Metastatic Esophageal Tumors from Distant Primary Lesions: Report of Three Esophagectomies and Study of 1835 Autopsy Cases

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Three cases of esophagectomy for secondary esophageal carcinoma metastasized from the ovary, breast and lung are reported. Long-term survival, 14 and 4 years, after esophagectomy was achieved in two patients. The intervals between surgery for primary cancer and dysphagia onset in these two patients were 16 and 7 years, respectively. An aggressive surgical approach appears to be the therapeutic procedure of choice for metastatic esophageal carcinoma when the primary tumor growth rate is suspected to be slow. Autopsy data on 1835 cases revealed 112 (6.1%) had metastasis to the esophagus. The lung was the most common primary tumor-bearing organ and the diffusely infiltrative type was the most common esophageal tumor observed macroscopically which corresponded to the findings in our three patients. When an esophageal stricture with normal mucosa is encountered, a metastatic tumor must be taken into consideration.

Key words: esophageal cancer – ovarian cancer – breast cancer – lung cancer – secondary neoplasms

INTRODUCTION

Local treatment for metastatic lesions in the esophagus from other organs usually cannot be justified because such lesions are often manifestations of systemic disease or mediastinal carcinomatosis. Recently, however, surgical resection was reported to provide excellent palliative therapy and long survival (1,2). We have encountered three patients with secondary carcinomas of the esophagus among the 1475 with esophageal carcinomas operated upon in our Institute. In this report, we present three cases of esophagectomy for metastatic esophageal carcinoma and 1835 autopsy data and also review the literature to discuss treatment strategies for this disease.

CASE REPORTS

CASE 1

A 50-year-old woman was admitted with dysphagia of 3 months duration. Sixteen years earlier (1962) she had undergone bilateral salpingo-oophorectomy for ovarian malignancy. Detailed data concerning the histology and extent of her disease were not available. Following this surgery, radiation therapy was administered to the pelvic region. Roentgenograms of her esophagus taken on November 30, 1978, showed a 5 cm long stricture with a smooth surface in the lower thoracic esophagus (Fig. 1) and endoscopic examination revealed a severe stricture 29 cm from the incisors (Fig. 2). Examination of a biopsy specimen revealed a papillo-tubular adenocarcinoma. Radiation (3090 rad) and chemotherapy [750 mg of 1-(2-tetrahydrofuryl)-5-fluorouracil by suppository] were given preoperatively and on January 22, 1979, subtotal esophagectomy and esophagogastrostomy were performed through a right thoracotomy and an abdominal incision. The tumor had invaded a portion of the lung and the pericardium was excised with the esophagus. The tumor in the resected specimen was covered with normal esophageal mucosa. Histological examination revealed infiltration of the submucosal and deeper layers by cancer cells, but the overlying squamous epithelium was intact. The tumor was a serous papillotubular adenocarcinoma with psammoma bodies (Fig. 3), findings characteristic of ovarian cancer, suggesting that the tumor was a metastatic lesion from her previous ovarian cancer. Her postoperative course was uneventful, but in 1988, 10 years after esophagectomy, local recurrence of cancer invading the lung and bronchus was found in the mediastinum. This recurrent tumor together with the pericardium and left atrium were excised by a right pneumonectomy. The histological appearance of this tumor...
Figure 1. Barium esophagram showing a 5 cm long stricture with a smooth surface in the lower thoracic esophagus of case 1.

was basically the same as that of the esophageal tumor. The patient died of recurrent disease on March 1, 1993, 14 years after esophagectomy.

CASE 2

A 56-year-old woman underwent left radical mastectomy for carcinoma of the breast in May 1978. Tumor stage at the time of surgery was pT3N0M0, stage IIb (3). She remained well until February 1985, when she became unable to swallow solid foods. A barium swallow revealed a mild stricture with a smooth surface in the lower thoracic esophagus and endoscopic examination revealed a protruding tumor covered with normal esophageal mucosa 34 cm from the incisors. Despite examination of multiple biopsy specimens endoscopically, only normal squamous epithelium without tumor cells was found. In May 1985, she underwent esophagectomy via a thoracotomy and a median laparotomy incision. One involved lymph node had invaded the thoracic aorta and lower lobe of the right lung. Although the lower lobe of the right lung was partially resected, some tumor was left in the wall of the thoracic aorta. The tumor in the resected specimen was covered with smooth normal mucosa and histological examination revealed adenocarcinoma cells in the submucosal and muscular layers (Fig. 4). The histological pattern of the tumor was similar to that of the ductal carcinoma of the breast which had been removed 7 years earlier (Fig. 4, c). These findings suggested that the tumor was a metastatic lesion from her previous breast cancer. Following the operation she received chemotherapy with adriamycin (60 mg, intravenously, every 4 weeks, total dose 720 mg), cyclophosphamide (100 mg/day, orally, for 2 out of every 3 weeks, for 2 years) and tamoxifen citrate (20 mg/day, orally). She continued to improve and did well for 4 years until June 1989, when she was readmitted with dyspnea. She was found to have developed lymphangitic pulmonary metastases and later died.
CASE 3

