



Case report

## Fibrin glue-induced eosinophilic pleural effusion after pulmonary resection: A case report



Nobutaka Kawamoto<sup>a,\*</sup>, Riki Okita<sup>a</sup>, Masanori Okada<sup>a</sup>, Kosuke Ito<sup>b</sup>, Katsutoshi Hirazawa<sup>c</sup>,  
Hidetoshi Inokawa<sup>a</sup>

<sup>a</sup> Department of Thoracic Surgery, National Hospital Organization Yamaguchi Ube Medical Center, 685 Higashikiwa, Ube, Yamaguchi 755-0241, Japan

<sup>b</sup> Department of Respiratory Medicine, National Hospital Organization Yamaguchi Ube Medical Center, 685 Higashikiwa, Ube, Yamaguchi 755-0241, Japan

<sup>c</sup> Department of Breast and Gastrointestinal Surgery, National Hospital Organization Yamaguchi Ube Medical Center, 685 Higashikiwa, Ube, Yamaguchi 755-0241, Japan

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ABSTRACT

**Introduction and importance:** Prolonged air leakage after pulmonary resection is a common complication, and fibrin glue is used as a sealant to reduce this. Fibrin glue-induced adverse events are generally rare. Herein, we describe a rare case of fibrin glue-induced eosinophilic pleural effusion (EPE).

**Case presentation:** A 77-year-old man underwent partial pulmonary resection for right lower lobe lung cancer, and the pulmonary staple stump was subsequently covered with fibrin glue. Antibacterial drugs were administered for the treatment of postoperative pneumonia. However, re-elevation of the inflammatory cell number was observed, and computed tomography revealed an increase in right pleural effusion. Although thoracoscopy was performed based on a possibility of empyema, no empyema was observed. The eosinophil count in the pleural effusion was 11%; thus, the patient was diagnosed with EPE, which was resolved after thoracic drainage, without corticosteroid administration. Fibrin glue was identified as the causative agent, using a drug-induced lymphocyte stimulation test.

**Clinical discussion:** EPE is defined as an eosinophil count of  $\geq 10\%$  in the pleural effusion. If pleural effusion on the surgical side, with fever or an elevated inflammatory cell number, is observed in the early postoperative period after pulmonary resection, empyema should be considered foremost. In this case, the administration of antibacterial drugs was ineffective, and the patient was eventually diagnosed with EPE.

**Conclusion:** EPE should be considered as a rare fibrin glue-induced adverse event after pulmonary resection. It is recommended that the leukocyte fraction be examined, if pleural effusion is collected for postoperative pleural effusion.

### 1. Introduction

Prolonged air leakage is a common complication after pulmonary resection, that reportedly occurs in approximately 8%–15% of patients [1]. Fibrin glue is often used as a sealant to reduce its incidence [2,3]. Fibrin glue-induced adverse events have been occasionally reported, most of which being allergies caused by bovine aprotinin (which is mixed in with fibrin lysate to prevent fibrin clots from being dissolved by plasmin) [4,5]. In the field of thoracic surgery, there are few case reports of fibrin glue-induced adverse events after pulmonary resection [6]. To

the best of our knowledge, only one case report of fibrin glue-induced eosinophilic pleural effusion (EPE) has been published, and it is a Japanese literature [7]. Herein, we report a rare case of fibrin glue-induced EPE, mimicking empyema.

This case report has been reported in line with the SCARE Criteria [8].

