Primary gastric Ewing sarcoma/primitive neuroectodermal tumor

Yu Ye[1,4,*], Xiaoming Qiu[1,4,*], Jixin Mei[1,4],
Dongyun He[3] and Ailing Zou[2,4] iD

Abstract

A rare and highly malignant small round cell tumor, Ewing sarcoma/primitive neuroectodermal tumor (ES/PNET) usually occurs in the pelvis, long-axis bones, and femur. In contrast, extraosseous ES is more often found in the paraspinal region, limbs, and retroperitoneum, but is extremely rare in the stomach. We report a case of a 55-year-old woman who presented with fatigue, fever, and black stool. Preoperative computed tomography (CT) imaging showed a large ulcerative lesion of approximately 5.5×5.0 cm in the stomach and irregular thickening of the ulcer wall. Upper endoscopy revealed a large, irregular ulcer in the posterior wall of the stomach. Histopathological examination suggested that the mass with the largest diameter (7.5 cm) was ES. Immunohistochemistry indicated positivity for CD99. Enhanced CT of the whole body was performed but no definite masses were found in other organs, and the patient was diagnosed with primary gastric ES. The patient underwent radical distal gastrectomy with Roux-en-Y gastrojejunostomy, but refused chemoradiotherapy.

[1]Department of Radiology, Huangshi Central Hospital, Affiliated Hospital of Hubei Polytechnic University, Edong Health Care Group, Huangshi, Hubei, China
[2]Department of Dermatology, Huangshi Central Hospital, Affiliated Hospital of Hubei Polytechnic University, Edong Health Care Group, Huangshi, Hubei, China
[3]Department of Pediatrics, Shishou People's Hospital, Jingzhou, Hubei, China
[4]Hubei Key Laboratory of Kidney Disease Pathogenesis and Intervention, Huangshi, Hubei, China

*These authors contributed equally to this work.

Corresponding author:
Ailing Zou, Department of Dermatology, Huangshi Central Hospital, Affiliated Hospital of Hubei Polytechnic University, Edong Health Care Group, 141 TianJin Road, Huangshi, Hubei 435000, China.
Email: 70289952@qq.com

Introduction

Ewing sarcoma (ES) and primitive neuro-ectodermal tumors (PNETs) are highly malignant, small round cell tumors. Despite having different degrees of neuroectodermal differentiation, they both contain EWSR1-ETS fusion proteins and belong to the Ewing sarcoma family.[1] The most common chromosomal rearrangement is a translocation between chromosomes 11 and 22, t(22;11)(q24;q12), which can lead to new EWSR1-ETS fusion proteins as transcription factors that regulate target genes and lead to cell transformation, resulting in tumors with the morphology and gene expression characteristics of ES.[2] ES usually occurs in the pelvis, long-axis bones, and femur. Extraosseous ES (EES) is more often found in the paraspinal region, limbs, and retroperitoneum[3] but is extremely rare in the stomach. Herein, we report a case of primary gastric ES to aid in disease recognition for clinicians and radiologists.

Case report

A 55-year-old woman presented with a 10-day history of fatigue and fever, and having defecated mushy black stool twice 4 days prior. During the course of the disease, the patient suffered from poor mental health and sleep, and she had lost some weight. She had a 3-year history of hypertension and a 2-year history of type 2 diabetes and was taking oral medications (nifedipine, acarbose, metformin, and glimepiride) to treat these conditions. She had no family history of genetic disorders. Physical examination showed an anemic appearance, with no obvious enlarged lymph nodes and normal signs in the heart, lungs, and abdomen. Routine blood work indicated a red blood cell count of 2.26×10^{12}/L (reference range: $3.5–5.5 \times 10^{12}$/L) and hemoglobin (Hb) of 57 g/L (reference range: 110–150 g/L).

Kidney, liver function, and gastrointestinal tumor markers were within normal limits.

Imaging examination using a 64-row and 128-slice spiral computed tomography (CT) system (LightSpeed, General Electric Co., Boston, MA, USA) showed that the gastric wall in the gastric body was irregularly thickened, nodular mass shadows were positioned locally, and enlarged lymph nodes were absent around the stomach (Figure 1a). The coronal profile showed a large ulcerative lesion of approximately 5.5×5.0 cm, with irregular thickening of the ulcer wall (Figure 1b). The volume rendering technique (VRT) of 3-dimensional (3D) post-processing volume reconstruction showed that the gastroduodenal artery was thicker than normal and passed through the gastric wall at the greater curvature of the gastric body (Figure 1c). The maximum density projection of 3D post-processing technology showed that the distal small branches of the gastroduodenal artery entered the thickened gastric wall vertically, and the local vessels were thickened and moved relatively gently (Figure 1d). Enhanced CT of the whole body was performed but we did not find any definite masses in other organs.

