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Case Report

Esophageal Squamous Cell Carcinoma with Intragastric Metastasis Invading Liver: A Case Report

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Abstract Esophageal squamous cell carcinomas often metastasized to lymph nodes and distant organs. The incidence of metastasis to the stomach from esophageal cancer was rare. However, early-stage esophageal carcinoma with gastric metastasis is very rare. We report a case of submucosal esophageal SCC arising in the mid-thoracic esophagus with a large metastasis tumor in the gastric cardia invading liver. A 54 year-old Thai male presented with sudden epigastrium pain for 3 days. He had melena 1 month previously. Endoscopic examination revealed a 0.5 cm small ulcerative lesion squamous cell carcinoma and a giant gastric tumor at cardia. Computed tomography showed that the gastric tumor was directly invading the liver. He underwent Ivor Lewis esophagectomy and wedge resection left lobe liver. Final pathological findings were superficial esophageal carcinoma invading the submucosal layer with gastric mass involving the gastric submucosa, the muscular propria, and partially extended into the adjacent liver. After chemotherapy cycle 3, computed tomography showed liver metastasis. The outcome for patients with esophageal carcinoma who have gastric metastasis is very poor, even after surgery and chemotherapy. Optimal management of gastric metastasis from esophageal cancer is not established yet.

Keywords: Early-stage esophageal carcinoma, Gastric metastasis, Intramural gastric metastasis, Liver invasion

Introduction

Squamous cell carcinoma (SCC) of the esophagus is associated with a poor prognosis. Many patients with this disease already have metastasis by the time the primary tumors are detected. Distant metastasis to other organs such as the liver, lungs, and bone are commonly found in advanced esophageal cancer cases, but not in the stomach, less than 70 cases were reported until now.[1] The incidence of metastasis to the stomach from esophageal cancer was 6.2% at autopsy[2] and 5.3-8.1% at endoscopic findings.[3,4] However, early-stage esophageal carcinoma with intramural gastric metastasis is very rare. The prognosis for patients with gastric metastasis is poor. Optimal management of gastric metastasis from esophageal cancer is not established yet. We report a case of submucosal esophageal SCC arising in the mid-thoracic esophagus with a large metastasis tumor in the gastric cardia invading liver.

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Report of A Case

A 54 years old Thai male presented with sudden epigastrium pain for 3 days. He wasn't complaining about dysphagia but a weight loss of 5 kg in 1 month. He had melena 1 month previously. He had no past medical and was not taking any regular medications. His social history was significant for smoking ½ pack of cigarettes for 30 years and drinking a ½ bottle of alcohol daily, 20 years previously. He had no significant family history.

He was alert and look cachexia. His blood pressure was 130/90 mm Hg, pulse 84/min, respiration 20/min, body temperature 36.7°C. His general examination revealed pallor and tenderness at the epigastrium. The complete blood count showed a white blood cell count of 22,430/mm^3, Hemoglobin 6.6 g/dL, platelets 498 × 103/mm^3. His blood chemistry was normal, with tumor markers carcinoembryonic antigen (CEA) 2.6 Ug/L. The chest X-ray showed no abnormality. He then underwent esophagogastroduodenoscopy (EGD). The endoscopic finding revealed a 0.5 cm small ulcerative lesion was seen at 33 cm from the incisor teeth and a 7 cm fulgurating mass was seen at cardia of the stomach below EGJ. (Figure 1) A biopsy of two specimens demonstrated moderately differentiated squamous cell carcinoma. CT scan shows heterogeneous mass, which was measured about 7.9 × 7.0 × 6.9 cm in greatest dimensions and shows central necrotic portion, arising from the gastric fundus. It causes mass effect and luminal narrowing without gastric wall thickening. Note that direct invasion of the gastric mass into the left lobe of the liver is seen. There is no obviously seen esophageal mass in the chest CT. Neither perigastric nodes nor mediastinal nodes are demonstrated (Figure 2).

