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Case Report

Mucosal Esophageal Squamous Cell Carcinoma With Intramural Gastric Metastasis Invading Liver and Pancreas: A Case Report

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A 59-year-old Japanese man was admitted to our hospital because of a 1-month history of dysphagia. Endoscopic examination revealed a superficial esophageal squamous cell carcinoma and a giant gastric tumor. Computed tomography showed that the gastric tumor was directly invading the liver and pancreas. Because of the risk of the gastric tumor causing obstruction and bleeding, we performed a subtotal esophagectomy, proximal gastrectomy, left lateral segmentectomy of liver, and pancreatosplenectomy with gastric tube reconstruction. Final pathological findings were superficial esophageal carcinoma penetrating the muscularis mucosae with an intramural gastric metastasis directly invading the liver and pancreas. The patient received postoperative adjuvant chemotherapy, yet died 8 months postoperatively of complications of local recurrence. Early-stage esophageal carcinoma with intramural gastric metastasis is very rare. To our knowledge, this is the first case of mucosal esophageal carcinoma with intramural gastric metastasis directly invading other organs.

Key words: Mucosal esophageal carcinoma – Intramural gastric metastasis – Direct invasion

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Esophageal squamous cell carcinomas often metastasize to lymph nodes and distant organs; intramural esophageal metastasis occasionally occurs. However, intramural gastric metastasis (IGM) is rare, the incidence in surgical specimens being 1% to 4.58%.[1–6] It is not unusual for rapidly growing IGMs to be larger than their primary esophageal carcinomas. IGMs have an extremely poor prognosis. Nearly all patients die within 1 year (median survival 5.8 months), and conventional radiotherapy or chemotherapy after surgery is ineffective in improving the prognosis.[3,7] The incidence of IGM is higher in advanced-stage disease; only a few cases of IGM in the early stage have been reported.[8–11] Herein, we report a case of mucosal esophageal carcinoma with a giant IGM invading the liver and pancreas. We also present a discussion of some related publications on this subject.

Case Report

In January 2011, a 59-year-old Japanese man was admitted to our hospital because of a 1-month history of dysphagia. He reported a 40-year history of smoking 20 cigarettes daily and drinking about 400 ml of Japanese sake daily. Blood tests showed an increased C-reactive protein concentration of 5.98 mg/dL. Other tests, including for tumor markers, were within normal limits.

Endoscopic examination showed a 2.0–cm-diameter, superficial, flat esophageal lesion 35 cm from the incisor teeth. Iodine staining did not stain this esophageal tumor but did show its margins more clearly (Fig. 1a). Biopsy of the lesion revealed poorly differentiated squamous cell carcinoma. In addition, the endoscopic examination showed a 10-cm-diameter submucosal tumor with contact bleeding in the cardiac portion of the stomach (Fig. 1b). Biopsy of the gastric tumor also revealed poorly differentiated squamous cell carcinoma. Computed tomography (CT) showed the gastric tumor had directly invaded the left lateral segment of the liver and the body of the pancreas (Fig. 2).

Because of the risk of the gastric tumor causing obstruction and bleeding, we performed a subtotal esophagectomy, proximal gastrectomy, left lateral segmentectomy of liver, and pancreatosplenectomy with gastric tube reconstruction in February 2011. Macroscopically, the esophageal tumor was a flat 13 × 19-mm lesion in the lower portion of the esophagus (Fig. 3a), and the gastric tumor was a 16 × 15 × 10-cm protruding lesion in the cardiac portion of the stomach (Fig. 3b). A sectioned slice of the gastric tumor showed direct invasion of the left lateral segment of the liver and the body of the pancreas (Fig. 3c and 3d).

