



# Diffusely infiltrative squamous cell carcinoma of the esophagus resembling scirrhous gastric cancer: a case report

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**Introduction and Importance:** Diffusely infiltrative squamous cell carcinoma of the esophagus is rare and difficult to diagnose.

**Case presentation:** The patient was a 75-year-old woman whose chief complaints were dysphagia and upper abdominal pain. Esophagogastroduodenoscopy and biopsy revealed squamous cell carcinoma at the abdominal esophagus. After neoadjuvant chemotherapy, esophagogastroduodenoscopy showed diffuse thickening and poor distensibility of the stomach wall. We suspected scirrhous gastric cancer and performed multiple biopsies, which revealed no evidence of malignancy. We then performed staging laparoscopy. There were no apparent changes in the serous membrane of the stomach, but peritoneal lavage cytology revealed squamous cell carcinoma. Thus, we made a diagnosis of squamous cell carcinoma of the esophagus with diffuse invasion of the stomach. Intraoperative pathological diagnosis revealed that there was greater diffuse submucosal invasion of the oral esophagus than we expected, and we had to resect the esophagus at the level of the middle thoracic esophagus. Despite multidisciplinary treatment (surgery, chemotherapy, and radiotherapy), the patient died 20 months after the initial diagnosis.

**Clinical discussion:** In this case, although biopsy did not lead to a diagnosis, peritoneal lavage cytology led to the correct diagnosis. Moreover, it was impossible to preoperatively predict the exact extent of the expansion because of diffuse submucosal invasion.

**Conclusion:** When diffusely infiltrative squamous cell carcinoma of the esophagus is suspected, peritoneal lavage cytology may be useful for confirming the diagnosis; however, it should be assumed that accurate preoperative evaluation of the range of diffusely infiltrative squamous cell carcinoma is difficult.

**Keywords:** case report, diffusely infiltrative squamous cell carcinoma, esophagus, peritoneal lavage cytology, scirrhous gastric cancer

## Introduction

Diffusely infiltrative squamous cell carcinoma of the esophagus is rare<sup>[1–3]</sup>, whereas diffusely infiltrative gastric cancer (scirrhous gastric cancer) is relatively common. Those tumors sometimes exhibit diffuse submucosal invasion, and malignant cells may elude detection by biopsy<sup>[2]</sup>, so those tumors are difficult to diagnose. We observed a rare case of diffusely infiltrative squamous cell carcinoma of the esophagus that resembled scirrhous

## HIGHLIGHTS

- Diffusely infiltrative squamous cell carcinoma of the esophagus is rare and difficult to diagnose.
- Peritoneal lavage cytology may help to diagnose diffusely infiltrative squamous cell carcinoma of the esophagus.
- Accurate preoperative evaluation of the range of diffusely infiltrative squamous cell carcinoma is difficult.

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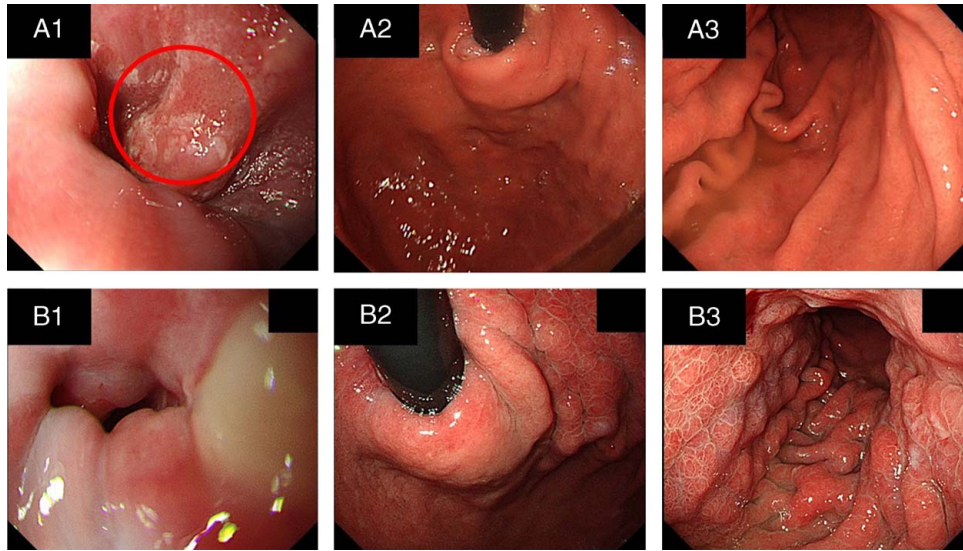
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gastric cancer. This case report has been reported in line with the Surgical CAse REport (SCARE) Criteria<sup>[4]</sup>.

