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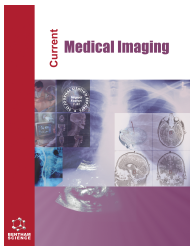

CASE REPORT

Perivascular Epithelial Cell Tumor of the Stomach Diagnosed Preoperatively by Endoscopic Ultrasound-Guided Fine-Needle Aspiration

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Abstract:

Introduction:

Perivascular Epithelioid Cell tumor (PEComa) is a rare mesenchymal neoplasm characterized by the co-expression of melanocytic and myoid markers. While PEComas can arise in diverse anatomical sites, gastric PEComas are exceedingly rare, with merely nine cases documented in the extant literature.

Case Presentation:

Herein, we have presented a case of gastric PEComa in a 65-year-old male patient who exhibited a 3-year history of epigastric pain, with notable exacerbation in the two months prior to diagnosis. For the initial evaluation of the patient's condition, Endoscopic Ultrasound-guided Fine Needle Aspiration (EUS-FNA) and Computed Tomography (CT) were employed, which enabled a preoperative diagnosis. Radiological assessment demonstrated a neoplasm exhibiting heterogeneous arterial enhancement, persistent delayed enhancement, and distinct margins. Subsequent to diagnosis, the patient underwent surgical resection and has maintained a disease-free status for one year postoperatively. This case report highlights the crucial role of EUS-FNA in facilitating preoperative histological diagnosis and optimizing surgical planning for gastric PEComa.

Conclusion:

This case constitutes the tenth documented instance of gastric PEComa in the global literature. In this case, EUS-FNA facilitated a preoperative histopathological diagnosis, thereby enabling precise surgical planning. An accurate preoperative diagnosis is crucial for devising an optimal treatment strategy.

Keywords: Perivascular epithelioid cell neoplasm, Gastric neoplasm, EUS-FNA, PEComa, Epigastric pain, Computed tomography.

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1. INTRODUCTION

PEComa is an uncommon mesenchymal neoplasm with an elusive etiology. According to the World Health Organization (WHO), PEComa is defined as “a mesenchymal neoplasm comprising histologically and immunohistochemically distinctive perivascular epithelioid cells” [1]. Perivascular Epithelioid Cells (PECs) were initially identified by Bonnetti *et al*. in 1992 [2]. As per the 2020 World Health Organization (WHO) classification of soft tissue and bone tumors [3 - 5], the PEComa family mainly includes angiomyolipoma, lymphangioleiomyomatosis [6], clear cell “sugar” tumors, clear-cell myomelanocytic tumors of the falciform ligament/ligamentum teres, and non-specific PEComas Not Otherwise Specified (PEComa-NOS) arising in sites, like the uterus, colon, and soft tissues. PEComa can occur in many anatomical locations. They are usually benign and can be surgically cured with a good prognosis. However, some PEComas exhibit aggressive behavior and metastasize. The gastrointestinal tract is one of the most common sites for PEComa, accounting for 20-25% of all reported PEComa-NOS cases [7, 8]. Only 9 cases of gastric PEComa have been reported so far [9], indicating the extreme rarity of PEComas arising in the stomach. Consequently, the clinical and imaging characteristics of gastric PEComas remain poorly understood.

Diagnosing PEComa using imaging alone is challenging,

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and definitive diagnosis requires preoperative histopathological examination. The previously reported 9 cases of gastric PEComa were not diagnosed by EUS-FNA prior to surgery. Here, we have presented a case of PEComa that was diagnosed by EUS-FNA, aiming to improve the clinical and imaging understanding of this rare disease.

2. CASE PRESENTATION

A 65-year-old male patient with epigastric pain for 3 years presented with aggravated symptoms for 2 months. The patient had visited our outpatient clinic 2 years prior for epigastric pain and paroxysmal vague discomfort accompanied by acid reflux, belching, and yellow pasty stools, without an apparent cause. Gastroscopy at that time revealed a gastric ulcer and chronic atrophic gastritis with intestinal metaplasia in the lower body of the stomach. The patient was treated with omeprazole, trimebutin, and bismuth magnesium. Two months before this visit, the patient's symptoms were aggravated again, and was treated with oral medications, such as acid suppressants and gastric protectants, but no significant improvement was found. Past medical history included anemia, chronic gastritis, Helicobacter pylori infection, duodenal diverticulum, hepatic cysts, hepatic space-occupying lesions, renal stones, and prostatic hyperplasia. Laboratory testing showed no specific changes except an elevated level of Carbohydrate Antigen 199 (CA199, 55.80 U/ml).

