True Carcinosarcoma of the Esophagus: Report of a Case

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Key Words

True carcinosarcoma of the esophagus · Immunohistochemical staining · Minimally invasive surgery

Abstract

Carcinosarcoma of the esophagus is a malignant neoplasm involving both carcinomatous and sarcomatous components. We report a patient with true esophageal carcinosarcoma who underwent laparoscopy-assisted surgery. An upper gastrointestinal barium study revealed a lobulated intraluminal filling defect in the lower intrathoracic esophagus. The patient underwent esophagectomy and regional lymphadenectomy with gastric tube reconstruction by laparoscopy-assisted surgery and thoracotomy. The esophageal hiatus was entered and the mediastinal esophagus was dissected using a laparoscopic approach. Microscopically, the tumor comprised poorly differentiated squamous cell carcinoma and spindle-shaped cells resembling leiomyosarcoma. Immunohistochemically, spindle-shaped sarcomatous cells displayed strongly positive reaction to vimentin and negative reaction to cytokeratin AE1/AE3 and CD68. No transitional zone was seen between sarcomatous and carcinomatous elements. The patient was finally diagnosed with true esophageal carcinosarcoma. Laparoscopic transhiatal esophagectomy seems to be a rational and safe procedure for lower esophageal neoplasms, even for patients with impaired respiratory function.

Introduction

Carcinosarcoma of the esophagus is a very rare malignant neoplasm comprising both carcinomatous and sarcomatous components. The oncogenesis of carcinosarcoma remains unclear. To date, a metaplastic concept and a collision concept have been

proposed. The former involves individual elements derived from a single common ancestor cell (so-called carcinosarcoma), while the latter involves two individual stem cells independently and simultaneously undergoing malignant transformation (true carcinosarcoma). According to a literature search using PubMed for 1981–2007, most reports detailed so-called carcinosarcoma, while reports of true carcinosarcoma were very rare. Partial or total esophagectomy with regional lymph node dissection was usually performed for esophageal carcinosarcoma [1–3]. Among 87 cases of carcinosarcoma described in the literature, 83 patients (95.4%) underwent surgical resection, 3 patients (3.4%) underwent local excision and 1 patient underwent endoscopic resection. Involvement of regional lymph nodes was seen in 31 of 59 patients (52.5%) [1]. In terms of prognosis, 5-year survival rates following treatment appear to be similar to those reported for squamous cell carcinomas [1, 2]. Although 3-year survival is higher for carcinosarcoma (62.8%) than for squamous cell carcinoma (28.1%), no significant difference in 5-year survival is apparent between the groups (26.7 vs. 22.4%). Prognosis is thus not as favorable as previously believed due to the high possibility of hematogenous metastasis in the late period [2]. Sanada et al. [4] reported that liver metastasis and peritoneal dissemination typically accompany sarcomatous components.

We report herein a case of true esophageal carcinosarcoma and discuss the characteristics of this disease with reference to the literature.

Case Report

A 79-year-old man was admitted to our hospital with complaints of dysphagia. He had undergone percutaneous transluminal coronary angioplasty for coronary atherosclerosis 2 years earlier. Upper gastrointestinal studies and gastrointestinal fiberoscopy revealed a lobulated intraluminal filling defect 6.5 cm long in the lower intrathoracic esophagus (fig. 1). The tumor surface was relatively smooth and esophageal compliance was maintained. Enhanced computed tomography showed a tumor in the lower intrathoracic esophagus (fig. 2), but no metastatic lesions including lymph node metastases were observed. Emphysematous changes and old tuberculosis were observed in both lungs. Endoscopic examination showed a polypoid, lobulated lesion in the lower intrathoracic esophagus. A biopsy specimen showed a tumor comprising squamous cell carcinoma with spindle cell components. Respiratory function testing showed that vital capacity was 4,090 ml, but forced expiratory volume in 1 s was 49.3%, indicating an obstructive ventilatory defect. Tumor markers were within normal limits, as follows: carcinoembryonic antigen, 2.7 ng/ml; squamous cell carcinoma-related antigen, 1.4 ng/ml.

