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Surgical Resection of Thoracic Esophageal Cancer with Interstitial Lung Disease: A Case Report

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ABSTRACT

Patients with esophageal cancer often have various comorbidities, and these sometimes limit treatment choices. We describe a patient with stage IA esophageal cancer accompanied by interstitial lung disease (ILD). Endoscopic resection and radiotherapy were not appropriate because of clinically diagnosed submucosal invasion and the patient was at high risk of ILD exacerbation. We therefore selected transhiatal esophagectomy without a thoracotomy considering the risk of postoperative respiratory complications, and administered methylprednisolone and sivelestat in the perioperative period for the reduction of surgical stress. To our knowledge, this is the first report of surgical treatment for esophageal cancer with ILD. The patient was discharged without postoperative complications. Transhiatal esophagectomy is an appropriate choice for patients with early-stage esophageal cancer without lymph node metastasis who are at high risk for postoperative respiratory complications. The appropriate selection of treatment is important for patients with esophageal cancer considering the risk of complications.

Key words: *Transhiatal esophagectomy, Inflammatory diseases*

Interstitial lung disease (ILD) is a slowly progressive inflammatory disease that is associated with a poor prognosis because it frequently induces life-threatening complications such as respiratory and heart failure. Estimates indicate that many patients with esophageal cancer would develop comorbid ILD because esophageal squamous cell carcinoma and several types of ILD are closely associated with smoking. However, treatment for esophageal cancer with ILD has not been described in the literature and selecting the optimal treatment for such patients can be a source of considerable anguish because clear treatment guidelines are unavailable. Here, we describe a patient with esophageal cancer complicated with ILD that was successfully treated by surgery. To our knowledge, this is the first report of surgical treatment for esophageal cancer with ILD.

CASE REPORT

Gastrointestinal fiberscopy of a 72-year-old man who was referred to our institution revealed multiple esophageal tumors. Endoscopic ultrasound indicated that a mid-thoracic tumor extending over two-thirds of the esophageal circumference had invaded the submucosal layer and the pathological diagnosis of biopsy specimens was moderately differentiated squamous cell carcinoma (Fig. 1). The other three esophageal tumors were thought to be mucosal cancers. Computed tomography (CT) did not show either enlarged lymph nodes or distant

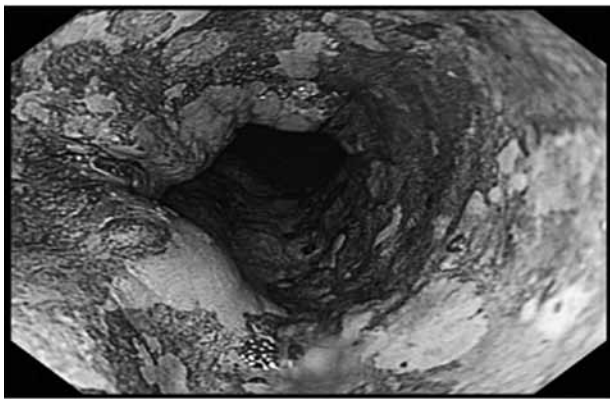

Fig. 1. Gastrointestinal fiberscopy of esophageal cancer. Tumor located 28 cm from incisors has extended over two-thirds of esophageal circumference. Submucosal invasion was suspected.

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metastasis. F-18-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) revealed abnormal tracer accumulation only in the mid-thoracic esophageal tumor with a maximum standard uptake value of 3.3. The levels of tumor markers such as squamous cell carcinoma (SCC)-related antigen were all within normal ranges. Based on these findings, stage IA esophageal cancer was clinically diagnosed according to the TNM Classification of Malignant Tumors 7th edition[19].

A medical history of ILD affected the treatment choice. The patient had attended a hospital with dyspnea upon physical exertion 18 months before esophageal cancer was identified. Chest X-ray and CT images revealed emphysema of the apex area and bilateral ground-glass and reticular opacities (Fig. 2A). Bronchoscopy revealed lymphocytosis in bronchoalveolar lavage fluid and blood chemistry findings showed significantly elevated levels of KL-6 (1030 U/mL). He was diagnosed with active interstitial lung disease, and was prescribed with prednisolone (10 mg/day). He had a smoking history of > 50 years, and stopped smoking upon receiving this diagnosis. The symptoms had almost completely disappeared and the KL-6 level had become normalized within six months, so the steroid medication was stopped at that time.

The KL-6 level was within the normal range, and the bilateral ground-glass and reticular opacities on CT images had improved but were still evident when the patient was diagnosed with esophageal cancer (Fig. 2B). His pulmonary function was within the normal value for %vital capacity (117%) and forced expiratory volume per 1s% (70.6%). However, the %diffusing capacity for carbon monoxide was very low (43.0%).

