Radiological unilateral pleuroparenchymal fibroelastosis as a notable late complication after lung cancer surgery: incidence and perioperative associated factors

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Received 22 March 2022; received in revised form 1 August 2022; accepted 20 August 2022

Abstract

OBJECTIVES: Pleuroparenchymal fibroelastosis (PPFE) is a rare idiopathic interstitial pneumonia characterized by pleural-parenchymal involvement, predominantly in the upper lobes. Unilateral upper lung field pulmonary fibrosis (upper-PF) that is radiologically consistent with PPFE reportedly develops after lung cancer surgery in the operated side and presents many clinical characteristics in common with PPFE. However, the incidence and perioperative associated factors remain unclear.

Key question

What is unilateral pleuroparenchymal fibroelastosis (PPFE) developing after lung cancer surgery?

Key finding(s)

Unilateral PPFE is a progressive upper lung field fibrosis which develops late after surgery with an incidence of 4.3%.

Take-home message

Unilateral PPFE is not a rare late complication after lung cancer surgery, which may be related to severe post operative clinical course.
INTRODUCTION

Pleuroparenchymal fibroelastosis (PPFE) is a rare form of interstitial lung disease characterized by pleural and subjacent parenchymal fibrosis predominantly in the bilateral upper lobes [1-3]. Patients with PPFE frequently have a low body mass index (BMI), deteriorated pulmonary function and poor prognosis [1, 3, 4]. In addition to idiopathic causes, a bone marrow, lung, or other organ transplant; radiotherapy; chemotherapy; recurrent lung infections; and an overactive immune system can cause PPFE [5].

More recently, upper lung field pulmonary fibrosis (upper-PF) radiologically consistent with PPFE has been reported to develop as a late complication after thoracic surgery [6, 7]. The upper-PF lesions were limited to the operated side but were similar to PPFE in terms of radiological and clinical characteristics. Most of the patients with unilateral upper-PF presented with respiratory symptoms and developed intra-/extrathoracic aberrant air suggestive of lung parenchymal air leak during their clinical courses [8], which might be related to the progression of unilateral upper-PF [7]. The prognosis was poor with a median survival time of 49.3 months, and all causes of death were respiratory diseases. Regarding respiratory complications after thoracic surgery, pneumonia is well known and can be caused by bacterial colonization of the atelectatic lung [9]. Pneumonia generally occurs in the early postoperative period and may improve with appropriate treatment. On the other hand, unilateral upper-PF occurs late after surgery [6, 7] and therefore may receive less attention compared to pneumonia. Although unilateral upper-PF is considered an important late complication after thoracic surgery, little is known about the incidence, mechanisms and perioperative-associated factors responsible for unilateral upper-PF development after lung cancer surgery. In addition, previous reports showed that almost all patients with unilateral upper-PF had a preoperative pulmonary apical cap in the apex of the lungs [6], and an autopsy showed findings consistent with postoperative chronic pleuritis [7]. However, the effect of a pulmonary apical cap and postoperative chronic pleuritis on disease development is also unclear. The purpose of this study was to determine the incidence, mechanisms and perioperative factors associated with the development of unilateral upper-PF.
associated with subpleural fibrosis in the upper lobes, but the distribution of these changes was not concentrated in the upper lobes nor were there features of coexistent disease elsewhere [1]. These criteria were applied only for a unilateral lung in the operated side. The diagnosis of upper-PF was made based on the consensus of at least 2 board-certified chest surgeons, chest physicians and chest radiologists.

We then reviewed the medical records of all eligible patients and compared the clinical characteristics, including age, sex, smoking history, BMI, results of respiratory functional analysis, operative approach (video-assisted thoracoscopic surgery or open thoracotomy), operative procedure (lobar resection or sublobar resection), the use of a polyglycolic acid (PGA) sheet and fibrin glue, a preoperative pulmonary apical cap and adjuvant chemotherapy between the 2 groups.

