

## Small Intestinal Metastasis from Esophageal Squamous Cell Carcinoma Presenting with Perforated Peritonitis

Osamu CHINO<sup>\*1</sup>, Hiroyasu MAKUUCHI<sup>\*1</sup>, Soji OZAWA<sup>\*2</sup>, Hideo SHIMADA<sup>\*3</sup>, Takayuki NISHI<sup>\*3</sup>, Soichiro YAMAMOTO<sup>\*2</sup>, Hirohito MIYAKO<sup>\*2</sup>, Eisuke ITO<sup>\*2</sup>, Yoshifumi KISE<sup>\*2</sup>, Tadashi HARA<sup>\*2</sup>, Akihito KAZUNO<sup>\*2</sup> and Hiroshi KAJIWARA<sup>\*4</sup>

<sup>\*1</sup>Departments of Surgery, Tokai University School of Medicine, Tokyo Hospital.

<sup>\*2</sup>Departments of Surgery, Tokai University School of Medicine

<sup>\*3</sup>Departments of Surgery, Tokai University School of Medicine, Oiso Hospital

<sup>\*4</sup>Departments of Pathology, Tokai University School of Medicine

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Metastatic tumors of the small intestinal tract from extra-abdominal sites are rare. We report herein a rare case of small intestinal metastasis from esophageal carcinoma that presented with perforated peritonitis. A 71-year-old man with dysphagia was referred to our hospital for further examination and treatment, and was diagnosed with type 3 advanced esophageal squamous cell carcinoma of the lower thoracic esophagus. Based on a diagnosis of Stage II cancer, a radical esophagectomy with three-field lymph node dissection was performed after neoadjuvant chemotherapy composed of 5-fluorouracil plus cisplatin. Pathological examination of the resected specimen revealed a moderately differentiated squamous cell carcinoma, extending into the adventitia with lymph node metastasis (T3, N2, M0, Stage III). During postoperative adjuvant chemotherapy, the patient complained of abdominal pain and was found to have perforated peritonitis. Emergency laparotomy was performed. A jejunal perforation with a submucosal nodule approximately 80 cm distal from the ligament of Treitz was detected, and completely resected by jejunal partial resection. Histopathology of the specimen showed a perforation of the small intestine due to metastasis of esophageal squamous cell carcinoma with mesenteric lymph node metastasis. The patient died of cancer 9 months after surgery. An extremely rare case of small intestinal metastasis from esophageal carcinoma presenting with perforated peritonitis was described.

**Key words:** esophageal cancer, small intestinal metastasis, perforated peritonitis, squamous cell carcinoma

### INTRODUCTION

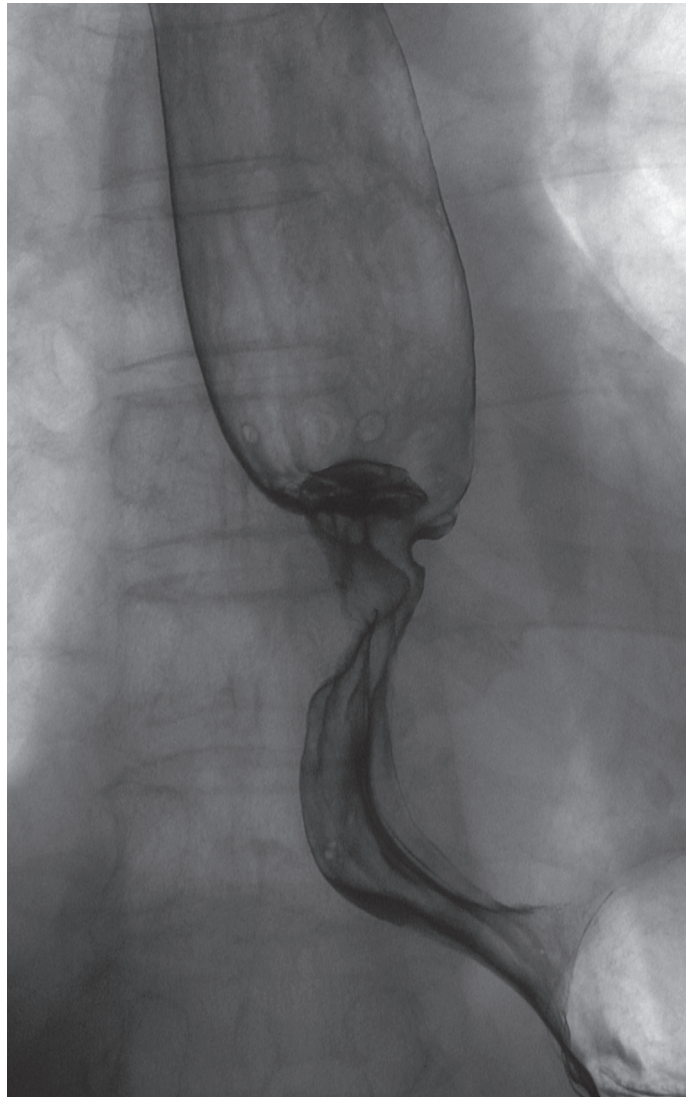
Squamous cell carcinoma (SCC) is the most common malignant neoplasm of the human esophagus. In esophageal cancer, the liver, lung, and bone are the common sites of metastases. Metastatic tumors of the intestinal tract from extra-abdominal site are rare. Metastasis to the small intestine from esophageal carcinoma is extremely rare, first described by Wang *et al.* in 1985 [1]. Herein, we report a case of a patient with small intestinal metastasis from esophageal SCC, which was detected through intra-operative findings and histopathological examination after surgery for small bowel perforated peritonitis.

