Curative resection of advanced esophageal cancer with metachronous stage IV breast cancer: A case report

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ABSTRACT
INTRODUCTION: Recent studies have shown the safety and efficacy of curative resection of esophageal cancer with multiple primary cancers. However, our literature search revealed no curative surgery cases for esophageal cancer in patients with multiple primary cancers with distant metastasis.

CASE PRESENTATION: A 75-year-old woman visited our hospital with dysphagia. She had a history of breast cancer with multiple bone metastasis. Esophagastroduodenoscopy revealed a circumferential mass in the upper intrathoracic esophagus. Histopathological examination of the biopsy showed squamous cell carcinoma. Other imaging findings revealed multiple nodules in the liver. The nodules were thought to have originated from the breast, but metastasis of esophageal cancer was considered a possibility. Intraoperative frozen sections of the liver and peritoneal nodules showed adenocarcinoma. Thoracoscopic esophagectomy was then performed. Following surgery, the patient received fulvestrant therapy, followed by capecitabine therapy, and the liver tumors decreased in size. She is currently alive after 1.5 years of the surgery without local recurrence of esophageal cancer.

DISCUSSION: Although the patient had metastatic breast cancer, her relapse-free interval of 20 years and good response to hormone therapy for 15 years were favorable prognostic factors. Her life expectancy was estimated to be a few years and surgery was performed.

CONCLUSION: Curative resection could be considered for patients with esophageal cancer who have an additional cancer with distant metastasis when the prognosis of the additional cancer is not poor.

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1. Introduction
Recent studies have shown the safety and efficacy of curative resection of esophageal cancer associated with multiple primary cancers. Multiple primary cancers are observed in 20.2% of esophageal cancers, and breast cancer is observed in 2.3% of these cases [1]. Although metastatic breast cancer is not a curative condition, an improvement in the survival time has been reported. However, our literature search revealed no surgery cases for esophageal cancers with multiple primary cancers showing distant metastasis. This work has been reported in line with the SCARE criteria [2].

2. Case presentation
A 75-year-old woman visited our hospital due to dysphagia. She had a history of left breast cancer and had undergone mastectomy at the age of 38 years. At the age of 60 years, she had experienced a local recurrence of cancer and had undergone a left chest wall excision and prophylactic irradiation with a total dose of 50 Gy. At the age of 68 years, she had experienced multiple bone metastasis. Her breast cancer subtypes were ER and PgR-positive and HER2-negative. She had received aromatase inhibitor therapy. Esophagastroduodenoscopy (EGD) revealed a circumferential mass in the upper intrathoracic esophagus, 21–24 cm from the incisors (Fig. 1a). Esophagography revealed stenosis and wall irregularity in the upper intrathoracic esophagus (Fig. 1b).