## Case presentation

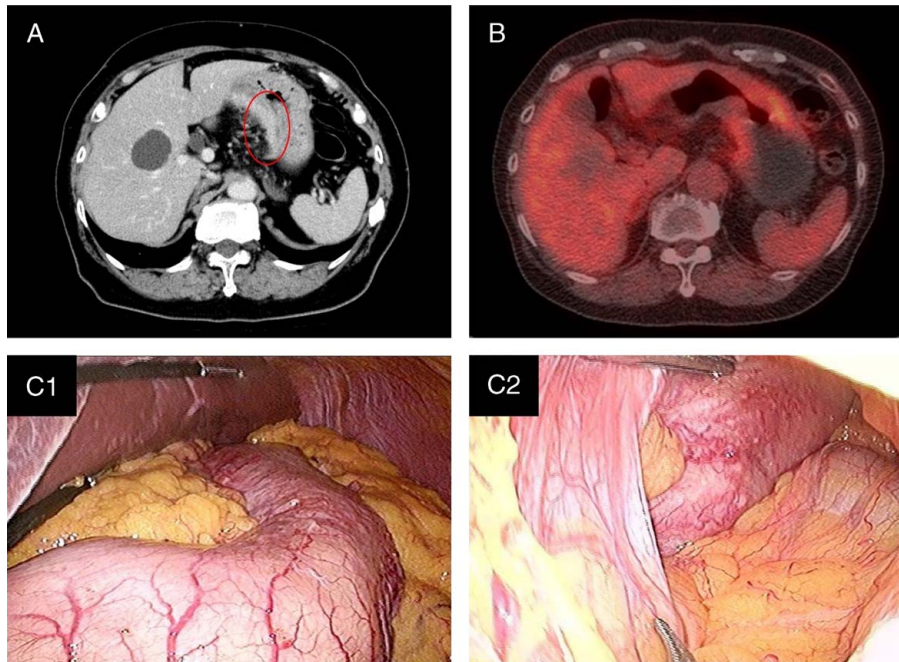
The patient was a 75-year-old woman whose chief complaints were dysphagia and upper abdominal pain. Esophagogastroduodenoscopy showed irregular ulcers at the abdominal esophagus (Fig. 1A), and biopsy revealed squamous cell carcinoma. The serum cytokeratin 19 fragments 21-1 and squamous cell carcinoma antigen level was elevated at 2.1 and 4.2 ng/ml, respectively. The serum carcinoembryonic antigen and carbohydrate antigen 19-9 levels were within the normal range. Computed tomography (CT) showed enlarged mediastinal lymph nodes. The clinical stage at the first diagnosis was III (T3N2M0, Union for International Cancer Control



**Figure 1.** (A) Esophagogastroduodenoscopy before neoadjuvant chemotherapy. (A1) Irregular ulcer at the abdominal esophagus. The biopsy revealed squamous cell carcinoma. (A2, A3) Mild chronic gastritis in the stomach. (B) Esophagogastroduodenoscopy after neoadjuvant chemotherapy. (B1) Partial response of the primary lesion. (B2, B3) Diffuse thickening and poor distensibility of the stomach wall. Multiple biopsies, including boring biopsy, revealed no evidence of malignancy.