Histologically, the esophageal lesion was a poorly differentiated squamous cell carcinoma penetrating the muscularis mucosae, with marked vascular and no lymphatic infiltration (Fig. 4a). The gastric lesion was also a poorly differentiated squamous cell carcinoma penetrating one layer deeper than the mucosa, consistent with an intramural metastasis from the esophageal carcinoma (Fig. 4b). Final pathological findings were mucosal esophageal

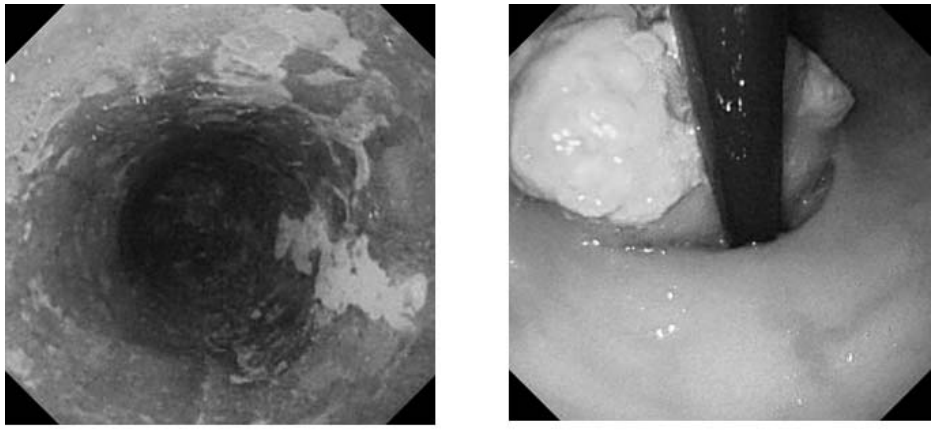

Fig. 1 Endoscopic examination. (a) A 2.0-cm-diameter, superficial, flat lesion was observed in the lower thoracic esophagus and delineated by iodine staining. (b) A 10-cm-diameter submucosal tumor was observed in the cardiac portion of the stomach.

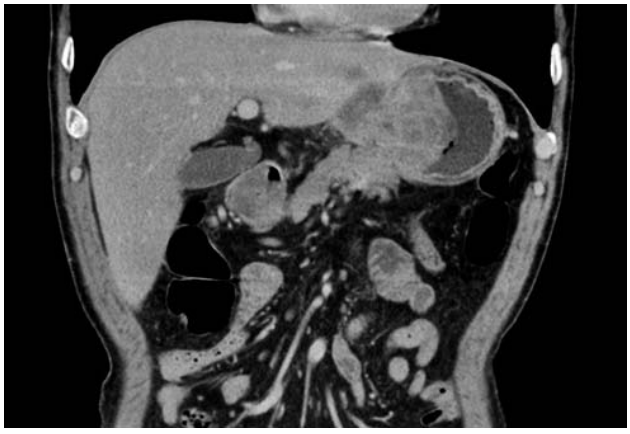

Fig. 2 A coronal CT slice revealed a gastric tumor directly invading the left lateral segment of the liver and the body of the pancreas.

carcinoma with intramural gastric metastasis directly invading the liver and pancreas.

Bile leakage from the resected surface of the liver 4 days after surgery complicated recovery. We inserted a drainage tube, and over the 30 days following surgery, the leakage improved. We discharged the patient 49 days postoperatively. He received 2 courses of adjuvant chemotherapy with a regimen of docetaxel, cisplatin, and 5-fluorouracil, but died of complications of local recurrence 8 months after surgery.

Discussion

IGM from esophageal carcinoma is rare, the incidence in surgical specimens being 1% to 4.48%.[1–6] Our previous study 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.[4] Another study reported detection of IGMs in 8/274 (2.9%) patients at autopsy, none of whom had had any evidence of gastric tumors when operated upon while still alive.[6] Takubo *et al*[12] reported that the incidence of intramural metastases from esophageal squamous cell carcinomas increases in parallel with the tumor stage. IGMs from mucosal esophageal squamous cell carcinoma are very rare; only 5 cases, including this case, have been documented in Japan.[8–11] Moreover, to the best of our knowledge, this is the first reported case of mucosal esophageal carcinoma with IGM invading the liver and pancreas.

