Esophageal Metastasis From Occult Lung Cancer

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A 66-year-old man with dysphagia was found to have a poorly differentiated esophageal carcinoma by incision biopsy. Following esophagectomy, reconstruction with a gastric tube was performed. Pathological examination and immunohistochemistry showed infiltration of adenocarcinoma cells with positive thyroid transcription factor 1-staining in the submucosal layer, which indicated metastatic esophageal carcinoma. Although no pulmonary lesion could be visualized by imaging or bronchoscopy, pulmonary origin was highly suspected as a result of positive thyroid transcription factor 1-staining. To the best of our knowledge, this is the first reported case of metastatic esophageal carcinoma from occult lung cancer (AJCC TNM stage TX). [*J Chin Med Assoc* 2010;73(6):327–330]

Key Words: esophageal surgery, lung cancer, metastasis

Introduction

Although the majority of secondary esophageal cancers are caused by direct invasion of tumors from nearby organs, metastatic esophageal carcinomas from distant primary malignancies, especially the lung, are relatively rare, and the optimal treatment remains unclear.[1] Here, we report a case of metastatic esophageal carcinoma with initial presentation of dysphagia. Although pulmonary origin was highly suspected by immunohistochemical staining, no definite lung lesion was detected by imaging studies, bronchoscopy and surgical exploration. To the best of our knowledge, metastatic esophageal carcinoma from occult lung cancer (AJCC TNM stage TX) is a very rare occurrence.

Case Report

A 66-year-old man was admitted to our hospital for progressive dysphagia and weight loss for 1 month. Physical examination and medical history were unremarkable. Esophagography showed eccentric narrowing of the middle third of the esophagus, with a smooth mucosal surface (Figure 1A). On esophagoscopy, external compression, with apparently normal overlying mucosa at 30 cm from the incisors, was noted. Biopsy revealed inflammation without malignant cells. Computed tomography (CT) (5-mm slice) demonstrated thickening of the esophageal wall and a mass lesion at the middle third of the esophagus (Figure 1B). No abnormal lesion was found in the bilateral lung fields. Laboratory data were unremarkable except for elevated carcinoembryonic antigen (CEA; 64.45 ng/mL) and carbohydrate antigen (CA) 19-9 (40.51 U/mL), which raised the possibility of malignancy. Both bronchoscopy and colonoscopy were performed to exclude bronchogenic and colorectal neoplasms.

Right-side muscle-sparing thoracotomy was carried out under the suspicion of esophageal cancer. One large mass lesion in the middle third of the esophagus was found, which was tightly adhered to the azygos vein, pericardium, aorta, bilateral main bronchus, and part of the lung. Incision biopsy of the mass was performed, and the frozen section showed poorly differentiated carcinoma. Therefore, the operation proceeded with subtotal esophagectomy, wedge resection of the adhered lung, reconstruction with a gastric tube via

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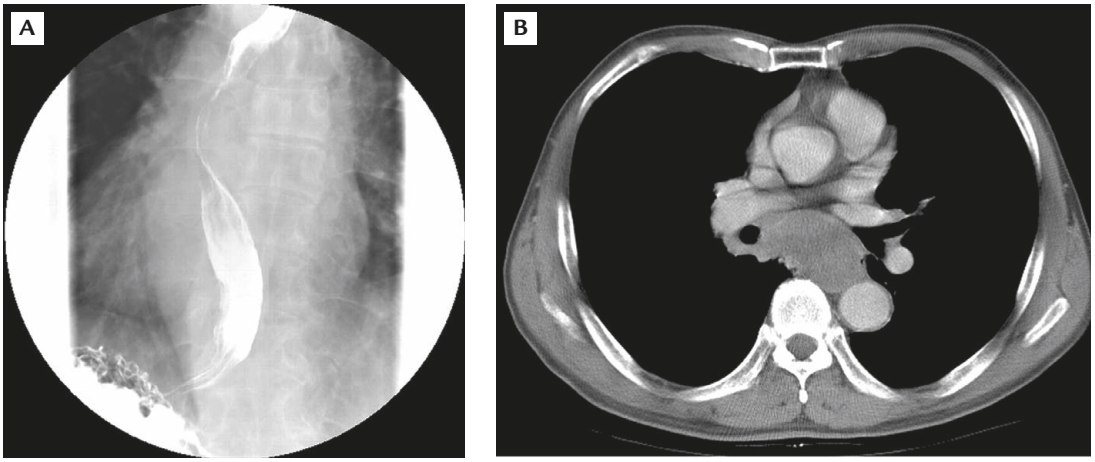

Figure 1. (A) Esophagography showed eccentric narrowing of the middle third of the esophagus, with a smooth mucosal surface. (B) Computed tomography of the chest demonstrated 1 mass lesion in the middle third of the esophagus, which occupied the subcarinal space.