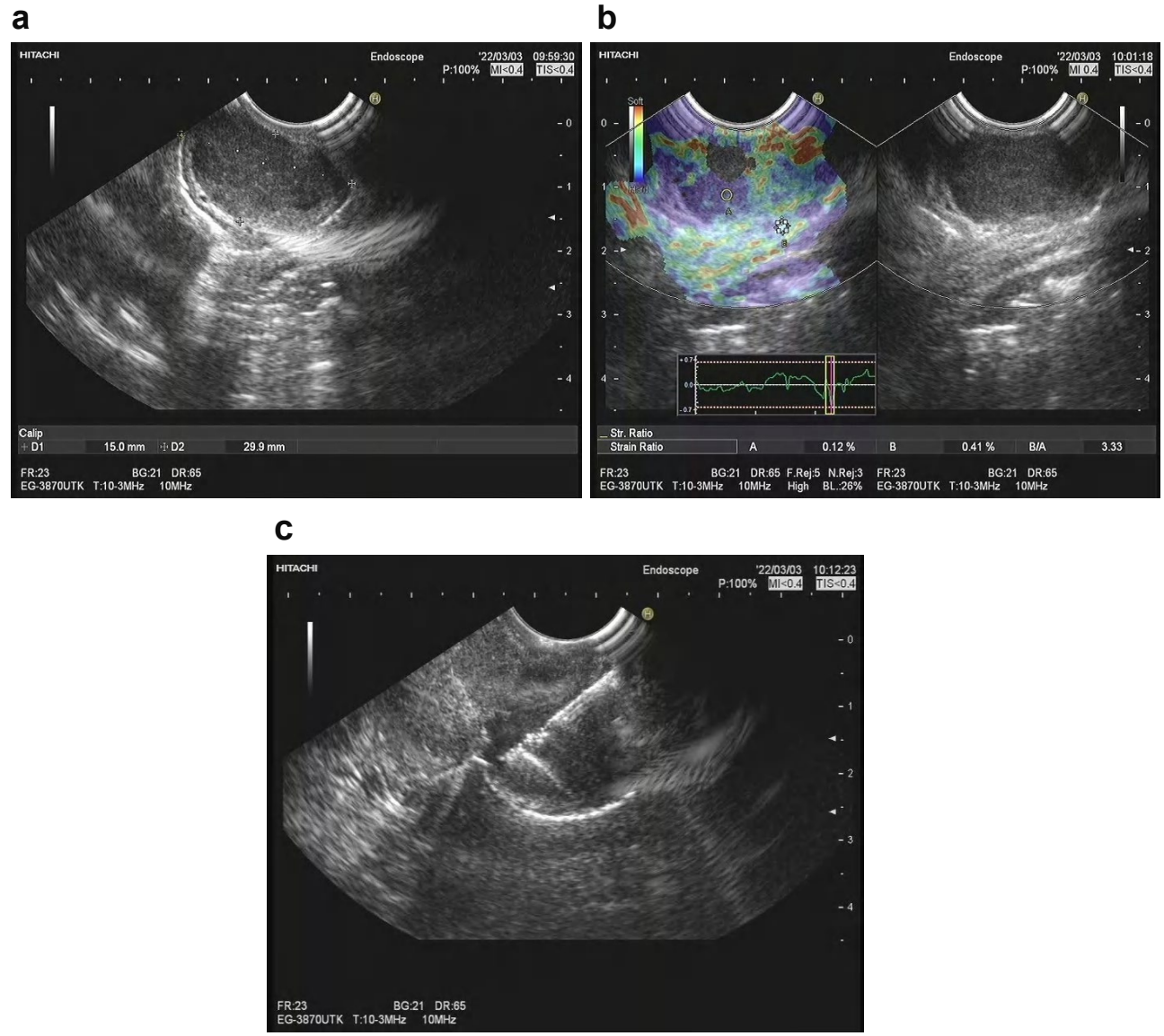

Fig. (1). Ultrasound gastroscopy with fine needle aspiration biopsy.
(**a**) The size of the section was 29.9x15mm; (**b**) the lesion could be seen in the residual intrinsic muscular layer with mixed echogenic changes, rich internal blood flow, elastic imaging with hard texture; (**c**) the 19G COOK puncture needle was used to puncture the lesion with micro-negative pressure and negative pressure of 10ml, and a total of 2 stitches were punctured.