**Operative procedure**

Lobar resection is a lobectomy (removal of a single lobe) or bilobectomy (removal of 2 adjacent lobes). Sublobar resection is wedge resection or segmentectomy. We routinely used the PGA sheet (Neoveil large size; 10.0 x 10.0 cm: Gunze, Kyoto, Japan) and 3 ml or 5 ml of fibrin glue (Bolheal: Teijin, Tokyo, Japan or Beriplast P Combi-Set: CSL Behring, Tokyo, Japan) to cover the dissected hilum when we performed a lobectomy, a bilobectomy and a segmentectomy, regardless of a lung parenchymal air leak. In the case of wedge resection, we covered them to the point of the air leak only when we confirmed the presence of an air leak.

**Definition of pulmonary apical cap**

A pulmonary apical cap is a wedge- and triangle-shaped opacity in the apex of the lung with broad pleural contact [10, 11]. The length of the pleural contact was reported to range from 7 mm to 6.0 cm on CT scans [10, 11]. Therefore, we evaluated the presence or absence of a preoperative pulmonary apical cap with a pleural contact of 5 mm or more on the operated side on CT.

**Radiological evaluation before and after lung cancer surgery**

In all eligible patients, thin-sliced high-resolution CT (1 mm) was routinely performed before and after lung cancer surgery. During the postoperative follow-up period, chest radiography and CT scans were performed alternately every 3 months for the first 5 years; thereafter CT was performed every 6 months, typically for up to 10 years. All images were interpreted using Synapse (Fujifilm Medical Systems, Japan).

**Pathological evaluation of the background of the lung specimen in patients who developed unilateral upper-PF later**

Histopathologic materials from all patients who developed unilateral upper-PF later were reviewed by a board-certified pathologist. The presence or absence of interstitial pneumonia in the area distant from the lung cancer was evaluated microscopically.

**Pleural effusion at 6 months after lung cancer surgery**

A previous report of an autopsy of a patient with unilateral upper-PF showed chronic pleuritis and suggested that chronic pleuritis following thoracic surgery contributes to the development of unilateral upper-PF [7]. Because all eligible patients were routinely evaluated with CT every 6 months, we assessed the presence or absence of pleural effusion on CT at 6 months after surgery, regardless of the amount of pleural fluid.

**Statistical analyses**

Descriptive statistics were expressed as n (%) or median and range. The Mann–Whitney U test and the Fisher exact test were used to compare continuous variables and categorical variables, respectively. A competing risk method was used to estimate the cumulative incidence of unilateral upper-PF. In this study, recurrence of lung cancer, treatment for metachronous multiple lung cancer or death of other diseases before unilateral upper-PF development was considered a competing risk event. Patients who had not developed unilateral upper-PF and had not died were censored at the time of the last follow-up. Gray’s test was used to test for differences in the cumulative incidence curves. The association between unilateral upper-PF and patient characteristics at lung cancer surgery were assessed using a proportional hazards model (Fine-Gray model). Statistical significance was set at a P-value < 0.05. Variables with P-values < 0.05 in univariable analysis were considered factors potentially associated with upper-PF development and used in subsequent multivariable analysis. Statistical analyses were conducted using EZR (Saitama Medical Center, Jichii Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [12].

**RESULTS**

**Patient characteristics**

Of the 943 patients with completely resected lung cancer, 587 patients were included. The study profile is shown in Supplementary Fig. 1. The median follow-up period was 5.1 years and the mean follow-up index was 0.84 (standard deviation: 0.23). Twenty-five patients (4.3%) developed unilateral upper-PF, and 562 (95.7%) did not. Patient characteristics are shown in Table 1. Twenty-five patients with unilateral upper-PF were significantly older (P = 0.035), more were men (P = 0.004) and more had a lower BMI (P = 0.014) than those without. Lobar resection was more frequently performed in patients with unilateral upper-PF than in those without (92.0% vs 73.1%, P = 0.036). The incidence of unilateral upper-PF development was 4.5% for lobectomy (19/426) and 50.0% for bilobectomy (4/8). The details of operative procedures for patients with unilateral upper-PF are shown in Table 2. Patients with unilateral upper-PF more
commonly had a preoperative pulmonary apical cap than those without (84.0% vs 39.7%, \( P < 0.001 \)). None of the patients received adjuvant radiotherapy.

