**Case
Report**

Acute Exacerbation of Idiopathic Pulmonary Fibrosis of Microscopic Usual Interstitial Pneumonia Pattern after Lung Cancer Surgery

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A 78-year-old man underwent right lower lobectomy for lung cancer. Histopathological examination led to the diagnosis of adenosquamous cell carcinoma. The background lung adjacent to the pleura showed idiopathic pulmonary fibrosis of microscopic usual interstitial pneumonia pattern, although preoperative computed tomography showed no apparent findings of interstitial pneumonia. The patient showed an acute exacerbation of idiopathic pulmonary fibrosis on the third postoperative day. We herein report a case of acute exacerbation of idiopathic pulmonary fibrosis of microscopic usual interstitial pneumonia pattern after lung cancer surgery.

Keywords: lung cancer, surgery, idiopathic pulmonary fibrosis, usual interstitial pneumonia, acute exacerbation

Introduction

Acute exacerbation of idiopathic pulmonary fibrosis (IPF) of usual interstitial pneumonia (UIP) pattern is a concept that is currently recognized as a diffuse alveolar damage pattern on UIP.¹⁾ In spite of the absence of computed tomography (CT) findings of interstitial pneumonia, histopathological examination of the lung rarely reveals UIP pattern in some patients, and such UIP pattern is called microscopic UIP.²⁾ Recently, we encountered a patient who showed the acute exacerbation of microscopic UIP after lung cancer surgery, and herein report the case.

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Case Report

A 78-year-old man was found to have a mass shadow in the right lower lung field on a chest X-ray in July 2008. He had a history of pulmonary tuberculosis at the age of 20 and of smoking 10 cigarettes per day for 45 years, but stopped smoking at the age of 65. He had clear breath sound, and he was in good health except for the chief complaints described above.

Blood chemistry showed no abnormalities except for elevations in CEA (9.9 ng/ml; normal range, 0–5 ng/ml). Chest X-ray revealed a mass shadow in the right lower lung field and extensive signs of old tuberculous infiltration at the apex of both lungs (**Fig. 1A**). Chest CT revealed a 38-mm-diameter, irregularly-bordered tumor in the right S8 and a small shadow just adjacent to the dorsal pleura, but no honeycombing or reticulation (**Fig. 1B**). Bronchoscopic brush cytology led to the diagnosis of non-small cell lung cancer. Preoperative pulmonary function tests were within normal limits.

Under the diagnosis of lung cancer, cT2N1M0, stage IIB, right lower lobectomy with lymph node dissection was performed. At thoracotomy, a small amount of pleural fluid was observed and it was diagnosed as malignant

Fig. 1 Radiologic findings. (A) Chest X-ray revealed a mass shadow in the right lower lung field. (B) Preoperative chest CT. (C) Chest X-ray film on the third postoperative day showed ground-glass opacity in extensive areas of both lower lung fields. (D) Chest CT on the third postoperative day. (E) Chest X-ray film on the 25th postoperative day showed that the infiltrative shadows had extended in all lung fields.

by intraoperative cytology; therefore, lymph node dissection was limited to hilar lymph node. Grossly, the tumor was irregularly-bordered and consisted of a mixture of grayish-white and yellow components (**Fig. 2A**). Postoperative histopathological examination showed a mixture of a well-differentiated papillary adenocarcinoma and a poorly-differentiated squamous cell carcinoma, leading to the diagnosis of adenosquamous carcinoma (**Fig. 2B**). Since the adenocarcinoma component reached the pleura, the tumor was diagnosed as p2. Small disseminations were scattered on the pleural surface away from the tumor, and intrapulmonary metastases were seen in S6 (pT4N1M0, stage IIIB). On the other hand, the background lung adjacent to the pleura showed patchy areas of alveolar septal fibrosis along with the rearrangement of alveoli (**Fig. 2C** and **2D**). The subpleural fibrosis was irregularly shaped and was composed of collagenous and elastotic fibrosis combined with mild chronic inflammation. There were enlarged, restructured airspaces due to interstitial fibrosis and architectural distortion. Many of the airspaces were lined by bronchiolar type epithelium and, in part, by squamous metaplasia. Smooth muscle hyperplasia was prominent in the subpleural fibrotic area. In addition to subpleural fibrosis and scarring, small active fibrotic foci were identifiable (**Fig. 2E** and **2F**).