Surgery was performed after obtaining informed consent. After preparation of isolated pulmonary ventilation during thoracic surgery, the patient was placed in the left half side lying position, and 5 trocars were introduced, including 1 trocar for laparoscopy via the navel. After exploration of the peritoneal cavity, the greater curvature was mobilized by dissecting the greater omentum from the transverse colon using Ligasure and Autosonix. The left gastric vessels were ligated at their origin, allowing en bloc lymphadenectomy. Mobilization of the greater curvature was continued from distal to proximal while the right gastric and gastroepiploic arteries were preserved. Both crura of the diaphragm were incised for loose passage of the gastric tube. The esophageal hiatus was entered and the esophagus was dissected cranially by laparoscopic surgery. After confirming that the gastric tube could be easily raised to the thoracic cavity once abdominal procedures were finished, esophagectomy and mediastinal dissection with lymph node dissection were performed through a right thoracotomy under isolated pulmonary ventilation at the fifth intercostal thoracotomy. Esophagogastric anastomosis was performed mechanically above the level of the azygos vein, using a circular stapling device with a 2-cm free margin.

Macroscopically, the resected tumor from the lower intrathoracic esophagus manifested as a lobulated polypoid lesion with a broad base and submucosal thickening of the esophageal wall. Histopathologically (fig. 3), the tumor showed permeation into the submucosal layer and consisted of poorly differentiated squamous cell carcinoma and a spindle cell sarcoma component (fig. 3a, b). Sarcomatous cells were arranged in broad, polygonal fascicles and displayed bizarre nuclei with abundant mitoses. Immunohistochemically, sarcoma components displayed strong positive results for vimentin, but negative results for cytokeratin AE1/AE3 (fig. 3c, d). Conversely the squamous cell carcinoma component showed positive results for cytokeratin, but not for vimentin. CD68 staining was

negative. Ki-67 (MIB-1) labeling index was high ($\geq 25\%$) in both components (fig. 3e). No transitional zone was seen between these components (fig. 3a–d). The tumor was finally defined as esophageal true carcinosarcoma. No evidence of metastasis was seen in the adjacent lymph nodes. It was finally diagnosed as an esophageal true carcinosarcoma.

The patient was discharged after an uneventful postoperative course and is now doing well as an outpatient at 9 months follow-up.

Discussion

Esophageal carcinosarcoma has recently been reported to account for only 0.5–2.4% of all esophageal tumors [2, 5] and has been classified as: (1) so-called carcinosarcoma; (2) pseudosarcoma; (3) true carcinosarcoma [6]. Most reported cases have involved so-called carcinosarcoma containing a transitional zone of carcinomatous and sarcomatous components. Immunohistochemical staining seems necessary to distinguish these lesions from true carcinosarcoma.

In this case, squamous cell components were positive for cytokeratin AE1/AE3. In contrast, spindle-shaped tumor cells were positive for vimentin, a marker of mesenchymal components. No transitional zone was seen, and the patient was finally diagnosed with true carcinosarcoma.

Some hypotheses have been nominated for the outbreak of carcinosarcoma, including: (1) stem cell origin theory, with tumor stem cells differentiating toward epithelial neoplasm and mesenchymal metaplasia; (2) tumor collision theory, with neoplasm derived from the collision of two distinct neoplasms, epithelial and mesenchymal in origin; (3) epithelial tumor theory, with a mesenchymal component that is nonneoplastic in origin, instead representing a reactive process to the presence of the epithelial neoplasm [7].

Oncogenesis is not completely elucidated, but some immunohistological reports using an electron microscope have indicated point mutation in a p53 gene. Iwaya et al. [3] reported that only sarcomatous cells were positive for p53, while Ohtaka et al. [8] reported both components as positive for p53. Histological features in the carcinomatous component have variously been described as squamous cell carcinoma or adenocarcinoma [8]. Conversely, sarcomatous components have also been reported as leiomyosarcoma, rhabdomyosarcoma, osteosarcoma [3, 9] or chondrosarcoma [9, 10].