A 65-year-old man was admitted with dysphagia in November 1981. No pulmonary symptoms were noted and chest X-ray findings on admission were interpreted as unremarkable. A barium swallow demonstrated marked constriction of the middle esophagus and esophagoscopy revealed a severe circumferential esophageal stricture with apparently normal mucosa 35 cm from the incisors. A two-staged operation was planned because of the patient’s past history of cerebral thrombosis with right hemiplegia. On November 30, 1981, he underwent thoracotomy and esophagectomy and cervical esophagostomy were carried out, during which, a tumor mass, measuring $3.0 \times 3.0$ cm, was noted at the base of the middle lobe of the right lung. Esophageal reconstruction with a gastric tube placed in the subcutaneous space was performed 2 months later. A postoperative chest X-ray showed a tumor shadow in the right lower lung field. The epithelial surface of the esophagus in the resected specimen appeared smooth and was stained with Lugol’s solution, providing evidence the mucosa was normal (4,5). Histological examination revealed that the tumor was in the muscle layer and infiltrating the submucosal and deeper layers, but the overlying squamous epithelium was intact. The histological type of the tumor was a poorly differentiated adenocarcinoma (Fig. 5), suggesting it was a metastatic lesion from a lung cancer, although no histological specimen of the pulmonary tumor was obtained. The patient died 231 days after surgery. Permission to conduct an autopsy was not granted.

AUTOPSY SERIES

A total of 1835 autopsies on patients who died of carcinomas at the National Cancer Center Hospital, Tokyo (NCCH), from January 1, 1979, through December 31, 1988, were reviewed. Of these autopsied patients, 161 had double cancers and 14 had triple cancers, giving a total of 2024 cancers in this series. In each autopsy case, two sections were sampled from the autopsied esophagus on average and we confirmed the esophageal sampling from all the autopsy cases. We defined esophageal metastasis as hematogenous or lymphatic metastasis from distant primary lesions. When an esophageal tumor was directly contiguous with
a regional lymph node metastasis, we judged it to be lymphatic metastasis to the esophagus. Metastases to the esophagus were found in 112 patients, an incidence of 6.1% (112/1835). The lung was the most common primary tumor-bearing organ associated with esophageal involvement. Fifty-one of 450 primary tumors of the lung (11.3%) showed metastasis to the esophagus without direct extension (Table 1). The most common histological cell type of primary lung cancer was adenocarcinoma (32/212, 15.1%), followed by small cell carcinoma (8/82, 9.8%), squamous cell carcinoma (8/99, 8.1%), large cell carcinoma (3/46, 6.5%) and others (0/11). The incidences of metastases to the esophagus from breast and ovarian cancers were 7.4% (14/188) and 2.5% (1/40), respectively (Table 1). The most common macroscopic type (6) observed on the esophagrams of the 112 patients with metastases to the esophagus was the diffusely infiltrative type (17.9%), followed by the protruding (9.8%) and ulcerative types (4.5%) (Table 2) and cancer cells in these tumors were located chiefly in the subepithelial layer. No macroscopic abnormalities were apparent in 76 cases (67.8%) and the metastases were only detected microscopically.

Table 1. Incidence of metastasis to the esophagus in autopsy cases (1979–88, National Cancer Center Hospital, Tokyo)

<table>
<thead>
<tr>
<th>Primary malignant tumor</th>
<th>No. of cases</th>
<th>Metastasis to the esophagus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>450</td>
<td>51 (34)* 11.3</td>
</tr>
<tr>
<td>Breast</td>
<td>188</td>
<td>14 (10) 7.4</td>
</tr>
<tr>
<td>Stomach</td>
<td>326</td>
<td>13 (9) 4.0</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>117</td>
<td>8 (5) 6.8</td>
</tr>
<tr>
<td>Tongue</td>
<td>51</td>
<td>5 (2) 9.8</td>
</tr>
<tr>
<td>Liver</td>
<td>170</td>
<td>4 (3) 2.4</td>
</tr>
<tr>
<td>Ovary</td>
<td>40</td>
<td>1 (1) 2.5</td>
</tr>
<tr>
<td>Others</td>
<td>682</td>
<td>16 (12) 2.3</td>
</tr>
<tr>
<td>Total</td>
<td>2024</td>
<td>112 (76) 5.5</td>
</tr>
</tbody>
</table>

*Figures in parentheses are the number of cases with microscopic metastasis.

