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Synchronous multiple primary malignancies of the esophagus, stomach, and jejunum: A case report

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Abstract

BACKGROUND

Treatment of synchronous multiple primary malignancies is quite often very challenging. Herein, we report on a rare case of synchronous multiple primary malignancies in the esophagus, stomach, and jejunum.

CASE SUMMARY

A 50-year-old man who was a heavy drinker and smoker with a poor diet, and had a family history of cancer sought treatment due to dysphagia lasting for 4 mo. He was finally diagnosed with lower esophageal squamous cell carcinoma (pT3N2M0, G2, stage IIIB), gastric angular adenocarcinoma (pT3N2M0, G2-G3, stage IIIA) with greater omental lymph node metastasis, and jejunal stromal tumor (high risk). The high-risk jejunal stromal tumor was found during surgery. In spite of radical resection and adjuvant chemotherapy, lymph node metastasis occurred 21 mo later. The patient responded poorly to additional chemotherapy and refused further examination and therapy. He died of widespread metastases 33 mo after surgery.

CONCLUSION

This case indicates a poor prognosis of synchronous multiple advanced primary malignancies and the importance of comprehensive assessment in the population at high risk for cancer.

Key Words: Multiple primary malignancies; Gastrointestinal tract; Diagnosis; Treatment; Case report

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Core Tip: This article presents a case with synchronous multiple primary malignancies, including esophageal squamous cell carcinoma, gastric adenocarcinoma, and jejunal stromal tumor. This patient had many cancer-related risk factors like heavy drinking, smoking, and family history. The high-risk jejunal stromal tumor was found during operation. Despite radical surgery and adjuvant chemotherapy, the patient died of widespread metastases 33 mo later. This case suggests a poor prognosis of synchronous multiple advanced primary malignancies and the importance of comprehensive assessment for high-risk populations.

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INTRODUCTION

Multiple primary malignancies are relatively common, accounting for about 2.4%-17.2% within 20 years of follow-up in a cancer population[1-2]. The prognosis of multiple primary malignancy varies much due to cancer type and stage at initial diagnosis. The treatment of patients with synchronous multiple primary malignancy, especially advanced ones, is still difficult[3]. Herein, we report one case with synchronous esophageal squamous cell carcinoma, gastric adenocarcinoma, and high-risk jejunal stromal tumor. This is the first case with synchronous primary malignancies in the esophagus, stomach, and jejunum, including both epithelial and mesenchymal tumors. The jejunal stromal tumor was found during surgery. This case suggests a poor prognosis of synchronous multiple advanced primary malignancies and the importance of comprehensive assessment for high-risk populations.

CASE PRESENTATION

Chief complaints

A 50-year-old man sought treatment for dysphagia lasting for 4 mo.

History of present illness

The patient had difficulty when swallowing solid and semiliquid food, without nausea, vomiting, thoracalgia, acid reflux, heartburn, abdominal pain, abdominal distension, melena, constipation, or weight loss, *etc.*

History of past illness

The patient had no previous medical history.

Personal and family history

The patient smoked 10 cigarettes per day for 30 years, drank alcohol 100 g/d for 30 years, and often ate hot food. His father died of lung cancer.

Physical examination

The patient's height and body weight were 169 cm and 61 kg, respectively. His general condition was good and physical examination revealed no special abnormalities.