**Table 1: Patient characteristics**

| Characteristics | All cases (n = 587) | With unilateral upper-PF (n = 25) | Without unilateral upper-PF (n = 562) | P-value |
|-----------------|---------------------|-----------------------------------|--------------------------------------|---------|
| Age (years) | | | | |
| Median (range) | 69 (25–86) | 73 (55–85) | 69 (25–86) | 0.035 |
| < 70, n (%) | 307 (52.2) | 8 (32.0) | 299 (53.2) | 0.042 |
| > 70 | 280 (47.7) | 17 (68.0) | 263 (46.8) | |
| Sex, n (%) | | | | |
| Male | 331 (56.3) | 21 (84.0) | 310 (55.1) | 0.004 |
| Female | 256 (43.6) | 4 (16.0) | 252 (44.8) | |
| Smoking history, n (%) | | | | |
| Yes | 356 (60.6) | 19 (76.0) | 337 (60.0) | 0.143 |
| No | 231 (39.4) | 6 (24.0) | 225 (40.0) | |
| BMI (kg/m²) | | | | |
| Median (range) | 22.2 (15.2–43.9) | 20.3 (16.0–26.1) | 22.3 (15.2–43.9) | 0.014 |
| %VC (%) | | | | |
| Median (range) | 104.9 (51.3–169.8) | 100.7 (72.4–129.5) | 105.1 (51.3–169.8) | 0.056 |
| &gt; 80, n (%) | 561 (95.6) | 22 (88.0) | 539 (95.9) | 0.093 |
| &lt; 80 | 26 (4.4) | 3 (12.0) | 23 (4.1) | |
| FEV1.0% (%) | | | | |
| Median (range) | 73.1 (29.0–100.0) | 74.1 (45.6–99.4) | 73.0 (29.0–100.0) | 0.325 |
| &gt; 70, n (%) | 376 (64.1) | 15 (60.0) | 361 (64.2) | 0.674 |
| &lt; 70 | 211 (35.9) | 10 (40.0) | 201 (35.8) | |
| Operative approach, n (%) | | | | |
| VATS | 554 (94.3) | 23 (92.0) | 531 (94.5) | 0.645 |
| Open thoracotomy | 33 (5.6) | 2 (8.0) | 31 (5.5) | |
| Operative procedure, n (%) | | | | |
| Lobar resection | 434 (73.9) | 23 (92.0) | 411 (73.1) | 0.036 |
| Sublobar resection | 153 (26.0) | 2 (8.0) | 151 (26.9) | |
| Use of PGA sheet and fibrin glue | | | | |
| Yes | 542 (92.3) | 25 (100) | 517 (92.0) | 0.246 |
| No | 45 (7.7) | 0 (0) | 45 (8.0) | |
| Pulmonary apical cap, n (%) | | | | |
| Absent | 343 (58.4) | 4 (16.0) | 339 (60.3) | &lt; 0.001 |
| Present | 244 (41.6) | 21 (84.0) | 223 (39.7) | |
| Adjuvant chemotherapy | | | | |
| Yes | 47 (80.0) | 1 * (4.0) | 46 (8.2) | 0.712 |
| No | 540 (20.0) | 24 (96.0) | 516 (91.8) | |

*Uracil-tegafur was administered orally.
BMI: body mass index; FEV1.0%: % forced expiratory volume in 1 s; lobar resection: lobectomy or bilobectomy; %VC: % vital capacity; PGA: polyglycolic acid; sublobar resection: wedge resection or segmentectomy; upper-PF: upper lung field pulmonary fibrosis; VATS: video assisted thoracoscopic surgery.