Upper endoscopy revealed a large irregular ulcer located at the posterior wall of the stomach, with a dirty, smelly ulcer surface and exposed blood vessels in the center (Figure 2). However, gastric biopsy suggested chronic inflammation of the mucosal tissue. Therefore, a laparoscopic exploration was performed on 14 May 2020. During the operation, an ulcerative mass of approximately 9×8 cm was found near the gastric antrum at the greater curvature of the stomach. The mass penetrated through the serous membrane and showed nodular infiltration of the surrounding area. No effusion was observed in the abdominal or pelvic cavity, and no obvious metastasis was found in the liver, gallbladder, spleen, pancreas, omentum, or
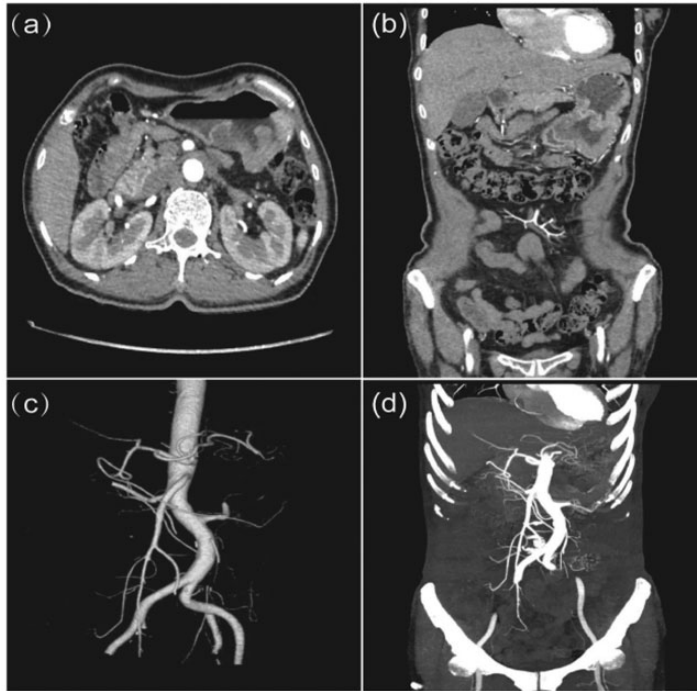
Figure 1. Preoperative computed tomography (CT) images: (a) enhanced CT axial showing the irregularly thickened wall in the gastric body and nodular mass shadows and the absence of definite enlarged lymph nodes; (b) coronal profile showing a large ulcerative lesion of approximately 5.5 × 5.0 cm with irregular thickening of the ulcer wall; (c) volume rendering technique of 3-dimensional post-processing volume reconstruction showing the dilated gastroduodenal artery passing through the thickened gastric wall at the greater curvature of the gastric body; (d) maximum density projection showing distal branches that were slightly dilated and relatively normal and curvature entering the thickened gastric wall vertically.

mesentery. The patient underwent radical distal gastrectomy with Roux-en-Y gastro-jejunostomy, which was performed using the laparoscopic technique. The operation lasted 4 hours; the patient had blood loss of 200 mL and received 2 units of red blood cells. The postoperative hospital stay was 10 days, without obvious complications.

Histopathological examination revealed that the mass with the largest diameter (7.5 cm) was an ES (Figure 3a), which invaded the entire layer of the gastric wall, with positive lymph nodes at the lesser curvature of the stomach (2/14) and all negative at the greater curvature of the stomach (0/10); the tumor did not invade the