Primary esophageal carcinomas located in the middle or lower portion of the esophagus and those with associated lymph node metastasis have a higher probability of metastasis to the stomach.[1,6] The most likely reason for the correlation between lymph node metastasis and gastric metastatic tumors is that the latter metastases occur via the lymphatic system; such a mode of spread would enable expansive growth in the submucosa.[1] The lymphatic ducts of the esophageal mucosa are not contiguous with those of the gastric mucosa.[13] However, the 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.[13] These connections might explain the predominant location of metastatic gastric lesions in the upper portion of the stomach, rather than in the body. In our patient, the primary tumor was in the lower thoracic esophagus and the IGM in the cardia of the stomach. However, we detected no lymph node metastases or lymphatic infiltration. Rather, we identified marked vascular infiltration.

A PubMed search (http://www.ncbi.nlm.nih.gov/pubmed) of case reports revealed only one similar previous case of IGM without lymphatic infiltration in the surgical specimen. In that case, an intramural metastasis developed in the body of the gastric tube postoperatively.[14] Other studies reporting metastases in reconstructed stomachs state that intramural metastases develop principally in the upper third of the gastric tube, but can also occur in the gastric body.[1,6] These findings suggest that IGM can occur without direct involvement of the lymphatic system.[14] In our case, the cells giving rise to the IGM could not have spread via the lymphatic system because the primary tumor was a mucosal carcinoma with no lymphatic infiltration of the submucosa; therefore, its lymphatic drainage did not connect with that of the stomach. Thus, IGMs must sometimes develop via routes other than the lymphatic system, including vascular routes.

As was true of our case, some IGMs are larger than the primary esophageal carcinoma from which they originated. Some possible explanations for the more rapid growth of IGMs concern their location.[8–11] First, the blood supply to the stomach is more abundant than that to the esophagus; this may facilitate gastric tumor growth. Second, loss of tumor cells occurs