Laboratory examinations

There were no abnormal laboratory data findings, including blood test, hepatic function parameters, renal function parameters, tumor markers, *etc.*

Imaging examinations

White light endoscopy revealed one soft nodular neoplasm with superficial erosion along the lower esophagus 35-37 cm from the incisors (Figure 1A), which was identified as squamous cell carcinoma following biopsy, and one hard nodular

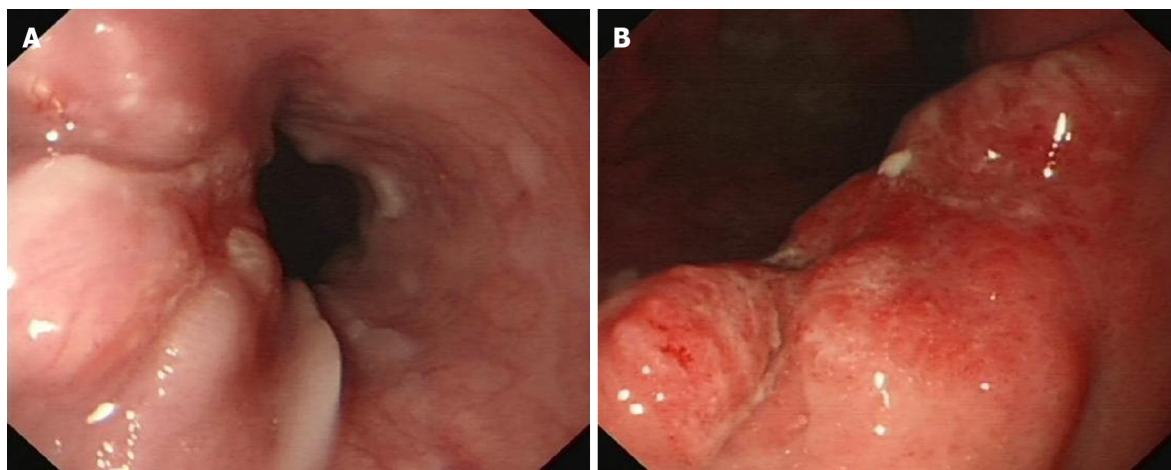


Figure 1 Preoperative endoscopy. A: Preoperative endoscopy showed one soft nodular neoplasm with superficial erosion along with the lower esophagus; B: Preoperative endoscopy showed a nodular neoplasm with superficial erosion and irregular boundary in the stomach angular notch.

neoplasm with superficial erosion and irregular bound in the stomach angular notch (Figure 1B) that was identified as adenocarcinoma following biopsy. Chest and upper abdomen enhanced computed tomography (CT) showed eccentrically enhanced thickening of the lower esophagus (Figure 2), without enlarged lymph nodes and distant metastasis.

FINAL DIAGNOSIS

The final diagnosis was lower esophageal squamous cell carcinoma (pT3N2M0, G2, stage IIIB), gastric angular adenocarcinoma (pT3N2M0, G2-G3, stage IIIA) with greater omental lymph node metastasis, and jejunal stromal tumor (high risk).

TREATMENT

Lower esophageal carcinoma resection and total gastrectomy were first planned. Entering the thoracic cavity through the right posterolateral 5th intercostal space, we found a fungating 3 cm × 3 cm × 2 cm tumor in the lower esophagus and enlarged lymph nodes. Entering the abdomen through the midline incision of the upper abdomen, we found a 4 cm × 3 cm × 3 cm superficial ulcerated tumor in the lesser curvature of the stomach and an 8 cm × 7 cm × 6 cm tough irregular nodular tumor in the jejunum 60 cm away from the Treitz ligament and multiple enlarged lymph nodes. The jejunum tumor was located in the pelvic cavity, and intraoperative freezing indicated a spindle-cell tumor. We finally performed lower esophageal cancer resection, total gastrectomy, segmental jejunal resection, systematic lymph node dissection, thoracic duct ligation, and esophagojejunostomy.