Intraoperative findings showed a 7 cm sized endophytic mass below Z-line that invade the left lobe liver and 0.5 cm mass at the mid-thoracic esophagus.

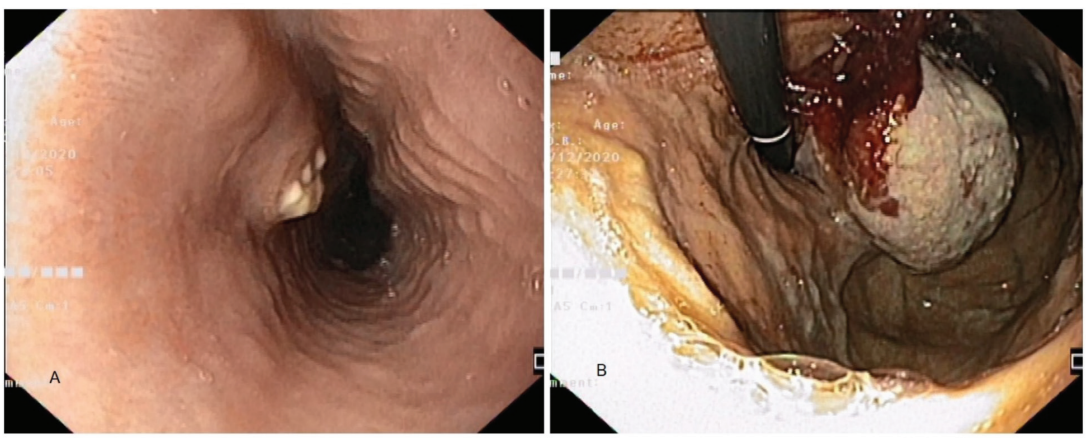

Figure 1 Endoscopic finding (a) small ulcerative lesion at the mid-thoracic esophagus. (b) fulgurating mass at cardia of the stomach below EGJ.

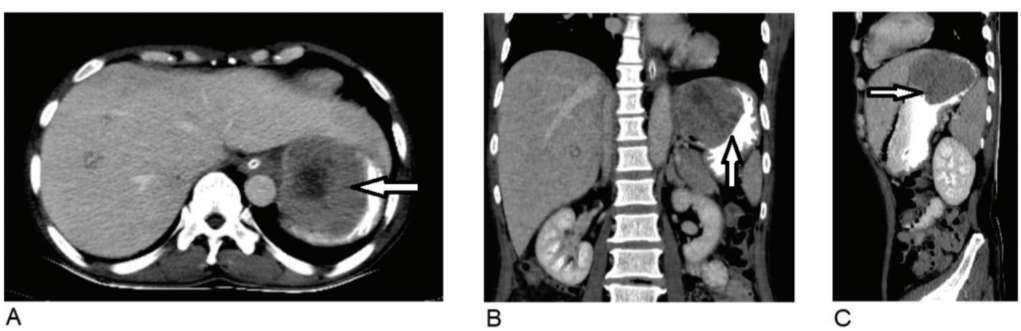

Figure 2 CT scan (a) Axial contrast-enhanced CT scan shows heterogeneous mass, which was measured about 7.9x7.0x6.9 cm in greatest dimensions and shows central necrotic portion, arising from the gastric fundus (arrow). (b) The coronal view shows the gastric mass causing luminal narrowing without gastric wall thickening (arrow). (c) The sagittal view shows the direct invasion of the gastric mass into the left lobe of the liver.