Table 2. Macroscopic type observed on the esophagrams

<table>
<thead>
<tr>
<th>Type</th>
<th>No. of autopsy cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffusely infiltrative</td>
<td>20</td>
<td>17.9</td>
</tr>
<tr>
<td>Protruding</td>
<td>11</td>
<td>9.8</td>
</tr>
<tr>
<td>Ulcerative</td>
<td>5</td>
<td>4.5</td>
</tr>
<tr>
<td>No MAD*</td>
<td>76</td>
<td>67.8</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>100</td>
</tr>
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</table>

*MAD = macroscopic abnormality detected.

DISCUSSION

Metastatic involvement of the esophagus from a distant primary lesion is rare. The incidence of metastatic esophageal tumors in patients undergoing esophagectomies at the NCCH was 0.2%, but our autopsy data showed that 6.1% of the patients had metastasis to the esophagus and in 67.8% of these, the metastatic tumors were detected only by microscopic examination. In autopsy series, the incidence of secondary esophageal involvement by a variety of primary neoplasms has been reported to range from 0.3 to 3.2% (7–9). Therefore, in comparison with these reports, the incidence of metastasis to the esophagus in our series is relatively high.

Since the first reported case of metastatic esophageal carcinoma from the prostate by Gross and Freedman in 1942 (10), a wide variety of tumors from various organs, such as the breast, larynx, thyroid, hypopharynx, stomach and others, have been reported (11–13). Our autopsy data indicated that the lung is the most common organ with a primary tumor that results in esophageal involvement. In case 3, who had esophageal metastasis from a lung tumor, no pulmonary symptoms and no remarkable chest X-ray findings were noted on admission. Therefore, when the primary tumor is not detected, a further work-up of the lung is necessary.

Metastatic esophageal carcinomas usually pose a diagnostic challenge because, at times, they are indistinguishable from primary esophageal carcinomas. In all three of our patients esophagoscopy showed a stricture with normal mucosa, which was the most common macroscopic feature in the autopsy study. Therefore, this esophagoscopy finding would appear to be a characteristic feature of metastatic esophageal carcinomas. In two of our three patients, the endoscopic biopsy specimens were negative for tumor. When an esophageal stricture with normal mucosa is encountered, a metastatic tumor must be taken into consideration, especially when the patient has a past history of malignant tumor. In addition, barium esophagography makes an important contribution to the correct diagnosis in these cases (14). On barium swallow, a smooth concentric esophageal stricture is often apparent.

As most patients with metastasis to the esophagus already have metastasis to other areas, the treatment of choice is usually chemotherapy and/or radiotherapy (13,15). Surgical resection has been performed for local control of the disease and has resulted in excellent palliation in patients with metastatic tumors from various primary tumors, such as breast cancer (1,16,17), malignant mixed Mullerian tumor of the uterus (2), lung cancer (18) and malignant melanoma (19). The placement of an esophageal prosthesis during the course of radiation therapy and/or chemotherapy is reported to be the treatment of choice for maintaining esophageal patency (20).

Kerr and Cadman reported that thoracic involvement was found in 44.5% of 357 ovarian cancer patients and that the mean time from the diagnosis of ovarian cancer to diagnosis of pulmonary metastasis was 9.3 months (21). No esophageal involvement was mentioned in their report, however. The prognosis for such patients is poor: only 5.6% of patients survived
for 5 years. Dauplat et al. (22) also reported poor prognoses for patients with distant metastasis from ovarian carcinoma; a median survival of 6 months for patients with pleural effusion and 8 months for those with parenchymal lung metastases. Therefore, our case 1 is atypical for ovarian cancer.

Metastases of breast cancer have been treated mainly by chemotherapy, radiotherapy and/or hormone therapy. However, good results with pulmonary metastatic resection (5 year survival rates of 40–50%) have been reported recently (23,24). The median disease-free interval between surgery for a primary breast tumor and the appearance of pulmonary metastases has been reported to be 2.2 years (25). Friedel et al. (26) indicated that one of the most significant prognostic factors for beneficial resection of pulmonary metastases of breast cancer was the disease-free interval. In our cases 1 and 2, the intervals between surgery for primary cancer and dysphagia onset were 16 and 7 years, respectively, and therefore the primary tumors were considered to be slow growing. In these patients surgical resection yielded satisfactory palliation and long-term survival, especially in case 1, who lived for 14 years after esophagectomy.

On the basis of the findings in our patients, an aggressive surgical approach appears to be the therapeutic procedure of choice for metastatic esophageal carcinoma when the primary tumor growth rate is suspected to be slow. Of course, the decision to resect such metastatic lesions should only be made after careful and prudent evaluation to ensure clinical benefit to the patients.

References