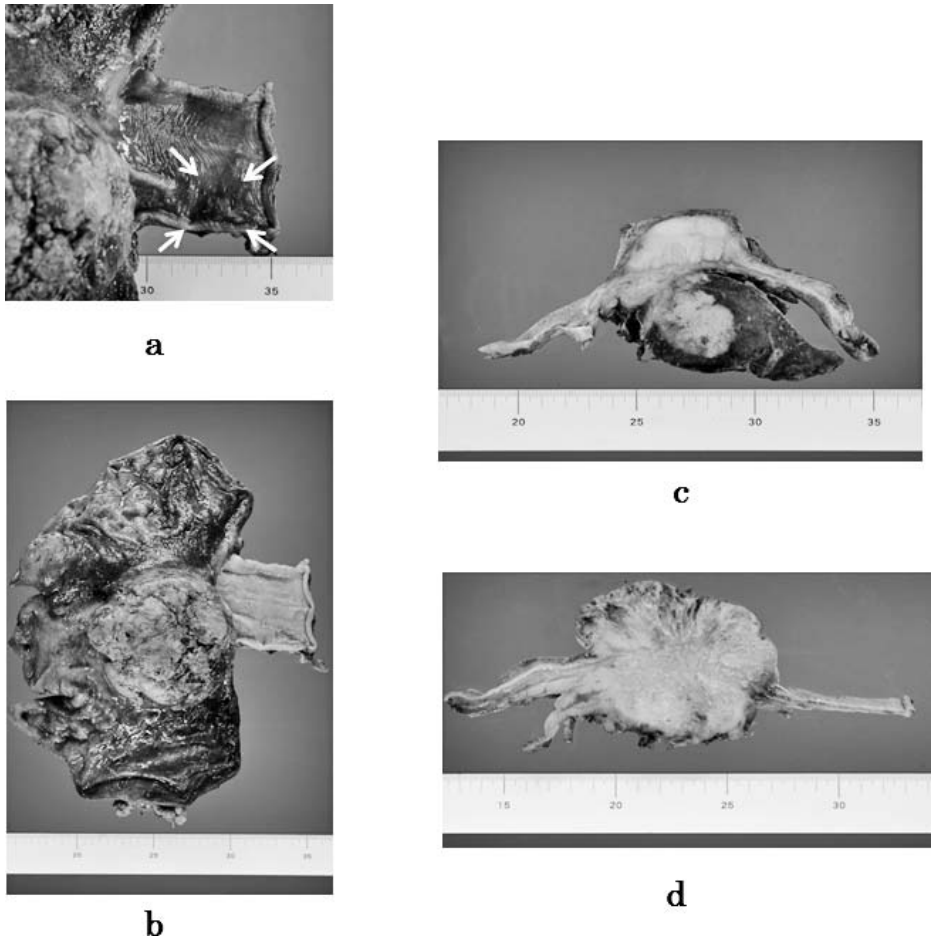

Fig. 3 Surgical specimens. (a) The esophageal tumor, a flat, 13 × 19-mm lesion in the lower portion of the esophagus, is delineated by iodine staining (arrow). (b) The gastric tumor is a 16 × 15 × 10-cm submucosal lesion in the cardiac portion of the stomach. (c, d) A sectioned slice of the gastric tumor shows direct invasion of the left lateral segment of the liver and the body of the pancreas.

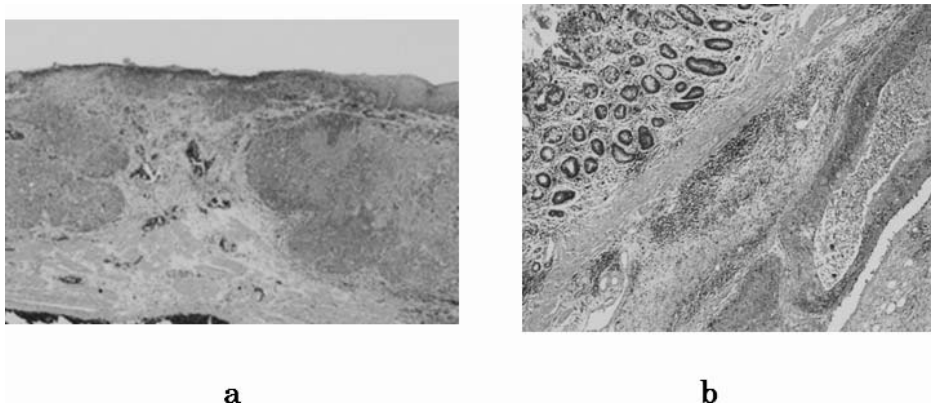

Fig. 4 Macroscopic examination. (a) The esophageal lesion is a poorly differentiated squamous cell carcinoma penetrating the muscularis mucosae. (b) The gastric lesion is also a poorly differentiated squamous cell carcinoma lying one layer deeper than the mucosa.

more easily at mucosal surfaces than in deeper layers.

Generally, the outcome for patients with esophageal carcinoma who have IGMs is very poor, even after aggressive treatment.[6] The mean survival time of patients in whom IGMs develop after esophagectomy is 5.8 months (range, 1–13 months).[3,6] We selected an extensive surgery, not neoadjuvant chemotherapy, because of the risk of IGM causing obstruction and bleeding, judging that esophageal carcinoma with IGM invading the nearby organs was resectable. Furthermore, we expected the efficacy of adjuvant chemotherapy to prevent the recurrence. However, our patient died of local recurrence 8 months after surgery despite adjuvant chemotherapy. Kato *et al*[2] reported no differences in survival rates between patients with IGMs who received no treatment and those who received chemotherapy or chemoradiotherapy. Therefore, it is necessary to examine combined modality therapy in patients with IGMs in the future.

In conclusion, our findings suggest that patients with mucosal esophageal carcinoma and an IGM that is directly invading other organs have extremely poor prognoses, even after adjuvant chemotherapy. Patients with esophageal carcinoma should undergo careful examination of their stomachs, even if their esophageal carcinoma is at an early stage.

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