### CASE REPORT

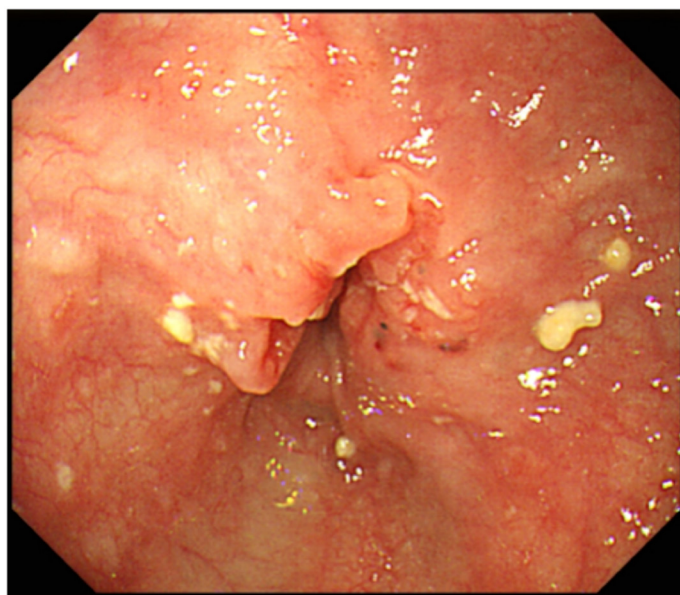
A 71-year-old man who had been suffering from dysphagia for 2 months underwent endoscopic examination in another hospital, which revealed an ulcerative lesion measuring 4-cm on the lower thoracic esophagus. The patient was referred to Tokai University Hospital for further examination and treatment. He was a heavy smoker and a habitual drinker since 50 years. General physical examination at admission did not reveal any abnormalities. All laboratory

data were within the normal ranges except for slight anemia, and squamous cell carcinoma antigen and carcinoembryonic antigen levels, which were 1.8 ng/ml and 3.7 ng/ml, respectively.