Postoperative pathology

The esophageal tumor turned out to be a moderately differentiated squamous cell carcinoma (Figure 3A) invading to outer membrane, with positive vascular cancer thrombus and negative margin. Metastasis of squamous cell carcinoma was detected in groups 8, 10, and 16 lymph nodes. The gastric tumor was a moderately to poorly differentiated adenocarcinoma (tubular adenocarcinoma and signet-ring cell carcinoma, Laurén mixed type) (Figure 3B) that invaded to the subserosal layer with a negative margin. Metastasis of adenocarcinoma was detected in groups 3, 17, and 20 and greater omentum lymph nodes. HER-2 expression was positive, but HER-2 FISH was negative. The jejunal tumor was a gastrointestinal stromal tumor (GIST) of spindle cell type (Figure 3C), with a mitotic rate ≤ 5/50HPF. Immunohistochemical staining showed CD117 (+), DOG-1 (+), SMA (+), CD34 (-), and S-100 (-). Gene testing showed *KIT* exon 11 insertion mutation (sequence TATGAT inserted between 90-91 bases).

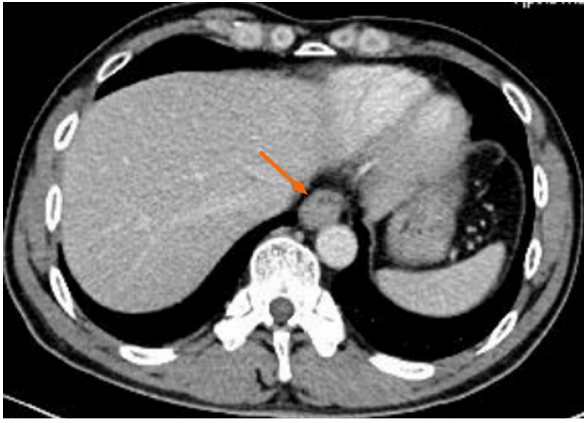


Figure 2 Preoperative computed tomography. Preoperative computed tomography showed that the wall of the lower esophagus was eccentrically thickening and enhanced, and the esophageal lumen became narrowed obviously (orange arrow).