**Table 2: Operative procedures of the patient with unilateral upper-PF**

| Operative procedures | n |
|----------------------|---|
| Lobal resection | 23 |
| Lobectomy | 19 |
| Right upper lobectomy | 4 |
| Right middle lobectomy | 1 |
| Right lower lobectomy | 8 |
| Left upper lobectomy | 5 |
| Left lower lobectomy | 1 |
| Bilobectomy | 4 |
| Right middle and lower lobectomy | 2 |
| Right upper and middle lobectomy | 2 |
| Sublobar resection | 2 |
| Left upper division segmentectomy | 1 |
| Left lower lobe wedge resection | 1 |

upper-PF: upper lung field pulmonary fibrosis.

**Cumulative incidence of unilateral upper-PF after lung cancer surgery**

The cumulative incidence of unilateral upper-PF gradually increased 2 years after lung cancer surgery (Fig. 1A). For the entire population, the 3-, 5-, 10- and 12-year cumulative incidences of unilateral upper-PF were 2.3%, 3.3%, 5.3% and 6.9%, respectively.

**Pleural effusion at 6 months after lung cancer surgery**

We investigated the presence or absence of postoperative pleural effusions at 6 months after surgery and found that pleural effusion was more common in patients with unilateral upper-PF than in those without (96.0% vs 24.2%, \( P < 0.001 \)) (Table 3). This trend was also observed regardless of the operative procedure (lobar resection and sublobar resection). Of note, pleural effusion in all patients with unilateral upper-PF persisted and was accompanied by pleural thickening and fibrosis adjacent to the pleura.
Figure 1: (A–E) Cumulative incidence curves of unilateral upper-PF after lung cancer surgery. upper-PF: upper lung field pulmonary fibrosis; VC: vital capacity.
Clinical and radiological courses of patients with unilateral upper-PF

The median interval from lung cancer surgery to the diagnosis of unilateral upper-PF was 36.3 months (range, 4.8–121.8) (Table 4). We carefully examined the radiological findings on CT scans in order to detect intra-/extrathoracic aberrant air such as subcostal and pneumothorax air. Aberrant air was detected in 17 patients (68.0%), although the degree of all aberrant air was slight, as shown in Supplementary Fig. 2. During their radiological courses, the upper-PF lesions initially showed only slight fibrosis adjacent to the pleura in all patients. However, the upper-PF lesions deteriorated with cystic changes in 20 patients (80%), which occasionally resulted in pulmonary aspergillus and nontuberculous mycobacterium infection, whereas 5 patients (20%) presented with radiological deterioration without any cystic changes. Eighteen patients (72.0%) had some adverse events caused by unilateral upper-PF. The typical case of pulmonary aspergillus infection following unilateral upper-PF progression is shown in Supplementary Fig. 3. The median follow-up period after unilateral upper-PF diagnosis was 29.7 months (range, 3.1–57.6). During this period, 6 patients (24.0%) died of unilateral upper-PF-related causes.

The pathological background of lung specimens resected for lung cancer in 25 patients who later developed unilateral upper-PF

Interstitial pneumonia was pathologically observed in 2 patients (8.0%) despite no radiological evidence of interstitial shadow. One was the usual interstitial pneumonia and the other was indeterminate for interstitial pneumonia. In addition, centrilobular emphysematous change was commonly observed in 18 patients (72%).

Perioperative factors associated with the development of unilateral upper-PF

Multivariable analysis showed that male sex (subdistribution hazard ratio [SHR] = 4.25, P = 0.010), %VC < 80% (SHR = 3.56, P = 0.047), lobar resection (SHR = 4.31, P = 0.038) and presence of pulmonary apical cap (SHR = 6.47, P = 0.0032) were independent perioperative associated factors for unilateral upper-PF development (Table 5). A proportional hazards model (Fine-Gray model) could not be performed concerning the use of a PGA sheet and fibrin glue because no patients developed upper-PF without the use of such materials. On the other hand, Gray's test (P = 0.13) showed no significant difference in the cumulative incidence of upper-PF development between patients with and without the use of such materials.