The esophageal cancers were multiple, and four lesions existed throughout thoracic esophagus. Furthermore, the mid-thoracic esophageal cancer occupied over two-thirds of the circumference and was thought to have invaded the deep submucosal layer. Overall, these esophageal cancers were not considered an indication for endoscopic resection in

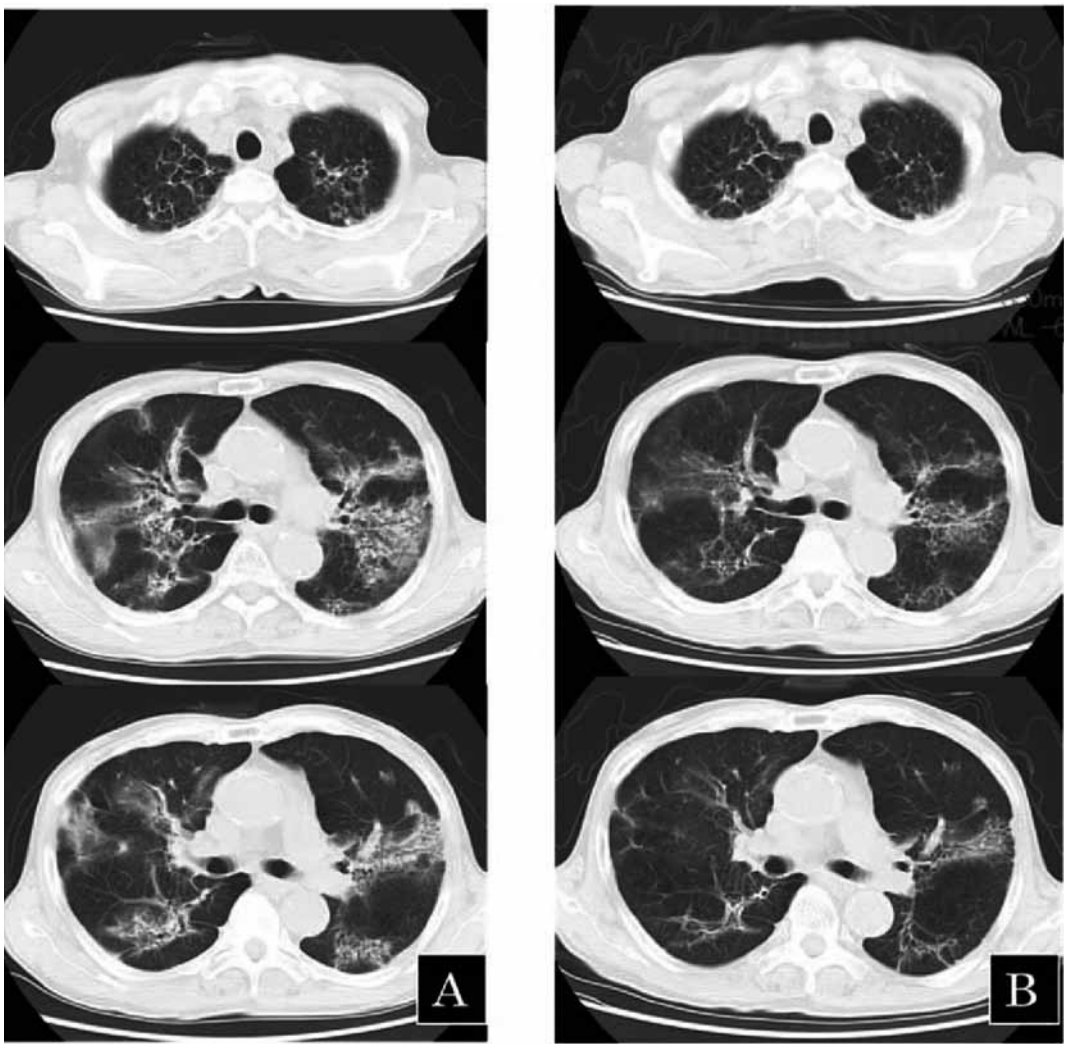

Fig. 2. Chest CT images.
(A) Bilateral ground-glass and reticular opacities 18 months before esophageal tumors were identified.
(B) Bilateral ground-glass and reticular opacities have improved but remain extant at the time of surgery.

view of curability and feasibility by a gastroenterologist. The radiologist also judged that radiotherapy would be incompatible because even minimal irradiation of the pulmonary parenchyma would exacerbate ILD.

We wavered in treatment choice, but it seemed that we had no other treatment choice but surgical resection. Therefore, we obtained the patient's informed consent after detailed explanation of the advantages and disadvantages of surgical therapy, and planned to surgically resect the esophageal tumors. We considered that a procedure via thoracotomy and one-lung ventilation would be very challenging for this patient, due to a high risk of postoperative respiratory complications such as ILD acute exacerbation. Therefore, he was treated with transhiatal esophagectomy (THE) without a thoracotomy. The operative duration was 210 min, and 130 g of blood was lost. The patient was administered with methylprednisolone (250 mg/body) at the start of surgery and sivelestat (300 mg/day) was administered from immediately after surgery until postoperative day (POD) 7. The postoperative course was good, and he was discharged on POD 25 without postoperative complications. Histopathological assessment showed that the esophageal tumor had slightly invaded the lymphatic vessels to the depth of the muscularis mucosa.