Ultrasonic gastroscopic fine-needle aspiration biopsy was performed. Ultrasound imaging revealed a 29.9 x 15 mm lesion originating from the intrinsic muscular layer with mixed echogenicity, rich internal blood flow, and hard texture on elastography (Fig. **1a**,**b**). The lesion was punctured using a 19G COOK needle with a micro-negative pressure suction of 10 ml. The fine needle aspirate consisted mostly of blood clots, with scant glandular epithelium and lamina propria seen in one area, vascular endothelium and fibrous tissue hyperplasia in the lamina propria in another area, and vascular endothelium with scattered lymphocytic infiltration in a 0.8 mm diameter fragment of tissue (Fig. **1c**).

Hematoxylin and eosin staining of the tissue sections showed round epithelioid cells with abundant eosinophilic cytoplasm. Immunohistochemistry demonstrated focal positivity for SMA and desmin. Staining was weakly positive for Melan-A and CD117, while Ki-67 was 2% (Fig. **2a** - **c**).

A Computed Tomography (CT) scan revealed a 27 mm soft tissue nodule in the lower body of the stomach with relatively well-defined borders and an approximate CT value of 31 HU (Fig. **3a**, **e**). On enhanced arterial phase imaging, the lesion displayed significant inhomogeneous enhancement with a CT value of about 147 HU (Fig. **3b**, **f**). The enhanced venous phase showed gradual uniform enhancement with a CT value of approximately 136 HU (Fig. **2c**, **g**). Delayed imaging demonstrated persistent uniform enhancement with a CT value of around 104 HU (Fig. **3d**, **h**).