This mixture of remote, inactive fibrosis and current, ongoing disease typified the temporal variability and led to the diagnosis IPF of microscopic UIP pattern.

The patient's postoperative course was uneventful, and chest auscultation revealed clear breath sound bilaterally until the third postoperative day, when he developed a fever of 39.0 °C and respiratory failure. Pronounced fine crackles were heard mainly in the lower lung fields on both sides. On examination, his finger tips and lips were cyanotic. The serum LDH level increased rapidly from the normal range (119–220 U/L) to 440 U/L. Arterial blood gas analysis indicated a marked decrease in PaO₂. A chest X-ray showed extensive areas of ground-glass opacity (**Fig. 1C**). Chest CT revealed reticular shadows with thickened interstitium in the dorsal portions of the right middle and left lower lobes (**Fig. 1D**), leading to the diagnosis of the acute exacerbation of microscopic UIP. The patient received steroid pulse therapy, which proved ineffective. Subsequently, he again received one cycle of steroid and cyclophosphamide pulse therapy, but the respiratory failure gradually worsened. He underwent tracheostomy and mechanical ventilation. Chest X-ray on the 25th postoperative day showed that the infiltrative shadows had extended in all lung fields (**Fig. 1E**). The patient died on the 25th postoperative day due to

Fig. 2 Pathological findings. (A) Gross appearance of the resected specimen. (B) Postoperative histopathological examination showed a mixture of adenocarcinoma and squamous cell carcinoma components (Hematoxylin and eosin staining). (C, D) Histology of microscopic UIP pattern in the background lung (C, Hematoxylin and eosin staining; D, Elastica-van Gieson staining). (E, F) Lightly staining areas of fibroblast proliferation are present (arrow) (E, Hematoxylin and eosin staining; F, Elastica-van Gieson staining).

respiratory failure. Autopsy was not performed.

Discussion

Even if preoperative CT shows no findings of interstitial pneumonia, histopathological examination of the background lung after lung cancer surgery rarely reveals a UIP pattern in some patients.²⁾ This report suggests that such a microscopic UIP pattern may become exacerbated after lung cancer surgery. On performing lung cancer surgery in the presence of a small shadow immediately

adjacent to the pleura, it is necessary to consider the possibility of microscopic UIP pattern. It was reported that preoperative CT revealed a small shadow, although localized, in 75% of patients who developed interstitial pneumonia after surgery and that the incidence of postoperative interstitial pneumonia was 25 times higher in patients with than in those without a subpleural shadow.³⁾ The following specific measures are reported to be effective to prevent the exacerbation of microscopic UIP pattern.^{1):} (i) accurate evaluation by high-resolution CT of small shadows, if any, on conventional CT, (ii) preoperative

abstinence from smoking, (iii) the avoidance of exposure to high oxygen concentrations and the use of the lowest possible concentration in intra- and perioperative respiratory management, (iv) avoidance of overextension of the lung during general anesthesia, (v) complete closure of alveolar leakage, shortening of the operative time, and, if possible, selection of limited surgery, and (vi) the prevention of postoperative respiratory infection.

There is, as yet, no clear evidence of the therapeutic effect of erythromycin, vitamin E, and a low dose of steroid. Future studies on the preventive effects of novel drugs such as pirfenidone are awaited.

In our hospital, postoperative histopathological examination revealed features of UIP pattern in 65 (16.8%) of 387 patients with non-small cell lung cancer who had undergone surgery between June 1995 and December 2008. Four of these patients developed acute exacerbations of UIP after surgery and died during hospitalization. Various researchers have reported that UIP pattern lesions are found in 12%–17% of patients undergoing lung cancer surgery, in agreement with our study.⁴⁾ Yano et al. reported that the mortality rate of patients who developed the acute exacerbation of UIP pattern after surgery was 91.7%.⁵⁾

In conclusion, we report a case of acute exacerbation of IPF of microscopic UIP pattern after lung cancer surgery.

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