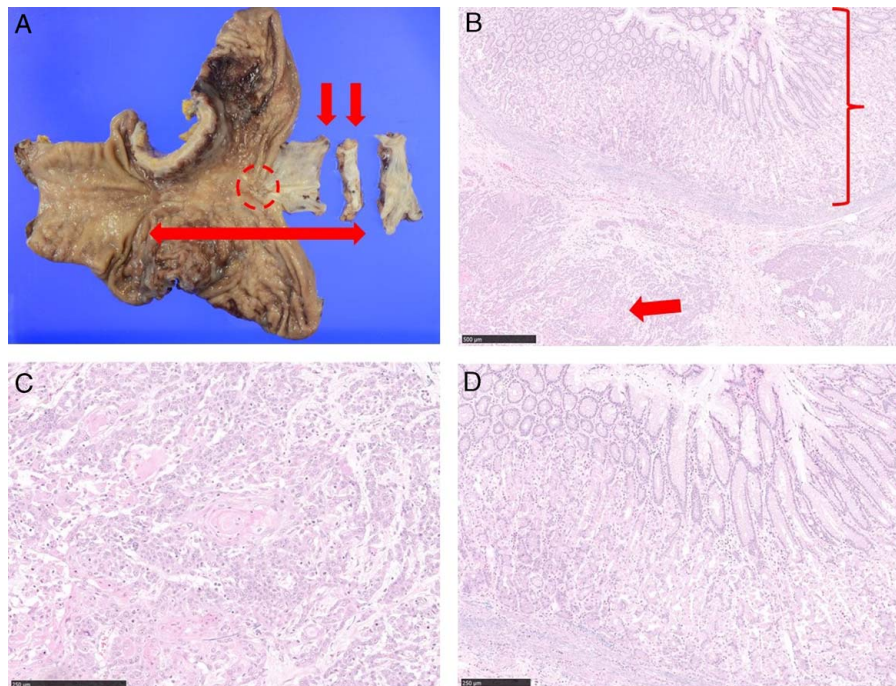
(UICC) 8th edition). She received two courses of cisplatin plus 5-fluorouracil (FP) as neoadjuvant chemotherapy. After this neoadjuvant chemotherapy, the serum cytokeratin 19 fragments 21-1 and squamous cell carcinoma antigen level improved to within the normal range. CT showed that the enlarged lymph nodes shrunk. Esophago-

gastroduodenoscopy showed a partial response at the primary lesion; however, there was diffuse thickening of the stomach wall and its distensibility was poor (Fig. 1B). Gastrography also showed poor distensibility of the stomach wall. Enhanced CT showed diffuse enhancement of the stomach wall (Fig. 2A), and positron emission tomography showed extensive uptake in



**Figure 2.** (A) Enhanced computed tomography showed diffuse enhancement of the stomach wall after neoadjuvant chemotherapy. (B) Positron emission tomography showed extensive uptake in the stomach [maximum standardized uptake value (SUVmax) = 4.79] after neoadjuvant chemotherapy. (C) In staging laparoscopy, there were no apparent changes in the serous membrane of the stomach, but peritoneal lavage cytology revealed squamous cell carcinoma.





**Figure 3.** Pathological findings. (A) The tumor was 115 × 85 mm. Areas of importance are indicated as follows: primary lesion (O); range of the tumor (⇔); and the surgical margin (→), which was positive twice. (b) Squamous cell carcinoma showed diffuse submucosal invasion in the stomach (→) and (C), while the mucosa of the stomach was almost normal (D). Scale bars: 500 μm in (B) and 250 μm in (C) and (D) (hematoxylin and eosin).