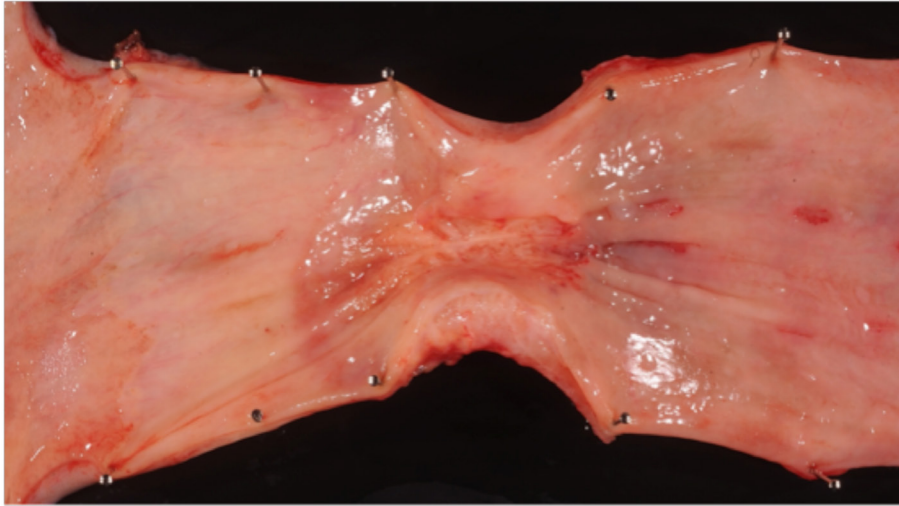
Double contrast esophagography demonstrated an ulcerative lesion with esophageal stenosis 4-cm in size longitudinally, and located on the lower thoracic esophagus (Fig. 1). Endoscopic examination revealed a type 3 advanced esophageal cancer with circular stenosis 35 cm from the incisor teeth on the conventional view (Fig. 2), and tumor staining with iodine by chromoendoscopy was negative. Pathological examination of the preoperative biopsy material revealed moderately differentiated SCC. Computed tomography (CT) scan of the thorax and abdomen and F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) showed no evidence of metastasis. The preoperative diagnosis was type 3 esophageal carcinoma invading the adventitia (T3) without lymph node or distant organ metastasis [2]. Based on a diagnosis of Stage II cancer, neoadjuvant chemotherapy (NAC) composed of 5-fluorouracil (800 mg/m<sup>2</sup>) plus cisplatin (80 mg/m<sup>2</sup>) was administered. Following the administration of NAC, the size of the primary tumor was slightly reduced. Clinical evaluation revealed stable disease. Liver dysfunction



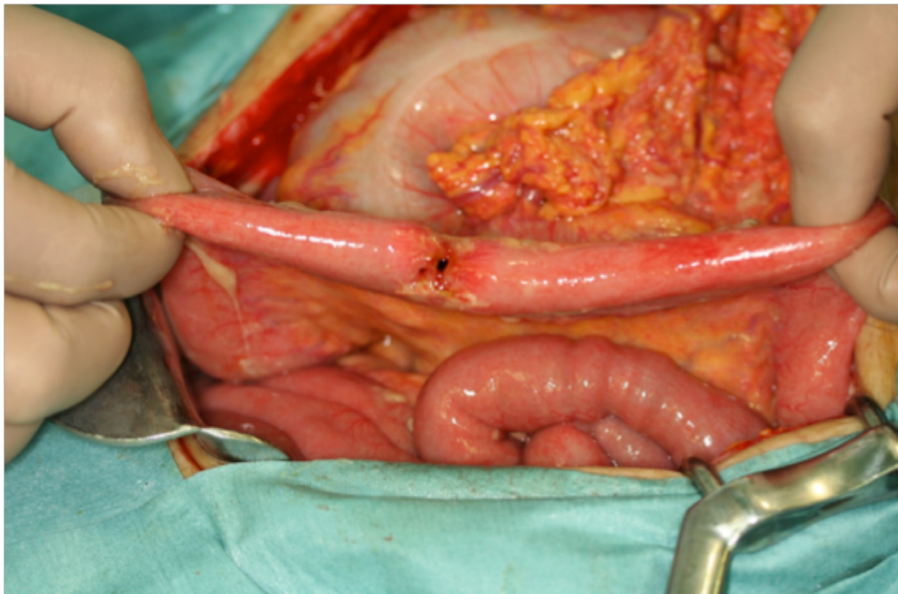
**Fig. 1** Double contrast esophagography revealed an ulcerative lesion with esophageal stenosis. The tumor was 4-cm in size longitudinally, and located on the lower thoracic esophagus.



**Fig. 2** Conventional endoscopic examination revealed a type 3 advanced esophageal cancer with circular stenosis 35 cm distant from the incisor teeth.



**Fig. 3** Macroscopic view of the resected esophageal specimen by subtotal esophagectomy.



**Fig. 4** Intraoperative finding of perforated peritonitis. A 5-mm jejunal perforation located approximately 80cm distal from the ligament of Treitz.