There was no intrathoracic and intraabdominal lymph node enlargement. He underwent Ivor Lewis esophagectomy and wedge resection left lobe liver. The microscopic examination of the esophagus revealed an infiltrative tumor that invaded the submucosal layer. There was an obvious transformation zone detected, showing the progression from the intraepithelial dysplasia into the invasive component. The tumor presented as irregular, cohesive nests/sheets surrounded by desmoplastic stroma. The squamous differentiation was identified by focal keratinizations, dyskeratotic cells, and the presence of intercellular bridges. (Figure 3) There were multiple tumor emboli with several esophageal nodal metastases seen. (Figure 4) The histologic sections of the stomach revealed an infiltrative tumor that almost exclusively involved the gastric submucosa, the muscular propria, and partially extended into the adjacent liver. The gastric mucosa was spared. Only a few focal ulcers were detected without evidence of intraepithelial dysplasia. (Figure 5) The gastric mass showed squamous differentiation similar to the esophageal primary. All of the perigastric nodes were negative for metastasis.

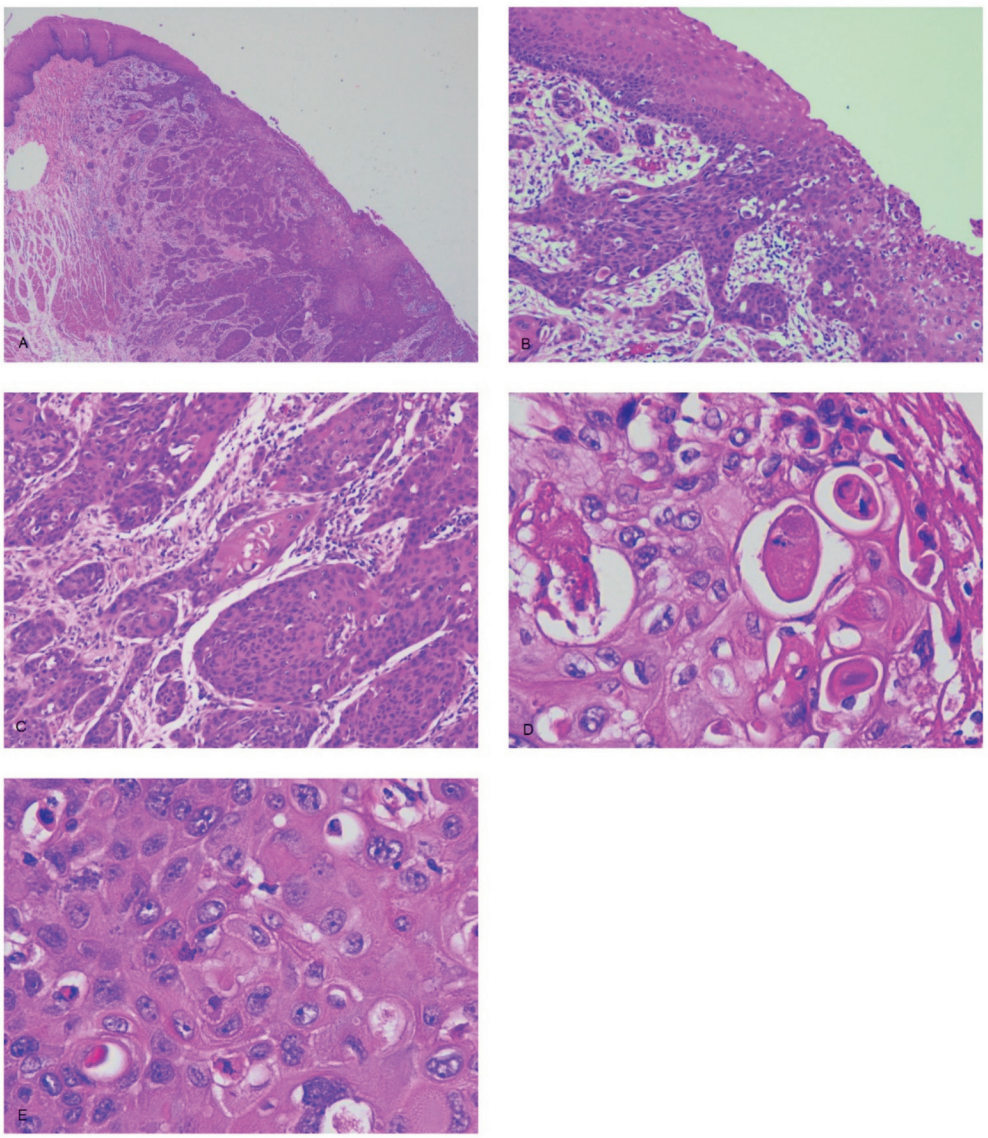

Figure 3 (a) The microscopic section of the esophagus revealed an infiltrative tumor that invaded the submucosa. (b) There was a transformation zone from the high-grade esophageal squamous intraepithelial neoplasia into the invasive component. (c) The tumor presented as irregular cohesive sheets with focal keratinization. (d) The tumor with dyskeratotic cells. (e) The neoplastic cells reveal focal intercellular bridges.

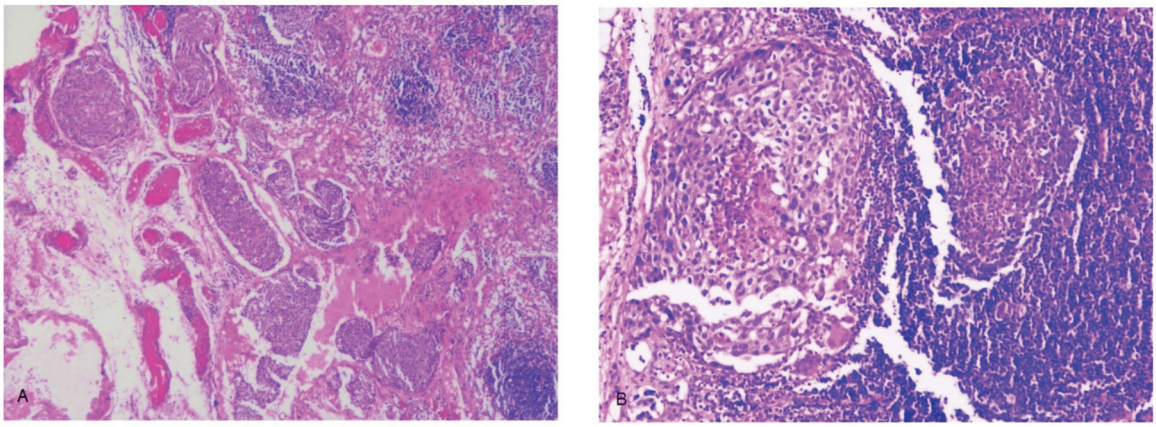

Figure 4 (a) Multiple tumor emboli identified in the nodal hilum. (b) The metastatic tumor in the periesophageal lymph node.