the stomach [maximum standardized uptake value (SUVmax)=4.79, Fig. 2B] and in the primary lesion (SUVmax=4.65). The patient was suspected of having two types of cancer, namely, esophageal cancer and scirrhous gastric cancer. We performed multiple biopsies for gastric lesions, including boring biopsy, which revealed no evidence of malignancy. We decided to perform staging laparoscopy to diagnose and determine whether radical resection was possible. In staging laparoscopy, there were no apparent changes in the serous membrane of the stomach (Fig. 2C), but peritoneal lavage cytology revealed squamous cell carcinoma. Thus, we diagnosed the patient with squamous cell carcinoma of the esophagus with diffuse invasion of the stomach. The final diagnosis was stage IV squamous cell carcinoma of the esophagus. There were no noncurative factors other than positive cytology, and the primary focus was esophageal stenosis; therefore, we decided to perform surgery to resect the primary lesion. We chose laparoscopic transhiatal esophagectomy and total gastrectomy. Pathological diagnosis during surgery revealed greater diffuse invasion of the oral esophagus than we expected. Although additional resection was performed laparoscopically, negative margins could not be secured. We added a thoracoscopic operation and resected the middle thoracic esophagus at the level at which there was no malignancy. We anastomosed the esophagus and the jejunum in the middle mediastinum. Pathological findings revealed that the tumor was 115 × 85 mm, T3 regarding the TNM classification, diffuse submucosal invasion of the squamous cell carcinoma in the stomach, and tumor cells in only a small area in the mucous membrane (Fig. 3). There were 30/106 metastatic lymph nodes, with positive nodes mainly in the gastric area, and no metastatic lymph nodes in the lower or middle

mediastinum. The postoperative course was good, and the patient was discharged 12 days after the surgery. Unfortunately, 19 days after surgery, late-onset anastomotic leakage occurred, and she underwent emergency drainage of the thoracic cavity and enterostomy. She recovered after the emergency surgery, and she started chemotherapy (docetaxel monotherapy) 71 days after the initial surgery. She underwent 10 courses of docetaxel monotherapy; however, 9 months after the surgery, metastatic lymph nodes appeared in the anterior and upper mediastinum. She underwent another course of chemotherapy (TS-1) with concurrent radiotherapy in the area (60 Gy/30 Fr). While the patient achieved a partial response to treatment for 6 months, she gradually declined and died 20 months after the initial diagnosis.

## Discussion

Diffusely infiltrative squamous cell carcinoma of the esophagus is rare and difficult to diagnose<sup>[1,2]</sup>. We reported a rare case of diffusely infiltrative squamous cell carcinoma of the esophagus that resembled scirrhous gastric cancer. Peritoneal lavage cytology was useful for proper diagnosis.

Only a few reports have been published on diffusely infiltrative squamous cell carcinoma of the esophagus, all from Japan<sup>[1–3]</sup>. In Japan, almost all cases of esophageal cancer are cases of squamous cell carcinoma; in contrast, in Western countries, cases of esophageal cancer mainly consist of adenocarcinoma. A few case reports have been published on diffusely infiltrative adenocarcinoma of the esophagus<sup>[5,6]</sup>, but the present study is the first to report diffusely infiltrative squamous cell carcinoma of the esophagus that resembled scirrhous gastric cancer.

In this case, peritoneal lavage cytology was helpful for diagnosis. In general, diffusely infiltrative carcinoma is difficult to diagnose<sup>[2]</sup>. We initially diagnosed the patient with squamous cell carcinoma of the esophagus, but we were not able to diagnose the stomach lesion even after multiple biopsies, including boring biopsy. Pathology revealed diffuse submucosal invasion of squamous cell carcinoma in the stomach, with tumor cells present only in a small area in the mucous membrane, leading to the difficulty in diagnosing the case from biopsy results. Similar difficulty occurs in scirrhous gastric cancer, and in such cases, peritoneal lavage cytology has been reported to be useful for diagnosis<sup>[7]</sup>. In this case, peritoneal lavage cytology led to the correct diagnosis; thus, peritoneal lavage cytology may be useful for diagnosing not only scirrhous gastric cancer but also diffusely infiltrative squamous cell carcinoma of the esophagus.