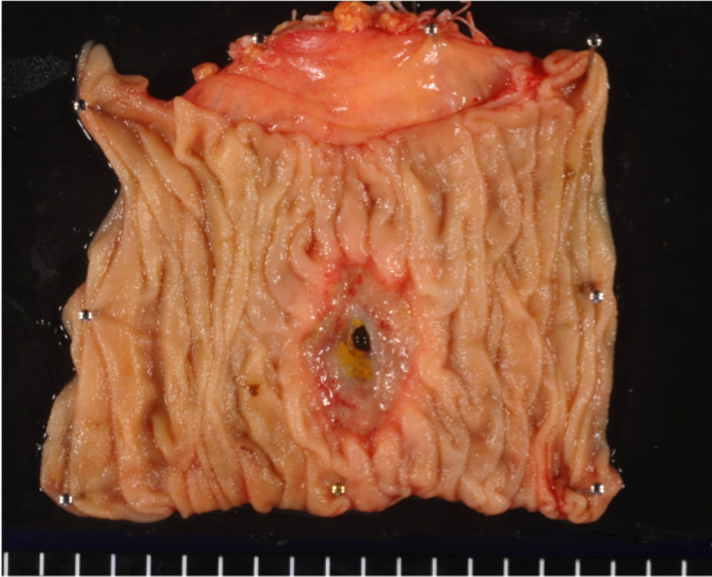
and progression of the esophageal stenosis due to NAC were noted as side effects. One month after NAC, a standard radical subtotal esophagectomy with three-field lymph node dissection and cervical esophago-gastrostomy using a right thoraco-laparotomy was performed. Operative findings showed no evidence of intra-abdominal metastasis at this initial surgery.

Gross findings of the resected specimens showed a type 3 lesion measuring 40 × 20 mm in size, and occupying approximately 4 / 5 of the circumference of the esophageal lumen with macroscopic stenosis (Fig. 3). On the basis of the pathological analysis, microscopic findings of the resected esophageal tumor was classified as moderately differentiated SCC, extending into the adventitia with metastasis in 3 mediastinal lymph nodes and 6 abdominal lymph nodes of 53 total dissected nodes. The infiltrative growth pattern was invasive (INF-c), and some lymphatic and blood vessel invasion was observed (ly1, v1) [2]. According to the

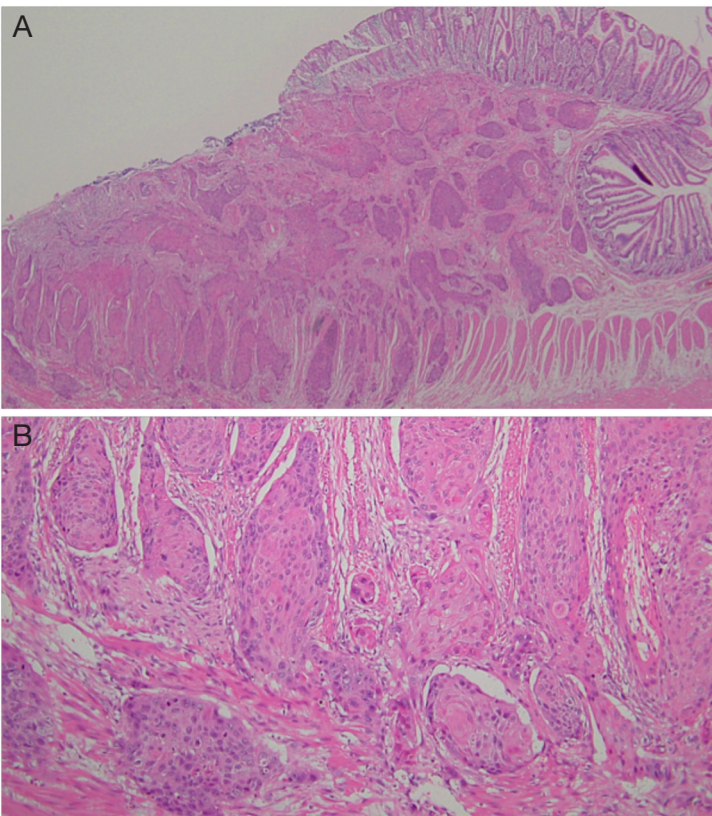
Japanese guidelines for clinical and pathologic studies on carcinoma of the esophagus, the pathological stage was classified as Stage III (T3, N2, M0) [2].