proximal and distal anastomosis or omentum. Immunohistochemistry was positive for cluster of differentiation (CD)99 (Figure 3b), CD57, CD56, and vimentin; focally positive for neuron-specific enolase (NSE); and negative for cytokeratin 7 (CK7), epithelial membrane antigen (EMA), CD117, CD34, DOG-1 (discovered on GIST-1), synaptophysin (Syn), chromogranin-A (CgA), leukocyte common antigen (LCA), S-100, human melanoma black (HMB45), MelanA, and desmin. The tumor cells were 40% positive for Ki-67. The patient was thus diagnosed with primary gastric ES. After surgical treatment, the patient refused postoperative
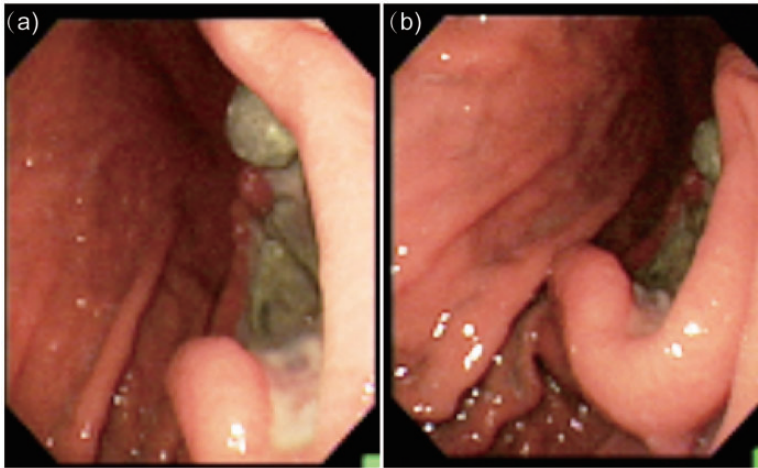
Figure 2. Upper endoscopy showing (a) an large irregular ulcer located at the posterior wall of the stomach, with dirty, smelly ulcer surface, and exposed blood vessels in the center; and (b) gastric mucosa with hyperemia and edema.
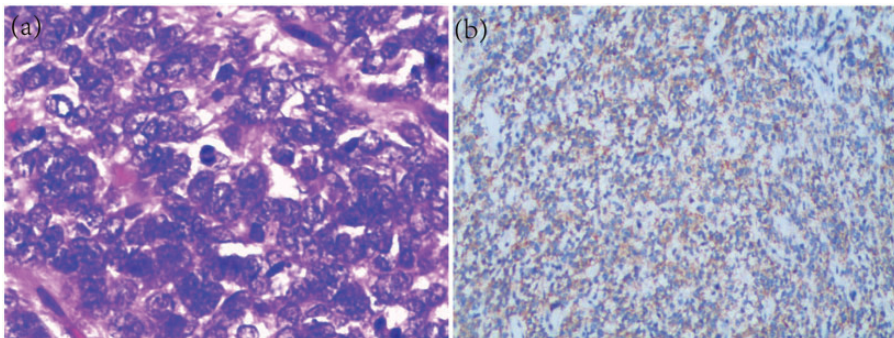

Figure 3. Postoperative pathological examination showing (a) small round cells with different sizes and mitotic figures (hematoxylin & eosin staining, original magnification, 400×); and (b) positivity for CD99 (immunohistochemistry staining, original magnification, 100×).

chemoradiotherapy and was discharged. Until now, no recurrence has been observed during follow-up.

Discussion

The ES/PNET group consists of classic ES of bone, EES, and peripheral PNETs of bone and soft tissue (including the so-called Askin tumor of the chest wall).[4] The histogenesis of these tumors remains unclear, but the tumor cells are most likely derived from primitive mesenchymal cells with the potential for limited neural differentiation,[5,6] hence their location in bone, peripheral nerve, and soft tissue.[7]

ES is an aggressive tumor and tends to occur in adolescents and young adults. It is common in the pelvis, long-axis bones, and femur[8] but can occur outside the bone.[9] Ewing et al. first reported the disease in 1921.[10] Its main specific imaging

Table 1. Clinical characteristics and outcomes in reported cases of gastric Ewing's sarcoma/primitive neuroectodermal tumor.