The treatment of esophageal cancer with positive cytology is controversial. In some cases of esophageal cancer, peritoneal lavage cytology may be positive<sup>[8]</sup>. Peritoneal lavage cytology for esophagogastric adenocarcinoma has been reported to be useful<sup>[9]</sup>. However, in clinical practice, peritoneal lavage cytology is not generally performed in cases of esophageal cancer. Thus, there is no consensus about the best treatment for esophageal carcinoma with positive cytology. In this case, we considered three treatment options: palliative treatment, such as stent placement and chemotherapy; surgical resection of the primary lesion; and radical treatment, including lymph node dissection in the upper mediastinum. As there was a positive cytology without any other noncurative factors, we chose laparoscopic transhiatal esophagectomy and total gastrectomy, which is a less invasive method than radical methods, such as lymph node dissection in the upper mediastinum. Some reports have shown that the transhiatal approach reduces pulmonary complications<sup>[10,11]</sup>. In this case, the tumor showed more diffuse invasion of the oral esophagus than we expected before the surgery, and we had to add thoracoscopic surgery; however, we were eventually able to complete minimally invasive surgery rather than thoracotomy. Accurate preoperative evaluation of the range of diffusely infiltrative squamous cell carcinoma is challenging. Therefore, it is important to confirm negative esophageal margins by intraoperative frozen section for diffusely infiltrative squamous cell carcinoma.

The prognosis for diffusely infiltrative squamous cell carcinoma of the esophagus is poor. Among 12 reported cases, only 33% (4 cases) of patients survived more than 1 year<sup>[1–3]</sup>. The average overall survival was 11 months (0–27 months). In the present case, the patient underwent surgery, chemotherapy, and radiotherapy, surviving for 20 months after the initial diagnosis. This duration of survival is longer than previously reported, but there remains room for further improvement. Unfortunately, the patient was not able to undergo early chemotherapy due to late-onset anastomotic leakage. The anastomotic leakage may have occurred due to neoadjuvant chemotherapy and anastomosis in the thoracic cavity. Additionally, the patient was not able to eat a full meal before the surgery; thus, we should have performed enterostomy at the initial surgery, which might have prevented anastomotic leakage and allowed earlier chemotherapy. Moreover, we used FP for neoadjuvant chemotherapy according to the result of Japan Clinical Oncology Group (JCOG) 9907<sup>[12]</sup>. Although the primary lesion and lymph nodes shrank in the patient during FP treatment, changes occurred in the stomach, and the response indicated disease progression. Other treatment options may have been more successful. The combination of neoadjuvant chemotherapy and radiotherapy is one choice that has been reported to be useful<sup>[13,14]</sup> and is widely used

in Western countries. A randomized controlled phase III trial (JCOG1109) showed that docetaxel and cisplatin plus 5-fluorouracil significantly improved overall survival over FP as neoadjuvant therapy for locally advanced squamous cell carcinoma of the esophagus<sup>[15,16]</sup>. Furthermore, nivolumab is now available as a treatment for recurrence<sup>[17,18]</sup>. Such treatments may improve the prognosis of diffusely infiltrative squamous cell carcinoma of the esophagus, and we should continue pursuing the best treatment.

## Conclusion

We reported a rare case of diffusely infiltrative squamous cell carcinoma of the esophagus that resembled scirrhous gastric cancer. The accurate diagnosis of this disease is difficult, but peritoneal lavage cytology may be useful. The treatment strategy should be determined based on the assumption that accurate preoperative evaluation of the range of diffusely infiltrative squamous cell carcinoma will be difficult.

## Ethical approval

None.

## Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

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## Author contribution

The manuscript was mainly written by H.A. and edited by H.K. and J.T. H.K., H.A., Y.H., A.S., and A.I. managed and followed up with the patients. JM, TY, and MK contributed to data collection. All authors read and approved the final manuscript.

## Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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