The postoperative course was uneventful, and the patient was discharged 3 weeks postoperatively. The patient received postoperative adjuvant chemotherapy composed of 5-fluorouracil plus cisplatin. During the second course of adjuvant chemotherapy, the patient complained of abdominal pain. Physical examination of the abdomen showed peritoneal irritation. A CT scan of the abdomen showed free air under the diaphragm and ascites, and perforated peritonitis was diagnosed. Emergency laparotomy was performed. A 5-mm jejunal perforation with a solitary hard nodule located approximately 80 cm distal from the ligament of Treitz on the anti-mesenteric side was detected (Fig. 4), which was completely resected via jejunal partial resection with intra-abdominal lavage.





**Fig. 5** Macroscopically, the resected jejunal specimen revealed an ulcerative lesion measuring 25 × 20-mm in size with a 5-mm perforation.



**Fig. 6** Photomicrographs showing microscopic findings of the resected jejunal specimen.  
A: Squamous cell carcinoma massively located in the submucosa and muscularis propria (original magnification ×2, H & E).  
B: Magnified findings showed moderately differentiated squamous cell carcinoma with lymphovascular permeation (original magnification ×20, H & E).

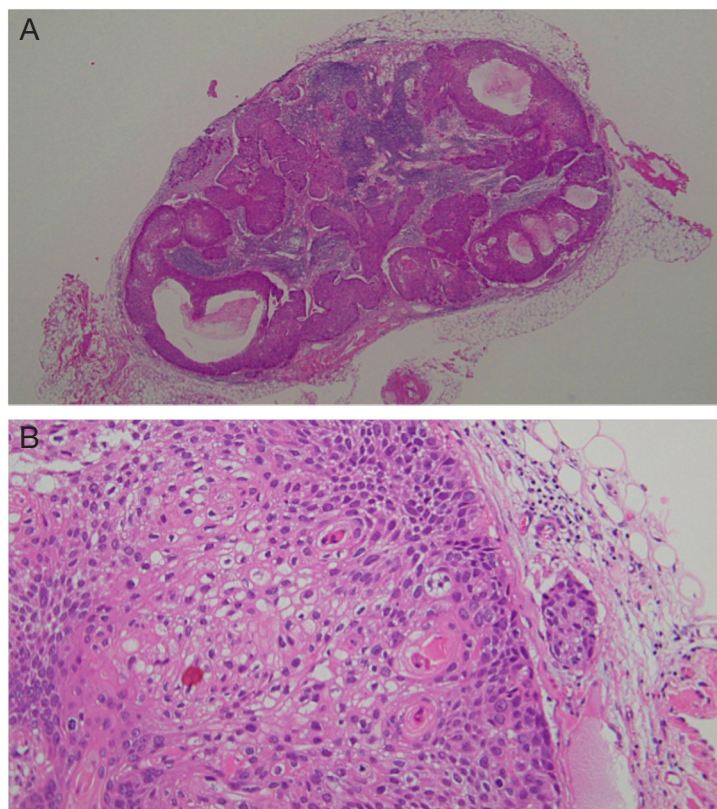
### **PATHOLOGICAL FINDINGS**

Macroscopically, the resected jejunal specimen revealed an ulcerative lesion measuring 25 × 20-mm in size with a perforation 5-mm in diameter (Fig. 5). Microscopically, viable tumor cells of keratinizing SCC were observed to have located mainly in the submucosa and muscularis propria with lymphovascular permeation (Fig. 6A, B). Mesenteric lymph node metastasis of SCC was also noted (Fig. 7A, B). Finally, histopathological examination of the jejunal specimen confirmed the diagnosis of jejunal perforation due to a solitary small intestinal metastasis of esophageal SCC with lymph node metastasis in the mesentery.

The patient was discharged 2 weeks postoperatively without complications. After 4 months, CT scan showed multiple bone metastases and lymph node metastases of the mediastinum and abdomen, and unfortunately, the patient died of cancer 9 months after surgery.

### **DISCUSSION**

Metastatic tumors of the intestinal tract from extra-abdominal sites are very rare [1, 3]. Hematogenous metastasis to the intestinal tract that developed from extra-abdominal cancer was initially reported in cases of melanoma and lung carcinoma [4–6]. SCC is the most common malignant neoplasm of the esophagus



**Fig. 7** Photomicrographs showing microscopic findings of the mesenteric lymph node specimen.

A: Metastatic squamous cell carcinoma with keratinization in the lymph node (original magnification  $\times 2$ , H & E).