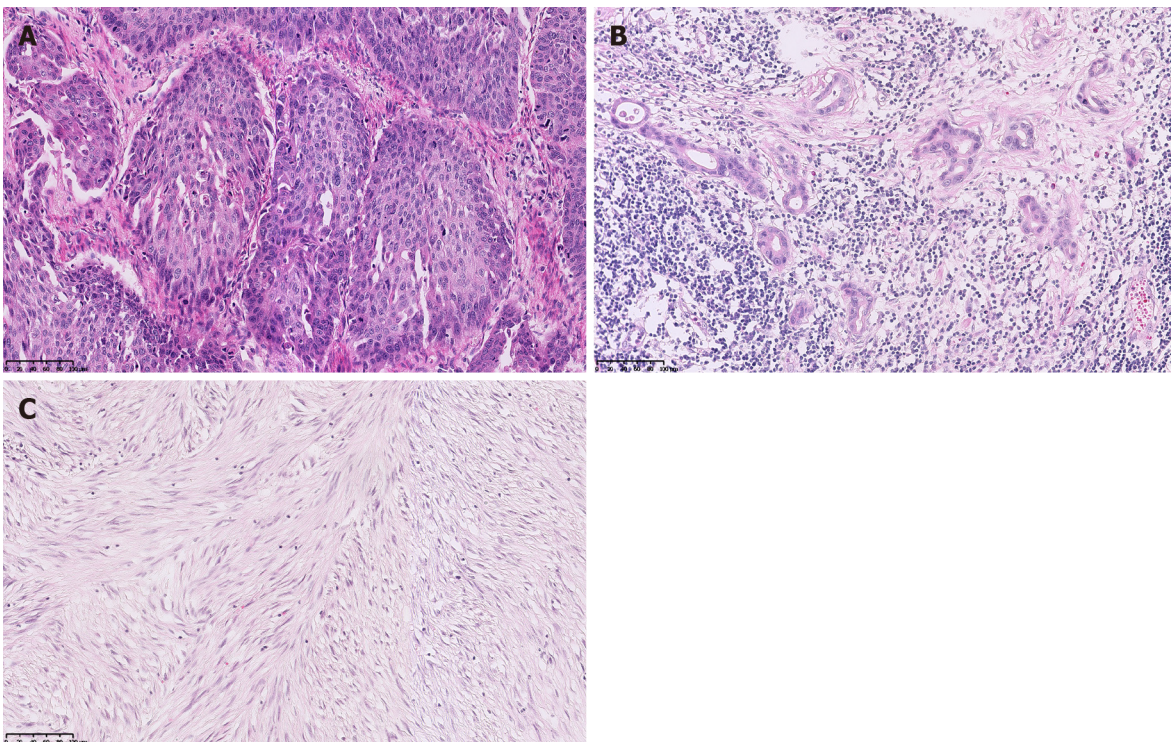


Figure 3 Postoperative pathology. A: Postoperative pathology showed that the esophageal tumor was a moderately differentiated squamous cell carcinoma with lymph nodes metastases (pT3N2M0, G2, stage IIIB); B: Postoperative pathology showed that the gastric tumor was a moderately to poorly differentiated adenocarcinoma (tubular adenocarcinoma and signet-ring cell carcinoma, Laurén mixed type) with lymph node metastases (pT3N2M0, G2-G3, stage IIIA); C: Postoperative pathology showed that the jejunal tumor was a gastrointestinal stromal tumor of spindle cell type (high-risk).

OUTCOME AND FOLLOW-UP

Enhanced head, neck, chest, abdomen, and pelvis CT and bone SPECT before adjuvant therapy showed no organic metastasis. A blood test showed a decreased white cell count at $2.54 \times 10^9/L$. Hepatic function and renal function parameters were normal. The patient was treated adjuvantly with six cycles of Oxaliplatin 200 mg d1 combined with Tegafur Gimeracil Oteracil Potassium capsules 50 mg bid d1-14 (SOX regimen). Re-examinations taken every 3 mo showed no relapse or metastasis within 18 mo postoperatively.

At the 21st mo after surgery, abdominal enhanced CT showed that the para-aortic and hepatogastric ligamentous lymph nodes enlarged (Figure 4A), and the concentration of CA72-4 was elevated to 10.18 U/mL. Additional Docetaxel 110 mg d1 combined with Cisplatin 35 mg d1-d3 (DP regimen) was given; however, nausea reached grade III at the first cycle and the latter three cycles were dose-reduced DP