The metastasis of the left supraclavicular lymph nodes developed 5 months after esophagectomy, and we performed lymph node dissection followed by chemoradiotherapy. Thereafter, the patient was followed-up without treatment by another hospital. Although the patient died of bone metastasis at 3 years after the first operation, he resumed normal activities at home without exacerbation of ILD until then.

DISCUSSION

Interstitial lung disease is a heterogeneous entity with various clinical presentations. Several types of ILD such as idiopathic pulmonary fibrosis, respiratory bronchiolitis-associated interstitial lung disease, and desquamative interstitial pneumonia are associated with smoking[1]. A clinical evaluation of our patient could not result in a definite diagnosis. Smoking-related ILD was initially suspected because he was a heavy smoker and CT imaging had revealed emphysema. ILD is associated with a high risk of lung cancer[5,16], however the relationship between ILD and esophageal cancer is unclear.

Esophageal cancer combined with ILD poses a challenge in terms of cancer treatment, because therapeutic choices are limited. Radiation therapy is generally contraindicated for such patients, because it often acutely exacerbates ILD[6,21]. Several authors have also stated that thoracic surgery increases risk for patients with ILD. Some studies have investigated the surgical outcomes of lung cancer[3,9,11,22] or lung biopsies for ILD patients[10,18]. Reports indicate that ILD is a risk factor for developing postoperative morbidity, mortality and poor long-term survival. In particular, 13.5 - 25.0% of patients with lung cancer experienced acute exacerbation of ILD, and it induced acute lung injury and is often fatal. Postoperative mortality rate was reportedly 2.8% - 16.6%[3,9,22].

To our knowledge, the incidence of respiratory complications after resection of esophageal cancer with ILD has not been described. However, patients with esophageal cancer even without ILD often develop respiratory complications that sometimes induce acute lung injury[12,20]. Tandon et al investigated risk factors for acute lung injury after surgery for esophageal cancer. They reported that obesity, a history of smoking, the experience of the surgeon, the duration of both the operative procedure and of one-lung ventilation and the occurrence of postoperative anastomotic leak are risk factors for acute lung injury[20]. Surgical stress is generally considered to be associated with postoperative respiratory complications[12].

Indeed, several investigators have examined the application of drugs to suppress surgical stress. Administering corticosteroids before esophagectomy helps to prevent postoperative acute lung injury and respiratory failure[15,17]. The selective inhibitor of neutrophil elastase, sivelestat, should also help to reduce postoperative acute lung injury[14]. The perioperative administration of sivelestat helps to reduce postoperative hypoxia, suppresses postoperative hypercytokinemia, shortens the duration of systemic inflammatory response syndrome and improves postoperative respiratory function[8,13]. We routinely administer corticosteroids before starting esophagectomy and perioperatively administer sivelestat for patients at high risk of respiratory complications.

The surgical procedure is also important to reduce surgical stress. Transthoracic esophagectomy (TTE) with systematic lymphadenectomy is a standard procedure for treating thoracic esophageal cancer. On the other hand, THE, which comprises cervical and abdominal approaches, is thought to be limited by the impossibility of systematic mediastinal lymphadectomy[7]. Transhiatal esophagectomy is sometimes adopted to decrease postoperative risk because thoracotomy is not required. A meta-analysis of THE compared with TTE associated the former with a shorter surgical duration, significantly less respiratory complications and early postoperative mortality. Others have associated THE with a significantly shorter hospital stay[2,4].

Our patient had esophageal cancer with suspected deep submucosal layer invasion, but without evident lymph node metastasis upon clinical evaluation. However, he was considered to be at high risk for postoperative respiratory complications due to hav-

ing a history of corticosteroid-treated ILD and heavy smoking. Surgery with mediastinal lymphadenectomy via thoracotomy and one-lung ventilation for this patient was considered too invasive and likely to increase the risk of fatal adverse effects. Therefore, we prioritized the risk aversion of postoperative respiratory complications, and selected THE. The patient recovered safely without postoperative respiratory complications.

CONCLUSION

The optimal treatment for esophageal cancer with ILD is very difficult to determine. It needs more cases to establish a clear treatment choice. We selected surgical resection via a transhiatal approach with administration of methylprednisolone and sivelestat for the reduction of surgical stress, and the postoperative outcome was excellent. Therefore, THE is a useful option for patients with early-stage esophageal cancer without lymph node metastasis who are at high risk of postoperative respiratory complications. Appropriate treatment for esophageal cancer with respiratory comorbidities should be tailored to individual patients based on their current physical status and degree of disease progression.

Conflict of interest

The authors have no conflicts of interest to disclose.

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