B: Magnified findings showed squamous cell carcinoma with a permeation of the lymphatic vessel around the metastatic lymph node (original magnification  $\times 20$ , H & E).

in Japan. SCC of the esophagus is characterized by extensive local growth, contiguous spread, and extensive lymphatic metastasis in the mediastinum, abdomen, and cervix via the dual interconnecting longitudinal lymphatic system along the esophagus, depending on the location of the main tumor [7]. Retrograde spread to mesenteric and iliac lymph nodes in the abdomen is unusual [8]. The lymphatic network connecting the esophagus and intestine, lymphatic embolization, hematogenous spread, and peritoneal seeding of the tumor during the initial operation have been considered to be possible mechanisms of metastasis to the abdomen [4]. The intra-abdominal region can also be reached via the hematogenous route, especially via the vertebral venous plexus [9, 10]. In esophageal cancer, the liver, lung, and bone are the most common sites of hematogenous metastases. Metastasis to the small intestine from esophageal carcinoma is extremely rare [10, 11].

In the international literature, there have been only 5 reported cases of small intestinal metastases from esophageal cancer, including 3 Japanese cases [11]. In the Japanese literature, 14 cases of small intestinal metastases from esophageal cancer have been previously reported [12]. We analyzed the clinicopathological characteristics of the 18 Japanese cases, including our case. The patient age ranged from 44 to 85 (mean 62) year-old, and 16 male and 2 female cases were reported. The clinical symptoms included small bowel obstruction in 11 cases, perforation in 5 cases, and no symptom in 2 cases. The main locations of the primary esophageal cancer were middle thoracic esophagus in 9 cases, lower thoracic esophagus in 5 cases, and cervical esophagus in 4 cases. For all cases, the small intestinal metastases were detected incidentally during surgery.

Surgical treatment using laparotomy was performed in all cases. Thirteen patients had a solitary lesion, and 5 patients had multiple lesions. Pathological findings of the primary esophageal cancer revealed SCC in 16 cases, and basaloid carcinoma and undifferentiated carcinoma in one case each. With the exception of a single case of superficial esophageal cancer, the majority of cases were primary advanced esophageal cancer with a very poor prognosis.

In our case, acute abdomen with abdominal pain associated with perforated peritonitis was present. Surgical exploration was certainly indicated, and solitary small intestinal metastasis was detected incidentally during surgery. Pathologically, the resected specimen of the jejunum showed metastatic SCC mainly located in the submucosa to muscularis propria with lymphovascular permeation and mesenteric lymph node metastasis. The jejunal metastasis was not detected preoperatively on radiographic examinations. Multiple bone metastases and lymph node metastases were recognized after 4 months, and the patient died of cancer 9 months after surgery. Based on these findings, small intestinal metastasis from esophageal carcinoma is considered to be a late manifestation of highly malignant tumor behavior that might represent the rapid advance of systemic metastases due to the final breakdown of immunological barriers. In addition, small intestinal metastases from esophageal carcinoma might be a significant finding generally associated with a poor prognosis.

FDG-PET is generally a useful examination to detect solitary metastasis. However, FDG-PET can have a high incidence of artifact caused by many different intra-abdominal focuses of inflammation such as gastro-intestinal tract, which can make preoperative correct

assessment of the abdominal cavity quite difficult [13]. The solitary jejunal metastasis was not detected by preoperative FDG-PET in this case, also. An occult and widespread dissemination of the cancer cells into the abdominal cavity is possible, because of the extensive esophageal lymphatic system. Therefore, early detection of small intestinal metastases might be difficult based on clinical symptoms and imaging findings. Additional intra-operative evaluation of the small intestine and the abdominal cavity should be performed to detect occult intra-abdominal metastases in the surgical treatment of advanced esophageal cancer.

### CONCLUSION

Metastasis to the intestinal tract from esophageal SCC presenting with perforated peritonitis is extremely rare. It might be difficult to diagnose the small intestinal metastasis by symptoms or radiographic imaging preoperatively. For patients presenting with an acute abdomen such as pan-peritonitis, small bowel obstruction, and intussusception who have a past medical history of advanced esophageal cancer, a differential diagnosis of intestinal metastasis should be considered. Further studies and reports of similar cases are required.

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