Reference	Sex, age (years)	Clinical presentation	Location	Tumor size (cm)	Distant metastasis	Neoadjuvant chemotherapy	Surgery	Postoperative chemotherapy	Follow-up (months)	Outcome
Czekalla et al. (2004)[18]	M, 14	Inappetence, fatigue, epigastric pain	Anterior wall body	5	Liver	Yes	SG	No	24	Alive
Colovic et al. (2009)[19]	F, 44	Epigastric pain	Posterior wall body	10	No	No	Excision	No	20	Alive
Kim et al. (2012)[20]	F, 35	No special symptoms	Antrum	5.5	No	No	WR	No	11	Alive
Song et al. (2016)[21]	M, 55	Upper abdominal pain, vomiting	High body	6.5	Lymph nodes	No	TG	Yes	13	Alive
Kumar et al. (2016)[3]	F, 32	Epigastric pain	Lesser curvature	11	No	No	Excision	Yes	12	Alive
Khuri et al. (2016)[17]	F, 31	Upper gastrointestinal hemorrhage	Lesser curvature	11	Pancreas Splenic hilum	No	TDPSLA	No	36	Alive
Soulard et al. (2005)[22]	F, 66	Epigastric pain	Antrum	8	No	No	Gastrectomy	Yes	10	Dead
Rafailidis et al. (2009)[23]	M, 68	Abdominal pain, dyspepsia, weakness	Body	12	Liver	No	SG	Yes	13	Dead
Inoue et al. (2011)[24]	F, 41	Abdominal pain	Anterior wall body	9	Enterocoelia	No	DG	Yes	110	Dead
Maxwell et al. (2016)[6]	F, 66	Anemia, abdominal pain	Antrum	11	No	No	DG	Yes	NA	NA
Hopp and Nguyen (2019)[12]	M, 24	Abdominal pain, nausea, vomiting	Posterior wall	10	NA	Yes	DG	NA	NA	NA

SG, subtotal gastrectomy; CG, curative gastrectomy; WR, wedge resection; TG, total gastrectomy; TDPSLA, total gastrectomy + distal pancreatectomy + splenectomy + left adrenalectomy; DG, distal gastrectomy; NA, not available.

manifestations are bone destruction in the metaphysis of long bone.[11] EES accounts for 15% to 20% of tumors in the Ewing's family (ES/PNET plus EES).[12] Primary gastric ES is exceptionally rare, with only a few cases reported in the literature.[13] The growth rate of EES is relatively slow, and some lesions may grow into masses larger than 20 cm in diameter, but the clinical symptoms of a patient with EES are not obvious.[14] In our case, the lesion was large and the patient had no specific clinical manifestations. Thus, EES is not conducive to early detection and diagnosis; its diagnosis mainly depends on the pathological characteristics of small round cells and positive staining for CD99 on immunohistochemistry.[15] We summarize 12 reported cases of primary gastric ES in Table 1, describing clinical presentation, treatment, and outcome. We found that primary gastric ES is more common in female patients, the clinical presentation is not specific, most tumors are larger than 5 cm, and comprehensive treatment (combining surgery, radiotherapy, and chemotherapy) is often chosen.

The treatment of EES has no unified standard, and combination chemoradiotherapy and surgical excision are the main treatments.[16] In our case, the lesion was relatively limited, did not spread to the abdominal and pelvic cavities, and was thus completely excised. The patient declined to undergo chemotherapy and radiotherapy after radical surgery.

Few reports have described the imaging features of primary gastric ES. In our case, enhanced CT showed obviously irregular thickening of the gastric wall in the gastric body, multiple nodular mass in the greater curvature and the gastric wall of the gastric body, and mild progressive strengthening after enhanced CT. The CT imaging features were similar to those described in the literature by Khuri et al.[17] VRT showed that the gastroduodenal artery supplied the lesion. The vessels in the area of the lesion were dilated and tortuous, but no definite vascular erosion was observed. The imaging differential diagnoses included Borrmann IV gastric adenocarcinoma and gastric lymphoma. However, Borrmann IV gastric adenocarcinoma retains part of the mucosa and is stratified with the submucosa due to the infiltrating growth of tumor cells in the fibrous matrix along the submucosal layer; the strengthening pattern of the adenocarcinoma is stratified.[25] Gastric lymphoma is a primary tumor of lymphatic follicular cells in the lamina propria and submucosa, and its cells are densely arranged. The gastric wall shows diffuse thickening with relatively uniform density and no gastric stenosis.[26]

In conclusion, we present this rare primary gastric ES that, because of its rarity and lack of specific characteristics in symptoms, signs, and imaging, is difficult to diagnose early. Early recognition and diagnosis of this rare tumor by clinicians and radiologists is important and could be improved.

Ethics statement

Local ethics committee approval was not necessary because this was a case report. Written consent for publication was obtained from the patient.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Author contributions

ORCID iD

Ailing Zou 🔟 https://orcid.org/0000-0001-5357-9747

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