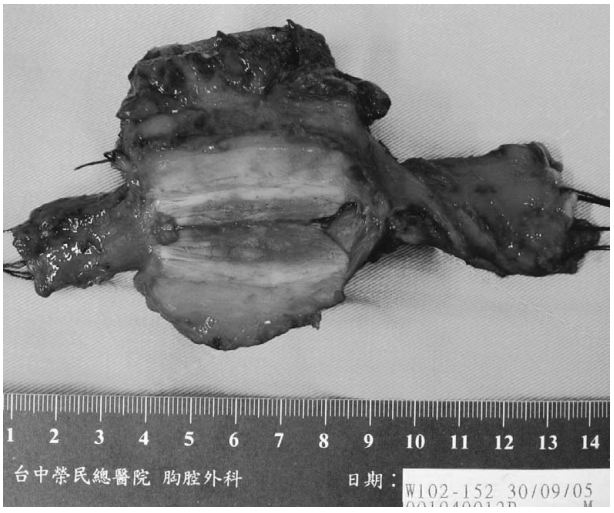

Figure 2. A specimen that consisted of *en bloc*-resected intrathoracic esophagus, including the tumor and lymph nodes. The esophageal mucosa was grossly intact.

the retrosternal route, and cervical esophagogastric anastomosis. Grossly, the esophageal tumor was firm, yellow, and 6 × 5 × 5 cm in size (Figure 2). No definite lesion was found in the nearby lung parenchyma. Microscopic examination revealed adenocarcinoma cells in the submucosal and muscular layers, with normal overlying mucosa (Figure 3A). Histological stains (PAS-D and mucicarmine) and immunohistochemical stains [pan cytokeratin AE1/AE3 and thyroid transcription factor 1 (TTF-1)] were positive (Figure 3B). Metastatic esophageal adenocarcinoma of pulmonary origin, which might be disseminated through a lymphatic or hematogenous route, was highly suspected. The tumor markers after resection showed marked decline (CEA, 27.79 ng/mL; CA19-9, 29.59 U/mL). The CEA level was 10.26 ng/mL 2 weeks after surgery. The patient's recovery was uneventful, and oral intake was well tolerated. He received adjuvant chemoradiation (gemcitabine and cisplatin) because of mediastinal lymph node involvement and possible residual tumor infiltration from outward growth. After 1 year of follow-up, there was no lung or endobronchial lesion by imaging and bronchoscopy. The tumor markers had all returned to their normal ranges.

Discussion

Secondary esophageal cancer usually occurs by 3 mechanisms. The most common mechanism is the direct extension of tumors from nearby organs.[1,2] The other 2 mechanisms include metastasis via the lymphatic system or the bloodstream from distant primary malignancies, which are relatively rare.[1,3] Mizobuchi et al reviewed a total of 1,835 autopsy reports on patients who had died of carcinoma. Metastases to the esophagus were found in 112 patients; an incidence of 6.1%.[3] However, less than one-third of these abnormalities could be macroscopically detected.[3] In another report of autopsy data on 423 cases of primary lung cancer, Antler and colleagues also found isolated esophageal metastasis in 6.4% of bronchogenic carcinoma patients.[4] Their study further showed that large-cell and small-cell carcinomas have the highest predilection for gastrointestinal metastases.[4]

Symptomatic metastatic esophageal carcinoma is extremely rare, and the presentation is usually progressive dysphagia.[1,2,4] Esophagography usually demonstrates esophageal narrowing, with a smooth mucosal surface, while CT usually depicts thickening of the esophageal wall over the stenosis.[1–3] The mechanisms