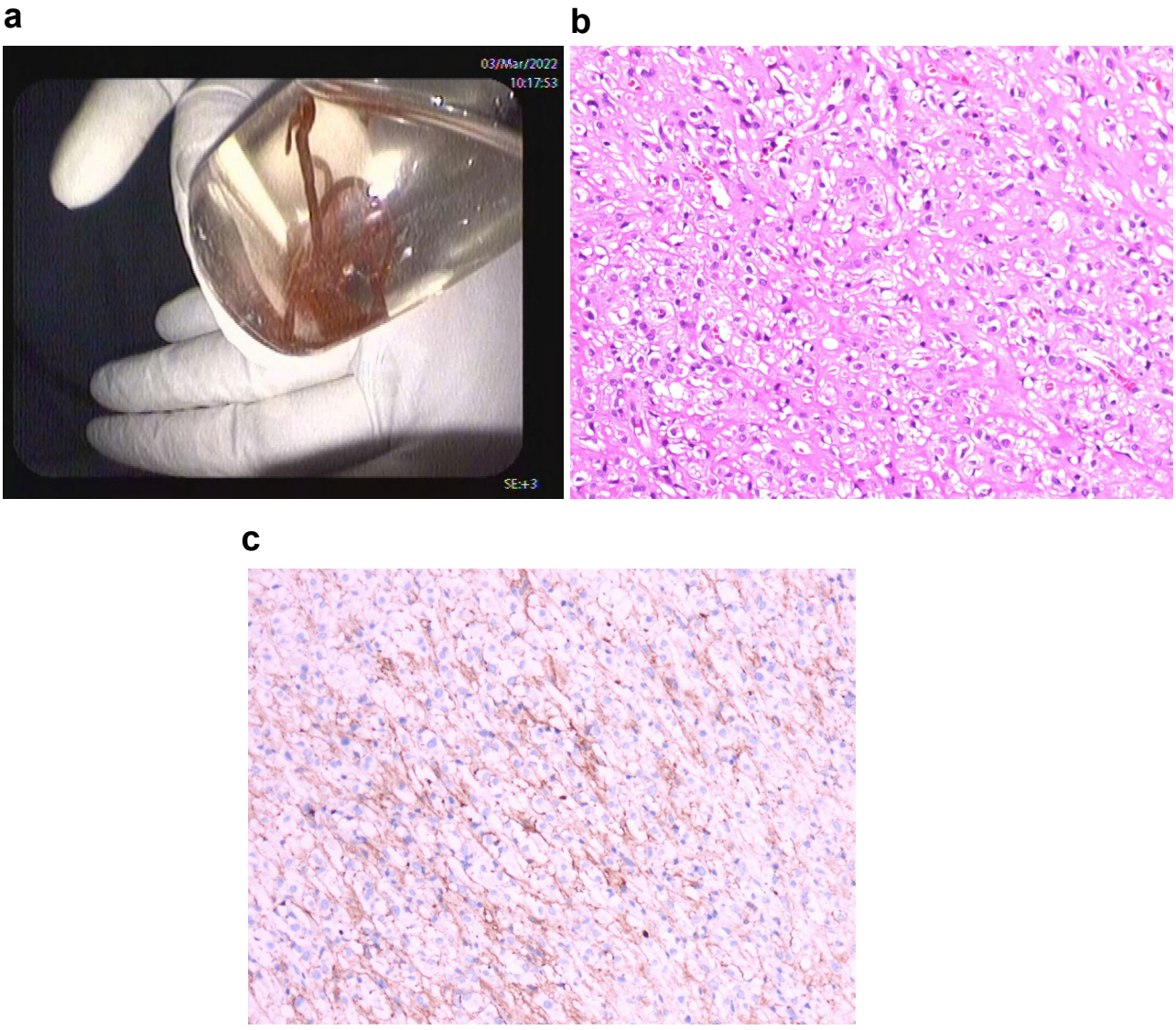

Fig. (2). Puncture needle biopsy tissue and pathological results.
Fine-needle aspiration biopsy tissue; (**b**) microscopically, the epithelioid cells were round-like in composition, with abundant cytoplasm and eosinophilic red color (Hematoxylin and Eosin staining ×200); (**c**) Melan-A also showed diffuse weak positivity in tumor cells (Hematoxylin and Eosin staining ×100).