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Histopathological examination of the biopsy showed squamous cell carcinoma. CT scans demonstrated swelling of the left recurrent nerve lymph node (#106recL) (Fig. 1c). PET-CT showed an uptake of 18F-fluorodeoxyglucose in the upper intrathoracic esophagus (maximum SUV of 11.9), vertebral bodies, pelvis, and ribs (maximum SUV of 2.5–3.2). Based on the findings of biopsy and CT, a clinical diagnosis of esophageal cancer [Ut, cT3N1(106recL) M0, cStage III] was made according to the eighth edition of the Union for International Cancer Control classification. Although the patient had metastatic breast cancer, her relapse-free interval of 20 years and good response to hormone therapy for 15 years were favorable prognostic factors. Her progression-free survival (PFS) was expected to be more favorable than the median PFS of advanced hormone-positive breast cancer [3], and her life expectancy was estimated to be a few years. The treatment plan included neoadjuvant chemotherapy (5-FU 800 mg/m² on days 1–5 and CDDP 80 mg/g/m² on day 1; two courses), followed by a thoracoscopic esophagectomy. She had difficulty in swallowing, and a nasogastric tube was inserted for nutrition. The evaluation of the primary lesion in the esophagus after chemotherapy using EGD and CT revealed a stable disease. PET-CT showed the fluorodeoxyglucose accumulation in the liver of segment III (maximum SUV of 4.3) (Fig. 2a). MRI revealed nodules in the liver of segment III (10 mm in diameter) and multiple small nodules (2–3 mm in diameter) in the liver (arrows). On examining previous PET-CT scans, we observed that the accumulation in the liver was present before neoadjuvant chemotherapy; however, liver metastasis was not observed on the follow-up examination of breast cancer. The multiple nodules in the liver were speculated to have originated from either breast or esophageal cancer metastasis. If the liver tumors had originated from the breast, we considered her prognosis not to be poor, because the metastatic liver tumor had not grown rapidly and aggressively, and several treatment options for her breast cancer were available. The treatment plan included partial resection of the liver and intraoperative frozen section, followed by laparoscopic esophagectomy. Macroscopic exploration of the abdomen revealed multiple small white nodules on the peritoneum and liver. Intraoperative frozen sections of the liver S4 and peritoneal nodules showed carcinoma. The histological type was more likely to be adenocarcinoma than squamous cell carcinoma. The possibility of poorly differentiated squamous cell carcinoma could not be eliminated, and a definitive diagnosis of metastatic lesion pended permanent section. Thoracoscopic esophagectomy with lymph node dissection was then performed. The reconstruction route was
posterior mediastinal because of the history of radiotherapy for breast cancer. Although the cytopathologic examination of pleural fluid was positive for malignant cells, no nodule was found macroscopically. The resected specimen showed a 30 × 20 mm lesion which could not be classified (Fig. 3a, b). Histopathological examination of the esophagus revealed well differentiated squamous cell carcinoma with invasion of the adventitia (Fig. 3c and d). The nodules on the peritoneum and liver of segment III were adenocarcinomas (Fig. 4a). Adenocarcinomas were also identified in regional lymph nodes of the esophagus, #106recL (Fig. 5a), #108, #110, #1, #2, and #7. On immunohistochemical examination, tumor cells in the liver, peritoneum, and 106recL lymph node were positive for ER and transcription factor GATA3, but negative for tumor protein p63 (Fig. 4b–d, 5b–d). The tumors were consistent with breast cancer metastasis. Final pathological diagnosis of the esophagus was pT3NoM0, G1, Stage IIA. The patient showed favorable progress following surgery and was discharged on the 11th postoperative day. Following surgery, the patient received fulvestrant therapy followed by capecitabine therapy, and the liver tumors decreased in size. No local recurrence of esophageal cancer has appeared 1.5 years after surgery.

3. Discussion

The patient course described in this report provides clinical suggestion. Curative surgery could be considered for patients with esophageal cancer who have multiple primary cancers with distant metastasis when the prognosis of additional cancer is not poor. Our literature search revealed no curative surgery case of esophageal cancer with synchronous or metachronous cancer with distant metastasis. A search of the last 30 years of our hospital records did not reveal such a case. However, several studies have reported that surgical resection can be safely performed in patients with esophageal cancer with multiple primary cancers, and no difference has been found in the overall survival or postoperative morbidity [4,5].

The patient had difficulty in swallowing because of stenosis. There was possibility of Complete response with chemoradiotherapy, but stenosis often remains after treatment. In this case, she had a strong wish for oral intake and intention to undergo surgery. In addition, good nutritional oral intake was beneficial for chemotherapy for breast cancer.

The prognosis of metastatic breast cancer depends on many factors. Median survival time according to subtypes has not been reported in literature. For example, a relapse-free interval of 2 years and hormone receptor positivity are favorable prognostic factors [6,7]. Liver metastasis is a poor prognostic factor compared with chest wall or bone metastasis [8]. In this case, the patient's relapse-free interval of 20 years and good response to hormone therapy for 15 years were favorable prognostic factors, while liver metastasis was a poor prognostic factor. However, liver tumors had not grown rapidly and aggressively, and several treatment options...
remained for treating her breast cancer. A recent study showed that median PFS of a hormone receptor-positive and locally advanced or metastatic breast cancer was 16.6 months in the fulvestrant group and 13.8 months in the anastrozole group [3]. Our patient's PFS was expected to be comparatively more favorable, and her life expectancy was estimated to be a few years.

4. Conclusion

Curative resection can be considered for esophageal cancer patients who have multiple primary cancers with distant metastasis.
Conflicts of interest
The authors declare that they have no competing interests.

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Ethical approval
Ethical approval has been exempted from our institution for this case report.

Consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author contribution
All authors conceived of the study and participated in its design and helped to draft the manuscript. TS checked and revised the manuscript. FF and HS supervised the work as pathologists. All authors read and approved the final manuscript.

Registration of research studies
This paper is a clinical report, no research involved.

Guarantor
Tadashi Sakurai and Takashi Kamei.

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