The cumulative incidence curves and the details of the cumulative incidence according to perioperative associated factors are shown in Fig. 1B-E and Table 6. The 10-year cumulative incidence was 6.3% in patients treated with lobar resection, 8.0% in male patients, 10.3% in patients with pulmonary apical cap and 14.5% in patients with low %VC, respectively.

Radiological courses of 2 patients with unilateral upper-PF

Figure 2 shows the radiological course of a 68-year-old male who underwent right lower lobectomy for stage IA lung adenocarcinoma. The patient was diagnosed with unilateral upper-PF 2 years and 3 months after the initial surgery. The cystic lesion deteriorated and resulted in nontuberculous mycobacteria infection and progressive body weight loss of 17 kg in 3 years.

Figure 3 shows the radiological course of a 78-year-old male who underwent right upper lobectomy for stage IB lung adenocarcinoma. The unilateral upper-PF lesion apparently worsened without cystic change, and the patient was finally diagnosed with
unilateral upper-PF. Although he was asymptomatic during the radiological course, a unilateral thoracic deformity apparently emerged.

**DISCUSSION**

The present study identified 4 clinical findings. First, the incidence of unilateral upper-PF development was 4.3% among all patients having lung cancer surgery, 4.5% for lobectomy and 50.0% for bilobectomy. The cumulative incidence gradually increased after lung cancer surgery, and the 10-year cumulative incidence was 5.3%. Second, 72% of the patients with unilateral upper-PF had some adverse events associated with the lesion. Third, pleural effusion at 6 months postoperatively was much more common in patients who later developed unilateral upper-PF than in those who did not. Fourth, multivariable analysis revealed male sex, low %VC, lobar resection and the presence of a pulmonary apical cap as perioperative factors associated with the development of unilateral upper-PF. These results provide the following 3 characteristics associated with unilateral upper-PF:

1. **First, unilateral upper-PF is an occasional but under-recognized late complication after lung cancer surgery.** Although there are many studies on early complications such as pneumothorax after lung cancer surgery [9, 13, 14], reports on late complications are limited. The present study showed that the 10-year cumulative incidence was 6.3% in patients treated with lobar resection, 8.0% in male patients, 10.3% in patients with pulmonary apical cap and 14.5% in patients with low %VC. Further, unilateral upper-PF usually resulted in a severe clinical course, including infection and respiratory failure. Therefore, unilateral upper-PF is a notable late complication after lung cancer surgery.

2. **On the operated side.**

| Table 5: Univariable and multivariable analyses for perioperative associated factors for unilateral upper-PF |
|---------------------------------------------------------------|
| Variables | Univariable analysis | Multivariable analysis |
|-----------|----------------------|------------------------|
|           | SHR  | 95% CI | P-value | SHR  | 95% CI | P-value |
| Age (≥ 70) | 2.50 | 1.09–5.76 | 0.031 | 2.07 | 0.84–5.02 | 0.11 |
| Sex (male) | 4.11 | 1.41–12.00 | 0.0096 | 4.25 | 1.40–12.84 | 0.010 |
| Smoking history (yes) | 2.13 | 0.85–5.32 | 0.11 | 1.25 | 0.33–2.79 | 0.57 |
| BMIF | 0.85 | 0.75–0.96 | 0.0078 | 0.89 | 0.76–1.05 | 0.18 |
| %VC (% < 80%) | 3.39 | 1.02–11.26 | 0.047 | 3.56 | 1.02–4.6 | 0.047 |
| FEV1, FVC (% < 70%) | 1.37 | 0.33–5.65 | 0.67 | 4.20 | 1.01–17.58 | 0.049 |
| Operative approach (open thoracotomy) | 7.71 | 2.64–22.52 | 0.00019 | 6.47 | 1.87–22.30 | 0.0032 |
| Operative procedure (lobar resection) | 4.20 | 1.01–17.58 | 0.049 | 4.31 | 1.08–17.15 | 0.038 |
| Use of PGA sheet and fibrin glue | N/E | 0.64 | 0.08–8.61 | 0.66 |
| Pulmonary apical cap (presence) | 7.71 | 2.64–22.52 | 0.00019 | 6.47 | 1.87–22.30 | 0.0032 |
| Adjuvant chemotherapy (yes) | 0.64 | 0.08–8.61 | 0.66 |