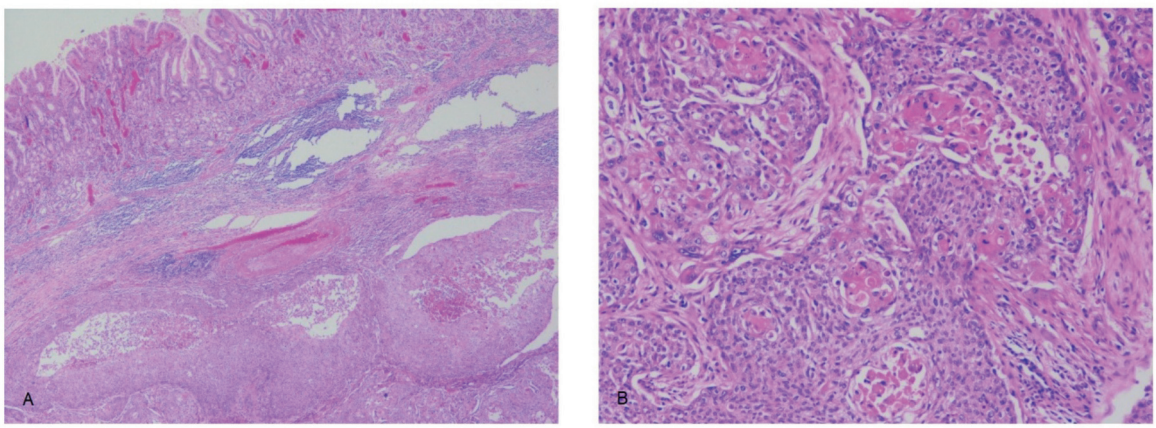

Figure 5 a) The gastric mass revealed an infiltrative tumor that almost exclusively involves the submucosa and muscular propria. The gastric mucosa was spared. There was no transformation zone detected. (b) The gastric tumor showed squamous differentiation similar to esophageal primary.

He was discharged on postoperative day 18 because of wound complications. He could eat semi-solid food before discharge and feed blenderized diet supplementally via jejunostomy. Chemotherapy was started at postoperative week[8]. He underwent chemotherapy for adjuvant treatment with cisplatin and 5-fluorouracil. Cisplatin 75 mg/m^2 was administered intravenously for 2 hours. After the completion of the cisplatin infusion on day 1. 5-Fluorouracil 1,000 mg/m^2/day was administered as a protracted intravenous infusion on days 1 to 4. Cycles of chemotherapy were repeated every 3 weeks.

After chemotherapy cycle 3, He came to the emergency room with abdominal distension and vomiting. The abdomen series showed small bowel dilatation with a different high in the same loop of the small bowel. He then underwent a CT scan of the abdomen. CT scan showed evidence of small bowel obstruction at the distal ilium and 4.2 × 3.9 × 4.8 cm hypodense lesion in hepatic segment VI/VII, possibly liver metastasis. The conservative treatment was done with NG and jejunostomy decompression. His clinical was improved 2 days after treatment. After discharge, he denies further chemotherapy and lost follow-up.

Discussion

The stomach is an unusual site for metastasis. Metastatic lesions to the stomach are found in 0.2% to 1.7% of populations in the autopsy series.[1,5] The common primary lesion was found to be melanoma, lung cancer, and breast cancer.[6-8]

Patient prognosis and survival outcomes are poor because the presence of gastric metastasis is associated with advanced disease.[3,5] The median survival period from the diagnosis of gastric metastasis was 3.0 months (range, 1.0 to 11.0 months).[3]

The presence of metastases within the stomach from esophageal carcinoma is rare. The incidence of metastasis to the stomach was 6.2% at autopsy2 and 5.3- 8.1% from endoscopic findings in the era of high-definition (HD) endoscopes.[3,4] Although 11.5% of the esophageal cancer patients had synchronous gastric tumors. The most common synchronous gastric tumor was adenocarcinoma of the stomach.[9]

Gastric metastatic firstly involved the submucosa and then might invade to the other layers of the stomach wall.[2] The pathological report was different from primary gastric squamous cell carcinoma. Primary Squamous cell carcinoma of the stomach is defined according to the following diagnostic criteria proposed by the Japanese Classification of Gastric Carcinoma: (1) all tumor cells are SCC cells, with no adenocarcinomatous components in any sections and (2) distinct evidence that SCC arises directly from the gastric mucosa.[10] Early in 1960-1980, EGD wasn't used routine for preoperative before gastrectomy. Some cases that reported primary SCC stomach, revealed another lesion at the esophagus in pathologic specimens.[11,12]

The mechanisms underlying gastric metastasis have not been clearly explained and are probably different for each primary tumor. Four pathways may be involved in the metastatic spread of original primary cancers to the stomach: peritoneal dissemination, hematogenous dissemination, lymphatic spread, and direct tumor invasion.[1] Saito et al. (1985) reported that gastric metastasis in esophageal cancer spread via the lymphatic route. From their report, examination of the surgical specimens revealed that not only lymphatic invasion but also lymph node metastasis was present in almost all patients. They summarized that metastases within the stomach are produced by the lymphatic invasion of carcinoma cells from the primary carcinoma in the esophagus.[2,12] Thus, it is considered that stomach metastasis is induced mainly via the lymphatic route rather than via the bloodstream route that is common in other types of distant organ metastasis.[2,13] But there had a case report that revealed the case of gastric metastasis without lymphatic infiltration in the surgical specimen because the primary esophageal tumor was a mucosal carcinoma with no lymphatic infiltration of the submucosa.[14]