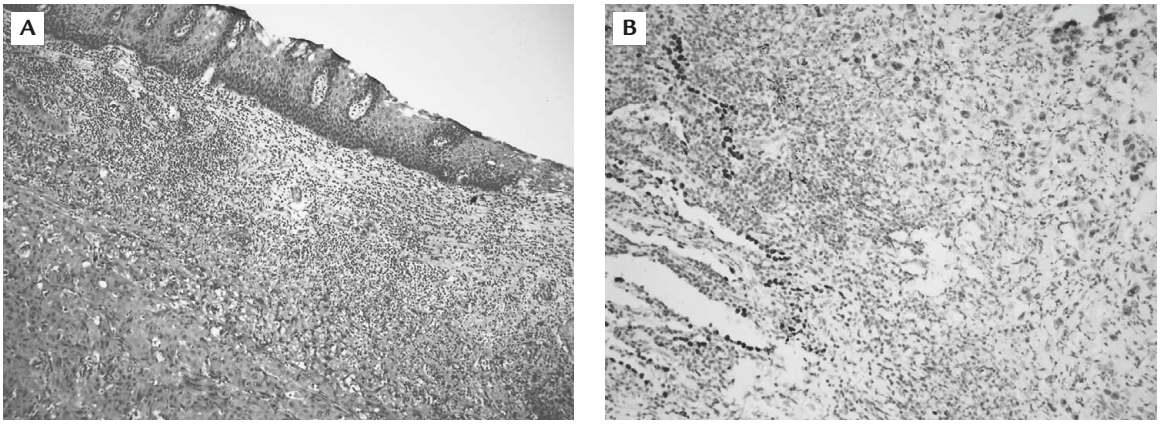

Figure 3. (A) Histological examination showing adenocarcinoma cells in the submucosal layer, with normal overlying squamous epithelium (original magnification, 100×). (B) Tumor cells (right half) were positive for thyroid transcription factor 1 staining. The nearby lung parenchyma (left half) served as a positive internal control (original magnification, 200×).

of lymphatic or bloodstream dissemination to the esophagus result in the submucosal location of the esophageal metastasis with normal overlying mucosa, which makes diagnosis by endoscopic biopsy difficult,[1] as in our case, in which the overlying mucosa was normal and accurate biopsy was not feasible. With the advent of positron emission tomography and endoscopic ultrasound, the biopsy of submucosal lesions under ultrasound guidance could potentially overcome the diagnostic challenge and help establish definitive diagnosis before surgical exploration, thus providing better options for some patients with inoperable tumors.[1]

Although many cancers, e.g. breast, kidney, gastrointestinal tract, lymphoid tissue, and prostate cancer, have been shown to metastasize to the esophagus, metastatic esophageal carcinoma from lung cancer has rarely been reported, and the optimal treatment remains unclear.[1] Most patients with metastasis to the esophagus are already in an advanced stage of disease. Therefore, many authors have advocated sequential dilation and/or stenting for local palliation, and chemotherapy and/or radiotherapy for systemic control.[1,3] The experience of surgical resection for metastatic esophageal carcinoma of pulmonary origin is limited. Inoshita et al reported the case of a 65-year-old man who presented with progressive dysphagia.[5] During surgery for the esophageal lesion, squamous cell carcinoma of the lung in the right lower lobe was incidentally discovered. The lung and esophageal lesions were resected simultaneously. In a report by Oka et al, a 54-year-old woman presented with dysphagia 5 years after left lower lobectomy and adjuvant chemotherapy for adenocarcinoma.[2] Resection of the esophagus was performed, and the histological patterns of the esophageal tumor were similar to those of primary lung cancer. In our case, the patient had no history of malignant tumor. Preoperative workup, including chest and abdominal CT, bronchoscopy and colonoscopy, found no abnormal lesion other than the esophageal mass. Manual palpation at exploratory thoracotomy and surgical specimens also showed no definite lung lesion. However, the results of immunohistochemical staining supported adenocarcinoma (PAS-D and mucicarmine positive) and epithelial origin (pan cytokeratin AE1/AE3 positive). Although the positive TTF-1 staining indicated lung or thyroid origin, the normal thyroid gland appearance on preoperative CT and elevated CEA level made the possibility of thyroid origin less likely. Furthermore, TTF-1 has sensitivity and specificity of 88% and 100%, respectively, in recognizing lung adenocarcinoma for determining the primary sites of metastatic cancer.[6] In a study that used TTF-1 for identification of carcinoma origin, pulmonary origin of metastases was confirmed in 27 of 37 cases with positive TTF-1 staining, whereas thyroid origin represented only a minority of cases.[7] Wedge resection of the adhered lung was performed in our patient, along with esophagectomy. Thus, there was a possibility that the primary tumor (such as bronchoalveolar carcinoma) might be in the specimen. In addition, the characteristic submucosal infiltration of tumor cells in the esophagus raises the possibility of metastatic lesions instead of direct invasion. Based on results of clinical examination and pathological immunohistochemical staining, metastatic esophageal carcinoma of pulmonary origin was highly suspected. To the best of our knowledge, this is the first reported case of metastatic esophageal carcinoma from an occult TX stage lung cancer. The patient received subtotal esophagectomy with reconstruction and postoperative adjuvant chemotherapy. So far, he has remained disease-free and asymptomatic.

In conclusion, we reported a case of metastatic esophageal carcinoma. Based on the results of clinical examination and immunohistochemical staining, pulmonary origin was highly suspected. Our experience suggested that, although chemotherapy is the rule of thumb for systemic control, esophagectomy in selected patients could provide excellent symptom palliation and local control.

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