*p upper-PF: upper lung field pulmonary fibrosis; BMI: body mass index; CI: confidence interval; FEV1, FVC: % forced expiratory volume in 1 s; lobar resection: lobectomy or bilobectomy; N/E: not evaluable because no patients developed upper lung field pulmonary fibrosis without the use of PGA sheet and fibrin glue; %VC: % vital capacity; PGA: polyglycolic acid; SHR: subdistribution hazard ratio.

| Table 6: Cumulative incidence of unilateral upper-PF according to perioperative characteristics |
|---------------------------------------------------------------|
| Perioperative characteristics | Cumulative incidence (95% C.I.) | 3-year | 5-year | 10-year |
|-----------------------------|--------------------------------|--------|--------|--------|
| Entire population | 2.3% (1.3–3.8) | 3.3% (2.0–5.0) | 5.3% (3.4–7.9) |
| Operative procedure | 3.1% (1.7–5.1) | 4.1% (2.5–6.3) | 6.3% (3.9–4.4) |
| Lobar resection | 0.0% (0.0–0.0) | 0.8% (0.1–4.2) | 2.6% (0.4–8.7) |
| Sublobar resection | 2.8% (1.4–5.1) | 4.5% (2.6–7.3) | 8.0% (4.9–12.2) |
| Sex | 1.6% (0.5–3.8) | 1.6% (0.5–3.8) | 1.6% (0.5–3.8) |
| Male | 4.6% (2.4–7.8) | 6.5% (3.8–10.2) | 10.3% (6.3–15.4) |
| Female | 0.6% (0.1–2.1) | 1.0% (0.3–2.6) | 1.8% (0.5–4.7) |
| Apical cap | 8.8% (1.4–25.0) | 14.5% (3.3–33.5) | 14.5% (3.3–33.5) |
| Present | 2.0% (1.3–3.5) | 2.8% (1.6–4.5) | 4.9% (3.7–5.5) |
| Absent | *Upper-PF: upper lung field pulmonary fibrosis; VC: vital capacity.**

*On the operated side. CI: confidence interval; lobar resection: lobectomy or bilobectomy; sublobar resection: wedge resection or segmentectomy; upper-PF: upper lung field pulmonary fibrosis; VC: vital capacity.
careful evaluation of radiological changes by thin-sliced CT findings every 6 months indicated that the upper-PF lesions initially showed only slight fibrosis adjacent to the pleura in all patients, and gradually became aggravated with or without cystic change. Thus, fibrobullous change may be one of the manifestations of unilateral upper-PF in the advanced stage.

Second, chronic pleuritis may be the first step in the unilateral development of upper-PF. To date, the mechanisms underlying unilateral upper-PF development after lung cancer surgery remain unclear. The autopsied case of unilateral upper-PF showed evidence of chronic pleuritis as well as secondary PPFE [7]. In addition, the previous study showed that almost all patients with unilateral upper-PF had aberrant air emerlence, suggestive of lung parenchymal air leak on CT during their clinical course [7]. Therefore, some visceral pleural disorders may contribute to the progression of unilateral upper-PF. In the present study, almost all patients who later developed unilateral upper-PF had pleural effusions in the residual space 6 months after surgery. The pleural effusion persisted, accompanied by pleural thickening and subpleural pulmonary fibrosis. These results indicate that chronic pleuritis contributes to the development of unilateral upper-PF. In fact, there was a case of bilateral tuberculous pleuritis progressing to upper-lobe-predominant pulmonary fibrosis mimicking PPFE 3 years thereafter [16], which supports our hypothesis. In addition, a PGA sheet and fibrin glue were used in all patients who later developed upper-PF. Because fibrin glue reportedly induced eosinophilic pleural effusion after lung resection [17], a PGA sheet or fibrin glue may play an important causal role in the development of upper-PF although the difference was not significant by Gray's test (p=0.13).

