorb higher levels of FDG. However, its uptake in the body is not absolutely specific. Cells in various physiological and pathological states may take up FDG (11). During surgery, a large number of tortuous blood vessels were observed on the mucosal surface of the esophageal mass. The presence of these blood vessels may have promoted the local aggregation of FDG (12), thus resulting in the high SUV value that was used for the diagnosis. Moreover, an SUV value of >2.5 obtained during PET analysis is often indicative of a malignant tumor.

Although the maximum SUV value range of FDG metabolism in esophageal leiomyoma is between 0 and 7.1, the SUV values of the majority of esophageal leiomyomas are <2.5 (13). However, the SUV value of the esophageal tumor in the present case reached 6.5, which may have led to the misdiagnosis. Thus, an overlap in SUV values between esophageal malignant tumors and esophageal leiomyoma may lead to complexities in obtaining accurate diagnoses. Based on the aforementioned reasons, during the process of tumor diagnosis, one should not rely solely on the imaging findings of PET-CT and the SUV value. Instead, a variety of factors, such as results from biopsy or other imaging tools, need to be comprehensively considered to reduce the risk of misdiagnosis. However, the muscular layer biopsy of the esophagus performed via endoscopic ultrasound is fraught with potential risks, such as bleeding and esophageal perforation. Generally, it is not recommended for clinical use. Some other imaging diagnostic tools, such as endoscopy, endoscopic ultrasonography, CT and magnetic resonance imaging (MRI), can be recommended for further differential diagnosis.

The specific mechanism underlying the increased FDG uptake of esophageal leiomyoma is yet to be fully understood; however, FDG also accumulates in uterine leiomyoma. Notably, FDG uptake is associated with the increased expression of basic fibroblast growth factor, transforming growth factor-β, granulocyte-macrophage colony-stimulating factor and Ki-67 (14). Results of previous studies revealed that high levels of metabolism in leiomyoma may be associated with high concentrations of growth factors that promote the increased proliferation of smooth muscle cells (15,16). Increased expression of the aforementioned cytokines may lead to increased vascularization, cell proliferation and cellular degeneration, which may lead to increased FDG uptake. The results of the present study revealed high levels of FDG uptake in the tumor; however, the results of the histological analysis did not reveal excessive proliferation of blood vessels or degenerated cells. Results of the immunohistochemical analysis also revealed weak positive Ki-67 expression (~1%), and this cytokine is a key marker of cell proliferation. In addition, the results of the present study revealed increased FDG uptake in the adrenal gland, and the post-operative histological diagnosis confirmed a primary adrenocortical adenoma. At present, the association between the high FDG uptake of adrenocortical adenoma and esophageal leiomyoma remains to be fully elucidated.

As an important imaging examination method, PET has several advantages, such as the ability to detect abnormal metabolic lesions throughout the body at an early stage, and it is of great significance for tumor staging and efficacy evaluation. However, the present found that esophageal leiomyoma adenoma and adrenal cortical adenoma can be a potential cause of a false-positive PET diagnosis, which increases the difficulty in diagnosing leiomyoma. To avoid unnecessary surgical interventions, instead of relying solely on PET, esophageal leiomyoma and adrenal cortical adenoma should be diagnosed by means of a comprehensive assessment that incorporates endoscopy, endoscopic ultrasound, CT, MRI and the pathological examination of tissue samples.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

LZ and HL contributed to the conception and the design of the study. XS obtained and analyzed the patient information, and contributed to manuscript drafting and critical revisions of the intellectual content. XS and LL performed analysis and interpretation of the PET-CT data. DF and YH performed the histological examination of the tissue. LZ, HL and XS confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent for publication of the article was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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