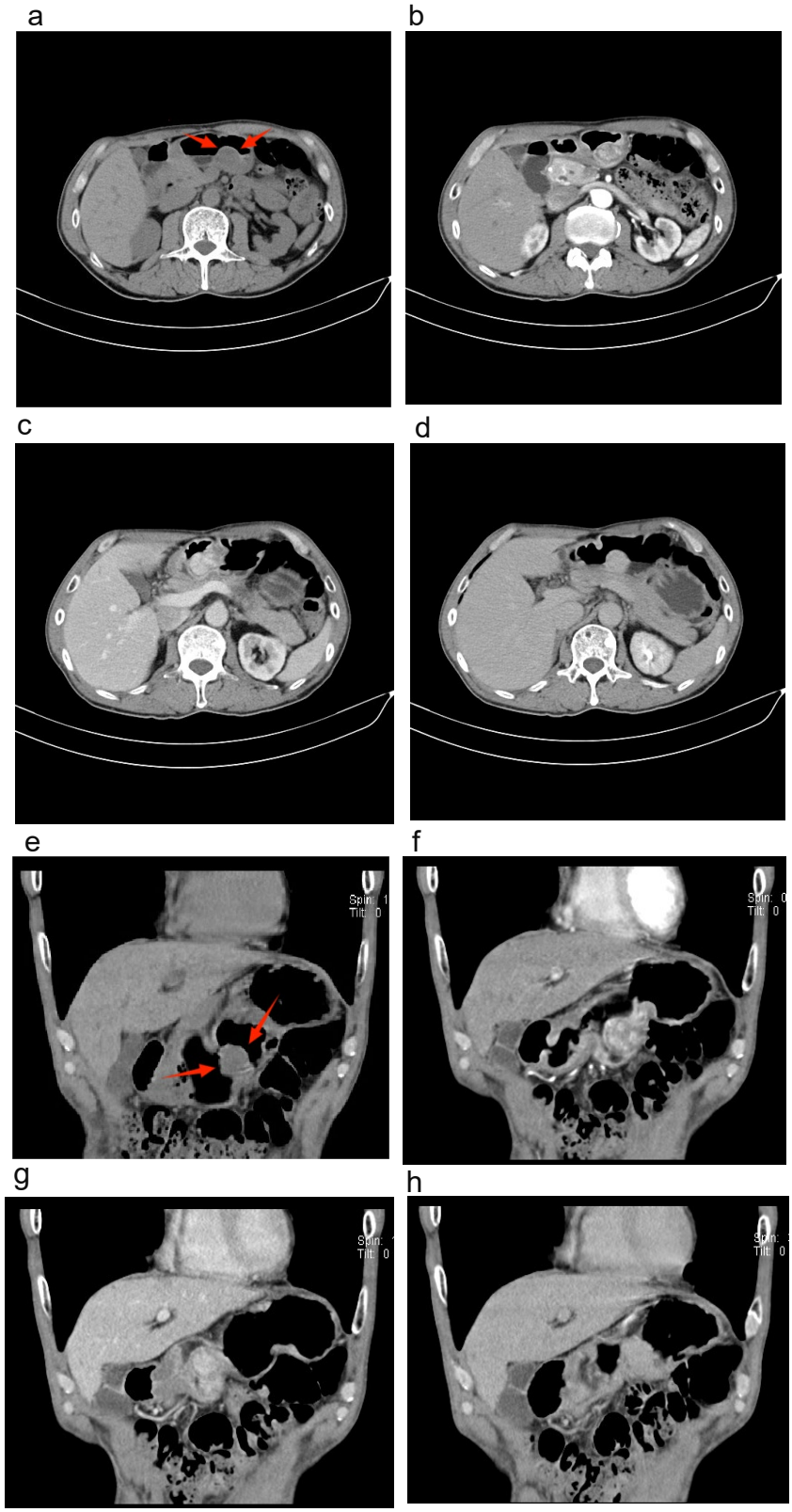

Fig. (3). Axial and coronal images from CT scan.
Axial (**a**-**d**) and coronal (**e**-**h**) images from CT scan; (**a**, **e**, arrows) A soft tissue density shadow in the posterior wall of the lower part of the stomach body was seen on the scan, which was round-like, with a size of about 27 mm and a CT value of about 31HU; (**b**, **f**) in the enhanced arterial phase, the lesion showed significant inhomogeneous enhancement with a CT value of about 147HU; (**c**, **g**) enhanced venous phase, showing gradual uniform strengthening, CT value of about 136HU; (**d**, **h**) delayed period of enhancement scan, showing continuous uniform enhancement with a CT value of about 104HU.

The patient underwent surgical treatment. Intraoperative exploration revealed no other abnormalities. Based on the pathology results, the treatment plan consisted of partial gastric resection and postoperative follow-up.

3. DISCUSSION

PEComa is a rare mesenchymal tumor that can occur anywhere in the stomach, mostly arising from the submucosa. PEComas occurring in the cecum and rectum are usually mucosal or submucosal in origin [10]. The age of onset for gastric PEComa ranges from 39 to 71 years, with an average of 55.3 years, and no significant sex predilection has been found. The main symptom of gastric PEComa is epigastric pain or discomfort, which may be related to mass effect, obstruction, and bleeding. These findings are consistent with other reports [8]. Due to the rarity of gastric PEComa, its true incidence and pathogenesis remain unclear [9, 11 - 15].

Definitive diagnosis still relies on immunohistochemistry, with HMB-45 considered the most sensitive marker [8, 13, 16]. However, HMB-45 has not accounted for more than half of cases and one study found 10-20% of PEComa cases to be negative for HMB-45 [12]. We found TFE3 positivity without MiTF expression, suggesting TFE3 may play a role in the myxoid phenotype in MiTF-negative PEComas. PEComas demonstrate a wide spectrum of biological behaviors ranging from benign to aggressive, and the commonly used grading system was proposed by Folpe *et al*. [16]. All reported cases of gastric PEComa, including ours, are summarized in Table **1**.