Kuwano et al. classified gastric involvement by esophageal squamous cell carcinoma pathologically into the following four patterns: (1) gastric invasion from metastatic lymph nodes, (2) intramural metastasis, (3) direct gastric wall involvement by the primary tumor, and (4) intraepithelial spread to the gastric mucosa. In conclusion, esophageal cancer that involves the gastric wall or epithelium by direct spread appears to have a similar prognosis to other esophageal tumors, but gastric involvement by metastases indicates a poor prognosis.[15]

Intramural metastasis (IMM) of esophageal carcinoma was first reported by Watson in 1933. Watson explained IMM as an extension by way of the submucous lymphatic spread. Takubo (1989) defined IMM as the metastatic tumor in the esophagus or stomach from the primary esophageal carcinoma, not located within a vessel lumen but rather invading the esophageal or gastric wall. The primary carcinoma and the focus of IMM were distant from each other.[16] The recent definition of IMM purposed by Hashimoto et al. (2013) is as follows: (1) separated from the primary tumor; (2) located in the wall of the esophagus, stomach, or duodenum; (3) having a gross appearance of a submucosal tumor without intraepithelial cancer extension; (4) having the same histological type as the primary tumor; and (5) lacking any evidence of intravascular growth. These criteria discriminated IMM from multiple primary tumors in the esophagus or stomach and intravascular tumor emboli around the primary tumor.[13] The incidence of IMM observed by five Japanese research groups varied from 7.0 to 14.3%.[16-18] and 1.0% had IMM to stomach.[18] Lymph node metastasis and distant organ metastasis were observed higher in IMM patients than patients without IMM. IMM patients resulted in significantly shorter overall survival than patients without IMM.[13,16,19]

There were two peaks in the distribution patterns of the sizes of the metastatic tumors: less than 2 cm and more than 4 cm in diameter from autopsy specimen.[2] Solitary metastases were reported to be more common than multiple metastases.[2,3] Metastatic tumors resembled submucosal tumors of the stomach.[2,3] In contrast, a large tumor could form a dome-like lesion or ulcerative lesion. It exhibited pronounced submucosal growth and equally pronounced invasiveness into the gastric wall or further into the neighboring structures or rupture.[2,20]

From another case report, metastasis tumors could be larger than the primary esophageal carcinoma from which they originated.[14,18,20] The explanation for the large metastasis tumor was the blood supply to the stomach is more abundant than that to the esophagus; this may facilitate gastric tumor growth.[14] Submucosal lymphatic drainage from the middle and lower esophagus is thought to be connected to the gastric lymphatic drainage from the cardia and fundus; thus, the submucosal lymphatic system may be the route taken by cells metastasizing to the stomach. These connections might explain the predominant location of metastatic gastric lesions in the upper portion of the stomach, rather than in the body.[14] We found one report that was similar to our case of esophageal SCC with gastric metastasis invading the liver. It was questionable that early T staging in esophageal SCC can have distant metastasis. Ebihara et al. report 1 case of IMM from stage T1 esophageal cancer from 1,259 patients with esophageal cancer who underwent surgical treatment.[18] Patients with esophageal carcinoma should undergo a careful examination of their stomachs, even if their esophageal carcinoma is at an early stage.[11,14]