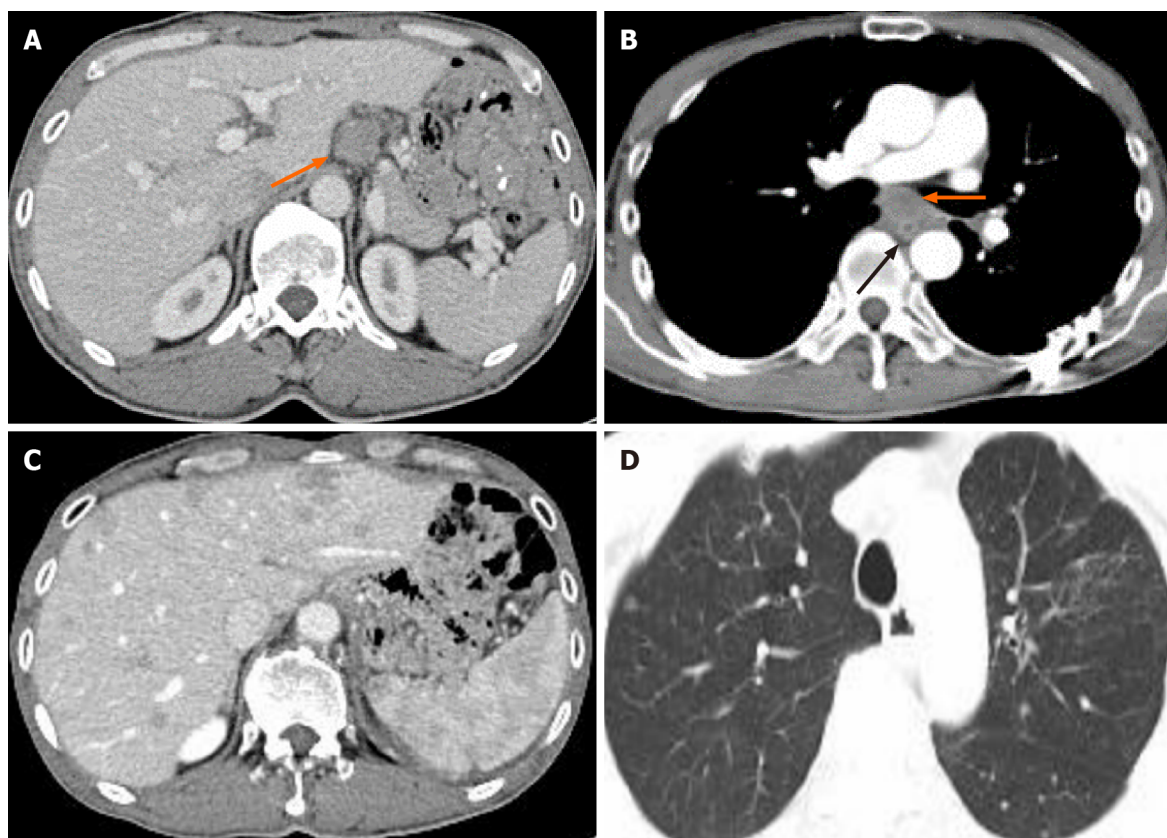


Figure 4 Computed tomography re-examination. A: Computed tomography (CT) re-examination showed that the hepatogastric ligamentous lymph node enlarged 21 mo after surgery (orange arrow); B: CT re-examination showed that the local thickening of the esophageal anastomotic site (black arrow) and enlarged subcarinal lymph nodes (orange arrow); C: CT re-examination showed multiple nodules in the liver; D: CT re-examination showed multiple nodules scattered in both lungs emerging 28 mo after surgery.

regimen (Docetaxel 90 mg d1 combined with Cisplatin 35 mg d1-d3). At the 24th mo after surgery, abdominal lymph nodes were further enlarged and the concentration of CA72-4 elevated to 17.9 U/mL. The patient refused biopsy and further treatment. At the 28th mo after surgery, local thickening of esophageal anastomotic site, multiple nodules in the liver, pancreatic invasion, small nodules scattered in both lungs, enlarged hepatogastric ligamentous and para-aortic lymph nodes, and enlarged subcarinal lymph nodes under enhanced CT (Figures 4B, 4C and 4D), and further elevated serum tumor markers (CA199 > 1000 U/mL, CEA 141.2 ng/mL, and CA72-4 > 300 U/mL) indicated rapid disease progression. The patient finally died of widespread metastases 33 mo after surgery. The timeline of his treatment is shown in Figure 5.

DISCUSSION

Multiple primary malignancies relate to more than one independent primary malignancy occurring simultaneously or successively in the same individual. When two or more advanced malignancies are simultaneously found in one patient, it is challenging to find appropriate anticancer therapy that could address all cancers without increased toxicity or relevant pharmacological interactions. In 2017, Vogt *et al* [3] reviewed the literature about multiple primary malignancy and recommended selecting a treatment strategy that could address all cancers or choose the most significant tumor in terms of prognosis and curative chance. Only several case reports about synchronous multiple primary malignancy are currently available in the literature, and lung cancer occurred in most of these cases. Moreover, gastrointestinal multiple primary malignancies were usually located in the colon, like Lynch syndrome. This is the first case of synchronous multiple primary malignancies in the esophagus, stomach, and jejunum, including epithelial and mesenchymal tumors. Our experience suggests a poor prognosis of synchronous multiple advanced primary malignancies and the importance of comprehensive screening in patients with high risk of cancer.