Typically, PEComa shows a wide range of biological behaviors, from benign to aggressive, with mostly having no recurrence after the surgery. The open abdomen is chosen for treatment following the diagnosis; the recently reported Vacuum-assisted, Mesh-mediated Fascial Traction (VAMMFT) method has proven to be effective and safe in terms of damage control surgery, secondary closure rates, and incidence of intestinal fistula formation [17]. However, one case of multiple liver metastases was found 6 months after surgery and one patient with malignant PEComa originating in the liver died (Table **2**). The commonly used grading criteria for these neoplasms have been proposed by Folpe *et al*. [16]. Indicators of poor prognosis include tumor ≥5 cm, infiltrative growth, heavy cellular anisotropy, coagulative necrosis, vascular infiltration, and nuclear schizophrenia >1/50 HPF. Patients with two or more of the above characteristics are considered to have malignant PEComa, those with only one of the above characteristics are considered to have PEComa of undetermined malignant potential, and those without the above characteristics are considered to have benign PEComa. Tumors with definite evidence of malignant behavior are usually >5.0 cm and have high mitotic rates.

Table 1. Clinical features of 10 cases of gastric PEComa.

Number	Authors/References	Gender	Age	Tumor Position	Tumor Size (cm)	Grading	Immunohistochemistry (positive)	Images
1	Mitteldorf *et al*. [14]	F	71	Gastric Sinus, submucosa	3.0x2.8x1.6	Moderate nuclear variation and discrete mitotic activity (1 mitosis/50 HPF)	Vimentin, SMA, desmin, Melan-A, CD56	Not mentioned
2	Waters *et al*. [15]	M	42	Gastric pylorus	10.0x7.0	Malignant	Melan-A, desmin, EMA	CT
3	Yamada *et al*. [11]	M	39	Gastric body, submucosa	3.0x7.0	Malignant	α-SMA, H-caldesmon, HHF-35, desmin, Melan-A, HMB-45, MiTF, CD10	CT
4	Shin *et al*. [13]	F	62	Gastric sinus, subcutaneous	4.2x3.2x2.0	The tumor cells showed mild pleomorphism, the mitotic count was 1 in 50 High Power Fields (HPF)	SMA, HMB-45, desmin	CT
5	Shin *et al*. [13]	M	67	Gastroesophageal junction, serosa	5.0x4.7x1.6	The nuclei showed marked pleomorphism and the mitotic counts were high (45/50 HPF)	SMA, Melan-A, CD117	Not mentioned
6	Kumar *et al*. [12]	F	48	Greater curvature of the stomach, submucosa	11.5x8.7x7.6	Malignant	SMA, Melan-A, TFE3, calponin, Ki-67 (25%)	CT
7	Toya *et al*. [20]	M	47	Gastric body, mucosal	4.0x3.0	Malignant	SMA, Melan-A, TFE3, desmin, H-caldesmon, vimentin, CD68, Ki-67 (53.9%)	CT
8	Xu *et al*. [9]	F	48	Gastric body, mucosal	1.5x1.2x1.0	Only mild nuclear pleomorphism	SMA, HMB-45, Melan-A, Desmin, CD68, Ki-67 (<3%)	CT

(Table 1) contd.....

Number	Authors/References	Gender	Age	Tumor Position	Tumor Size (cm)	Grading	Immunohistochemistry (positive)	Images
9	Xu *et al*. [9]	M	64	Gastric sinus, submucosa	5.0x3.0x3.0	Malignant	HMB-45, SMA, Melan-A, vimentin, CD117, Ki-67(3%)	CT
10	Present case	M	65	Gastric body, submucosa	6.0x4.0x3.5	Undetermined malignant potential	Melan-A, SMA, desmin, CD117, Ki-67 (2%)	EUS-FNA,CT

Notes: PEComa: Perivascular epithelioid cell tumor; HMB-45: Human melanoma black; SMA: Smooth muscle cell actin; MiTF: Microphthalmia transcription factor; α-SMA: α-smooth muscle actin; EMA: Epithelial membrane antigen; TTF-1: Thyroid transcription factor-1; TFE3: Transcription factor E3, CT: Computed tomography; EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration; F: Female; M: Male.

Table 2. Clinical symptoms and prognosis of 10 cases of gastric PEComa.