The GASTRIC group's meta-analysis of disease-free survival (DFS) in trials of adjuvant treatment for gastric cancer shows that DFS is an acceptable surrogate for overall survival (OS) in trials of cytotoxic agents for gastric cancer in adjuvant treatment. DFS is highly predictive of OS. The strong correlation between DFS and OS can be partly attributed to the short time interval between relapse and death in gastric cancer. Therefore, patients with a short DFS also tend to have a shorter OS.[21] However, a meta-analysis of studies of esophageal cancer showed that there was no correlation between progression-free survival (PFS) and OS, so PFS could not be a surrogate endpoint for OS.[22] A Cochrane meta-analysis revealed a clear survival benefit for the treatment of metastatic esophageal cancer with chemotherapy compared with best supportive care. The duration of response is only generally 4 to 6 months, with a median OS of 10 to 12 months.[23,24] In the report as mentioned before, the patient died of local recurrence 8 months after surgery despite adjuvant chemotherapy. They suggested that gastric metastasis invading other organs have extremely poor prognoses, even after adjuvant chemotherapy.[14] The outcome for patients with esophageal carcinoma who have IMM is very poor, even after aggressive treatment.[2,16] The mean survival time of patients in whom gastric metastasis develops after esophagectomy is 5.8 months (range, 1-13 months).[2,14] As was true of our case, the patient was recurrent in 4 months post-operative.

Conclusions

Patients with esophageal carcinoma should undergo a careful examination of their stomachs, even if their esophageal carcinoma is at an early stage. The outcome for patients with esophageal carcinoma who have gastric metastasis is very poor, even after surgery and chemotherapy. Optimal management of gastric metastasis from esophageal cancer is not established yet.

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Consent for Publication

The patient's wife provided consent for this case report to be published.

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บทคัดย่อ **รายงานผู้ป่วย : มะเร็งหลอดอาหารระยะต้น (T1b) ที่มีการแพร่กระจายไปยังกระเพาะอาหารและตับ**

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การกระจายของมะเร็งหลอดอาหารชนิด Squamous cell carcinoma มักพบที่ต่อมน้ำเหลือง และอวัยวะอื่นๆเช่น ตับ ปอด กระดูกเป็นต้น ซึ่งการพบกระจายของมะเร็งไปยังกระเพาะอาหาร (Intragastric metastasis) พบได้น้อยมาก และโดยปกติของการกระจายไปยังอวัยวะอื่นนั้นมักจะพบในมะเร็งระยะลุกลาม ในผู้ป่วยรายนี้ พบการกระจายของมะเร็งหลอดอาหารในระยะต้น และมีการกระจายไปยัง กระเพาะอาหารและตับ

รายงานเคสผู้ป่วยชายไทย อายุ 54 ปี มาโรงพยาบาลด้วยอาการปวดท้องบริเวณลิ้นปี่ 3 วันก่อนมาโรงพยาบาล และมีถ่ายดำมาก่อน 1 เดือนก่อน จากการส่องกล้องทางเดินอาหารพบแผลขนาด 0.5 เซนติเมตร ที่หลอดอาหาร และก้อนเนื้อขนาดใหญ่ที่กระเพาะอาหาร ผลชิ้นเนื้อทั้ง 2 ตำแหน่งเป็น Squamous cell carcinoma เอกซเรย์คอมพิวเตอร์พบว่าก้อนเนื้อที่กระเพาะอาหารติดกับตับซ้าย การรักษาผู้ป่วยรายนี้ได้ทำการผ่าตัด มะเร็งที่หลอดอาหารเป็นระยะ T1b และก้อนที่กระเพาะอาหารเป็น Intragastric metastasis หลังการผ่าตัด ผู้ป่วยได้รับเคมีบำบัด และหลังการให้เคมีบำบัด ครั้งที่3 ตรวจพบการกระจายไปยังตับขวา

การพยากรณ์โรคของมะเร็งหลอดอาหารที่กระจายไปยังกระเพาะอาหารตามที่มีรายงานพบว่ามีการพยากรณ์ของโรคที่แย่ แต่ในปัจจุบันยังไม่มี วิธีการรักษาที่เป็นมาตราฐาน รวมทั้งสูตรยาเคมีบำบัด