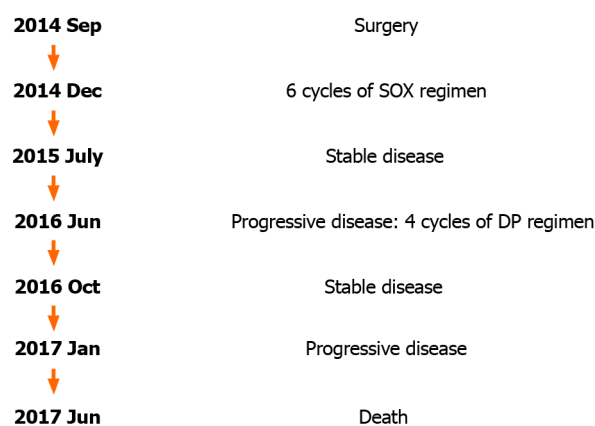


Figure 5 Timeline. The patient was diagnosed with multiple primary malignancies in September 2014 and was treated by radical surgery and adjuvant chemotherapy. Abdominal lymph node metastasis occurred in June 2016 (21 mo after surgery). Additional chemotherapy was carried out but was not well tolerated, and he refused further therapy. Widespread metastases occurred soon, and the patient eventually died in June 2017 (33 mo after surgery). SOX: Oxaliplatin 200 mg d1 combined with Tegafur Gimeracil Oteracil Potassium capsules 50 mg bid d1-14; DP: Docetaxel 110 mg d1 combined with Cisplatin 35 mg d1-d3.

Inherited predisposition to cancer, cancer promoting aspects of lifestyle (heavy drinking, smoking, high salt diet, frequent hot food, obesity, *etc.*), and hormonal and environmental factors have been associated with the occurrence of multiple primary neoplasms[4-6]. In this case, the patient had multiple risk factors like heavy drinking, smoking, frequent hot food, and family history. Cancer type and stage at initial diagnosis are related to the prognosis of synchronous multiple primary malignancies. This patient was diagnosed with esophageal squamous cell carcinoma at stage IIIB, gastric adenocarcinoma at stage IIIA, and high-risk jejunal stromal tumor. Despite radical resection and adjuvant chemotherapy, he died of multi-organ metastases 33 mo postoperatively. The 5-year overall survival (OS) of esophageal cancer and gastric cancer were 14.7%-23.5% and 20.4%-32.8%, respectively[7]. But the 5-year OS of early esophageal and gastric carcinoma may reach up to 63.2%-84%[8-10]. This sheds light on a poor prognosis of synchronous multiple advanced primary malignancies and the importance of comprehensive screening for high-risk population.

GIST is the most common mesenchymal tumor of the gastrointestinal tract, but many patients are asymptomatic because the tumor can grow inside the abdominal and pelvic cavity. Patients with gastrointestinal stromal tumor have a higher risk of additional cancers than the general population, reaching about 16.4%-37.9%[11-13]. In this case, the high-risk jejunal stromal tumor concealed in the pelvic cavity and we did not discover this lesion until performing esophagojejunostomy. GISTs in the small intestine have a poor prognosis, especially when the tumor size is larger than 5 cm, the mitotic rate is over 5/50 high-power fields, or the tumor is ruptured[14]. Also, surgery is the optimal therapy for localized primary GISTs. If we missed this GIST during this operation, the patient would have to encounter another major surgery. Therefore, for populations at high risk for malignancy, comprehensive cancer screening is crucial to avoid omission.

This case report had some limitations. First, it was unclear which malignancy the widespread metastases originated from because the patient refused to take biopsy after tumor recurrence and metastasis. Second, no genetic testing was performed to detect possible oncogene(s) for multiple primary malignancies.

CONCLUSION

Patients with synchronous multiple advanced primary malignancies have a poor prognosis, and comprehensive assessment of multiple primary malignancies is critical for patients at high risk for cancer.

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