Number	Symptom	Post-operative Follow-up
1	Black stool	No recurrence detected 19 months after surgery
2	Epigastric pain, black stool, weight loss	Malignant PEComa originating in the liver; survival <3 months
3	Epigastric pain, back pain	No recurrence detected 6 months after surgery
4 and 5	Not mentioned	No recurrence detected 7 years after surgery
6	Epigastric pain, intermittent nausea, and vomiting, loss of appetite, change in bowel behavior	Not mentioned
7	Not mentioned	Multiple liver metastases detected 6 months after surgery
8	Epigastric discomfort	No recurrence or metastasis detected after 17 months of ESD treatment
9	Epigastric pain, diarrhea	No recurrence or metastasis detected 18 months after surgery
10	Epigastric pain, acid reflux, belching, yellow pasty stools	No recurrence or metastasis detected one year after surgery

Note: ESD: endoscopic submucosal dissection.

Gastrointestinal PEComa should be differentiated from Gastrointestinal Stromal Tumors (GIST), clear cell sarcomatoid tumors, and malignant melanoma [9, 11 - 14]. Radiologically, gastrointestinal PEComas often resemble GISTs, and our case was initially considered a GIST. Gastrointestinal PEComas often resemble gastrointestinal mesenchymal tumors clinically and in imaging. Occasionally, cells express CD117, which can be established by the case in the present study and those reported by Shin and Xu *et al*. [9, 13], but they do not express Dog-1 and CD34. Morphologically, the cells were mostly epithelioid, and these results are consistent with those reported by Chen *et al*. [8], with a clear to pale eosinophilic cytoplasm and obvious nucleoli located in the central nucleus [10]. Clear cell sarcomatoid tumors occur mostly in the small intestine and are histologically epithelioid. In addition to lamellar and nested structures, cells may also appear as pseudo-papillary or pseudo-chrysalis structures, usually with small or inconspicuous nucleoli. EWSR1-related fusion genes can be detected in most patients. Malignant melanoma can also be epithelioid or spindle-shaped with distinct nuclei and is morphologically very similar to gastric PEComa; however, the cytomorphology of malignant melanoma is relatively more diverse, and S-100 is diffusely positive, even when S-100-negative melanoma lacks significant mitotic activity [10].

The diagnosis of gastric PEComa remains challenging based on imaging alone. Practically none of the tumors were prospectively diagnosed as PEComa on imaging and, in all cases, required pathologic diagnosis. Available literature focuses predominantly on pathology, while EUS-FNA is widely used to evaluate space-occupying lesions. Previous reports have shown that EUS-FNA can provide a preoperative definitive diagnosis of PEComa [18]. However, the diagnostic accuracy of EUS-FNA is limited without rapid on-site assessment, which can preclude making a definitive diagnosis prior to surgery.

Unenhanced CT showed isointense mass with heterogeneous arterial phase enhancement in our case, consistent with other reports that have found no significant imaging differences between benign and malignant PEComas [19]. One patient was reported to develop liver metastases [20], and a study found 77.8% of PEComas involving the kidney and gastrointestinal tract to initially metastasize to the liver. Although primary tumor imaging features are non-specific, differentiating large masses with well-defined borders, homogeneous delayed phase enhancement, and T2 hyperintensity can guide radiologists to detect metastatic disease early in malignant cases. A comprehensive preoperative approach integrating CT, MRI, and ultrasound findings is optimal for the evaluation of gastric PEComa.

CONCLUSION

In summary, we have utilized EUS-FNA preoperatively to diagnose this case of gastric PEComa, which would have been difficult to definitively diagnose by imaging alone. EUS-FNA is thus greatly significant for preoperative diagnosis of gastric PEComa. A comprehensive evaluation of CT and EUS-FNA findings together can prompt consideration of this rare tumor. Given the current lack of established protocols for diagnosis and management of gastric PEComa, long-term regular follow-up of this patient is imperative.

AUTHORS' CONTRIBUTION

L.M.W.: Drafted and critically revised the manuscript; J.Z.: Provided data and performed analysis and interpretation, critically reviewed the draft manuscript, and approved the final manuscript version.

LIST OF ABBREVIATIONS

PECs = Perivascular Epithelioid Cells

WHO = World Health Organization

CT = Computed Tomography

VAMMFT = Vacuum-assisted, Mesh-mediated Fascial Traction

GIST = Gastrointestinal Stromal Tumors

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient.

STANDARDS OF REPORTING

CARE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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