Osamura et al. [11] reported the common origin of carcinomatous and sarcomatous components of these mixed tumors, noting that mesenchymal metaplasia of squamous cells, the nonreactive nature of sarcoma-like cells and the metastatic potential of these cells strongly support the theory that carcinosarcoma and pseudosarcoma represent a single pathological entity. Iascone and Barreca [1] reviewed 127 carcinosarcomas and 56 pseudosarcomas, showing that these neoplasms display similar clinical and behavioral outcomes.

More than 80% of carcinosarcomas are located in the middle and/or lower esophagus [2]. Macroscopically, carcinosarcomas were 75% polypoid type and 15% ulcerative type [2]. When sarcomatous components are predominant, macroscopic type is polypoid because of the few stromal ingredients. Likewise, when carcinomatous components are predominant, ulcerative type is usual.

Tumor invasion was limited to the esophageal wall in 80% of carcinosarcomas and 40.6% of squamous cell carcinomas. Depth of invasion was limited to the esophageal wall more often in the carcinosarcoma group than in the squamous cell carcinoma group [2].

Partial or total esophagectomy with regional lymph node dissection was usually performed for carcinosarcoma of the esophagus [1–3]. Among 87 carcinosarcoma patients, 83 patients (95.4%) underwent surgical resection, 3 patients (3.4%) underwent local excision and 1 patient underwent endoscopic resection. Involvement of regional lymph nodes was seen in 31 of 59 patients (52.5%) with carcinosarcoma [1].

McCort [12] concluded in his review that carcinosarcoma has a more favorable prognosis compared to squamous cell carcinoma. Xu et al. [13] reported that the carcinomatous component of the tumor is usually at an early stage at the time of diagnosis and the incidence of lymph node metastasis is thus low. However, 5-year survival rates following treatment resemble those reported for squamous cell carcinomas [1, 2]. At 5 years after surgery, only 9 of 55 patients (16.4%) were reported alive and free from disease or dead of unrelated causes [1]. Iyomasa et al. [2] compared 20 cases of carcinosarcoma with 773 cases of squamous cell carcinoma. Although the 3-year survival rate was higher for carcinosarcoma (62.8%) than for squamous cell carcinoma (28.1%), no significant difference in 5-year survival is apparent between the two groups (26.7 vs. 22.4%). The prognosis is not as favorable as previously believed, due to the high possibility of hematogenous metastasis in the late period. Sanada et al. [4] have reported that liver metastasis and peritoneal dissemination typically accompany sarcomatous components.

There were few reports of radiotherapy and chemotherapy. Iwaya et al. [3] reported that radiotherapy could not control tumor growth. Sanada et al. [4] reported that chemotherapy (docetaxel + 5FU) and radiotherapy (66 Gy) for 2 months achieved a reduction rate of 45% for the primary lesion.

Our patient underwent laparoscopy-assisted gastrectomy which contributed to dissection of the lower thoracic esophagus via the esophageal hiatus and which led to shortened duration of thoracic procedures under isolated ventilation. The postoperative course was uneventful and he is now doing well without recurrence. We encountered an extremely rare case of true esophageal carcinosarcoma.

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Fig. 1. Upper gastrointestinal barium study and gastrointestinal fiberscopy revealed a lobulated intraluminal filling defect of 6.5 cm in the lower intrathoracic esophagus.

Fig. 2. Enhanced computed tomography showing tumor in the lower intrathoracic esophagus.

Fig. 3. Histopathological findings for tumor. **a** Hematoxylin and eosin (HE) $\times 10$. **b** HE $\times 20$. **c** Cytokeratin AE1/AE3 stain. **d** Vimentin stain. **e** Ki-67 stain.

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