Third, chest physicians and surgeons should be aware that the development of unilateral upper-PF may be correlated with perioperative patient characteristics including male sex, pulmonary apical cap, low %VC and lobar resection. To our knowledge, there is no definite reason for the predominance of male sex in the development of this disease. However, almost all patients with the above-mentioned “unilateral fibrobullous change” were male [15], which indicates that male sex is associated with disease development. With regard to low %VC and a preoperative pulmonary apical cap, patients with PPFE...
commonly have low %VC [1, 3, 4, 18], and a pulmonary apical cap has the same histological characteristics as PPFE despite being an anatomically localized, non-progressive lesion [1, 10, 19]. In addition, a pulmonary apical cap has been reported to be potentially caused by ischaemia in the upper lobes and low-grade inflammation in the lung parenchyma [1, 18] and is considered a potential risk factor for PPFE [20]. Therefore, we suppose that patients with low %VC and a pulmonary apical cap have some potential pathophysiological factors in common with those with PPFE. Furthermore, our results showed that lobar resection was also associated with unilateral upper-PF development. Generally, lobectomy, especially bilobectomy, is a wide resection of the lung compared to other procedures and is correlated with postoperative residual space. This postoperative residual space may cause persistent pleural effusion, which results in chronic pleuritis [21].

The limitations of this study include the following: a single-centre retrospective study, a small number of patients with unilateral upper-PF, a lack of pathological evaluations of the unilateral upper-PF lesions and no autopsy evaluations of the 6 patients who died. In addition, because no patients developed upper-PF without the use of a PGA sheet and fibrin glue, a proportional hazards model could not be used. Further study is needed to elucidate more detailed clinical and radiological characteristics, mechanisms and perioperative risk factors of unilateral upper-PF.

Figure 3: Radiological course of a 78-year-old male patient who underwent a right upper lobectomy for stage IB adenocarcinoma. (A) Preoperative radiological radiograph showed a small nodule (white arrow) in the right middle lung field, and chest computed tomography demonstrated a pulmonary apical cap (arrowhead) and a nodule (black arrow) in the right upper lobe. (B) Postoperative computed tomography at 6 months after surgery showed no abnormal shadows except for a small amount of pleural effusion (arrow) on the operated side. (C) At 4 years and 8 months after surgery, pleural thickening and subpleural fibrosis lesion emerged in the right upper lung field with unilateral thoracic deformity and thickened pleural effusion.
CONCLUSION

Unilateral upper-PF is an occasional but under-recognized late complication after lung cancer surgery. This complication may be correlated with perioperative patient characteristics including male sex, low %VC, pulmonary apical cap and lobar resection.

SUPPLEMENTARY MATERIAL

Supplementary material is available at ICVTS online.

ACKNOWLEDGEMENT

We would like to thank Editage (www.editage.com) for English language editing.

FUNDING

The study did not receive any funding.

Conflict of interest: The authors have no conflicts of interest to declare.

Data availability

All relevant data are within the manuscript and its supporting information files.

Authors’ contributions

Kenji Inafuku: Study design; Data interpretation; Data analysis; Akimasa Sekine: Study design; Data interpretation; Data analysis; Hiromasa Araí: Writing—review & editing; Eri Hagiwara: Writing—review & editing; Shigeru Komatsu: Writing—review & editing; Tae Iwasawa: Writing—review & editing; Toshihiro Misumi: Data analysis; Writing—review & editing; Noritake Kikunishi: Writing—review & editing; Michihiko Tajiri: Writing—review & editing; Koji Okudela: Pathological evaluations; Writing—review & editing; Yasushi Rino: Writing—review & editing; and Takashi Ogura: Writing—review & editing

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