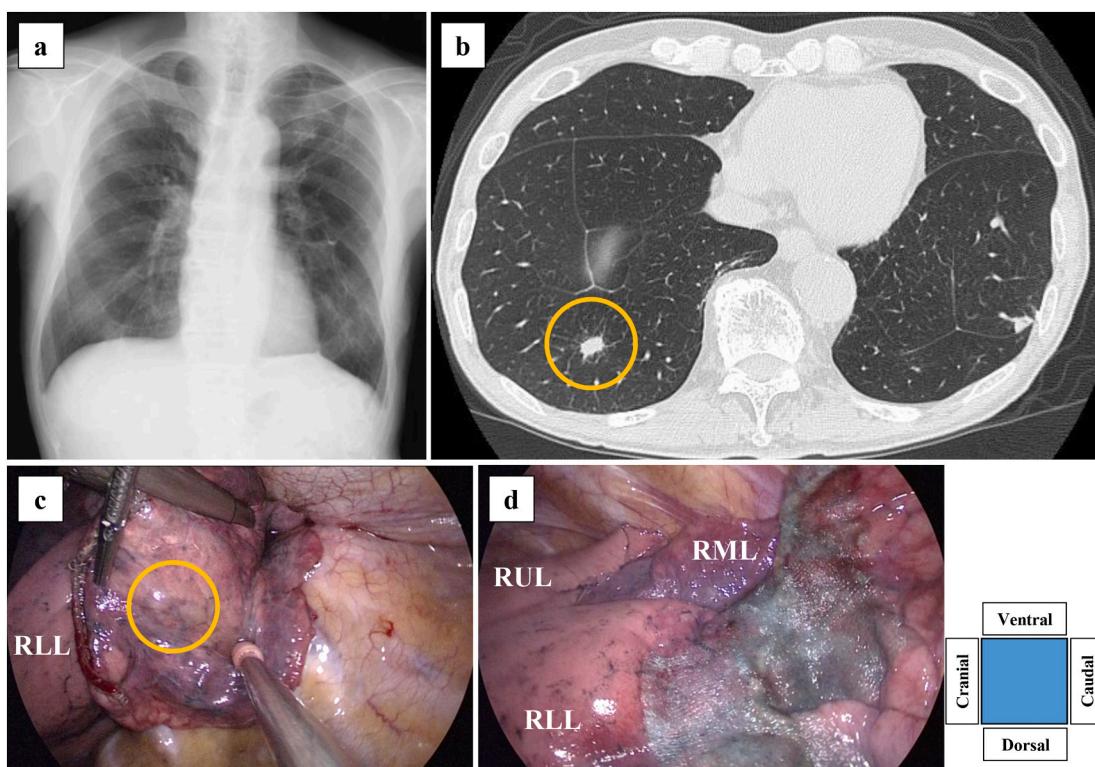
### 2. Presentation of case

A 77-year-old man with hypertension, emphysema, chronic kidney

**Abbreviations:** EPE, eosinophilic pleural effusion; CT, computed tomography; VATS, video-assisted thoracoscopic surgery; POD, postoperative day; DLST, drug-induced lymphocyte stimulation test.

\* Corresponding author.

E-mail address: [kawamotonobutaka@gmail.com](mailto:kawamotonobutaka@gmail.com) (N. Kawamoto).



**Fig. 1.** Preoperative and intraoperative imaging findings.

(a) Chest radiography showing no pleural effusion. (b) Computed tomography image showing a lung nodule in the right lower lobe (orange circle). (c) Surgical findings during partial pulmonary resection of the right lower lobe (orange circle, lung nodule). (d) Surgical findings after pulmonary staple stump covering with fibrin glue and polyglycolic acid sheet.

RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

disease, alcoholic liver dysfunction, and secondary eosinophilia due to cutaneous pruritus, underwent computed tomography (CT), which revealed a pulmonary nodule. The patient was taking nifedipine, verapamil, bisoprolol, bilastine, and calcium polystyrene sulfonate. The patient had a 56 pack-year smoking history, family history of pneumonia, heart failure, renal failure, and amyotrophic lateral sclerosis, and had no history of allergies. The patient underwent partial pulmonary resection for lung adenocarcinoma of the left lower lobe (T1bNxM0) at 74 years of age, and radiofrequency ablation for hepatocellular carcinoma (T1N0M0) at 76 years of age. The patient had no prior history of fibrin glue use. Chest radiography revealed no pleural effusion (Fig. 1a). CT revealed a 1.4 cm tumor in the lower lobe of the right lung (Fig. 1b). Partial pulmonary resection via video-assisted thoracoscopic surgery (VATS) was performed based on the suspicion of a right lower lobe lung cancer (Fig. 1c). Air leakage, which was observed at the pulmonary staple stump, was covered with fibrin glue and a polyglycolic acid sheet (Fig. 1d). Following pathological diagnosis, the lung adenocarcinoma was staged as IA2 (T1bNxM0).

The postoperative course is shown in Fig. 2. No air leakage was observed postoperatively, and the chest tube was removed on post-operative day (POD) 2. Antibacterial drugs were administered for postoperative pneumonia of the right lung on POD 3 (Fig. 3a, b). The inflammatory cell number temporarily improved and then re-elevated, and a CT scan revealed an increase in right pleural effusion, suggesting the possibility of empyema (Fig. 3c, d). Thoracentesis was performed on POD 12, and no bacteria were isolated. However, the inflammatory cell number was further elevated. We considered that thoracoscopy was necessary in order to observe the thoracic cavity, and the patient's informed consent was obtained. Although thoracoscopy was performed on POD 15, no empyema was observed (Fig. 4a, b). Intrathoracic lavage was performed using saline, and a chest tube was placed in the thoracic

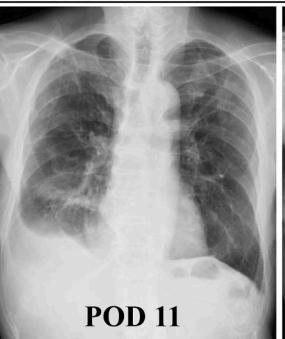
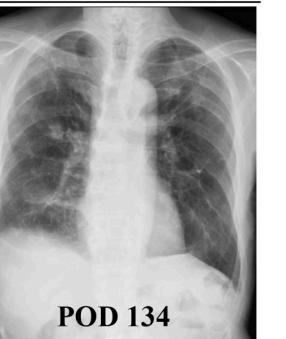
cavity. The eosinophil count in the pleural effusion were 21% (POD 12), and 11% (POD 15) (Table 1); the patient was diagnosed with EPE. On POD 18, the chest tube was removed. Although peripheral blood eosinophilia and right pleural effusion were observed, the inflammatory cell number had improved. The patient was discharged on POD 34.

A drug-induced lymphocyte stimulation test (DLST) for fibrin glue and polyglycolic acid sheet was performed on PODs 20 and 48. In fibrin glue, a stimulation index of 180% ( $\geq 180\%$  was considered positive) was obtained once (Table 2). Therefore, the patient was diagnosed with fibrin glue-induced EPE. At the patient's 3-month follow-up visit post-operatively, although chest radiography showed a small amount of right pleural effusion, no re-elevation of inflammatory cell number was observed.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

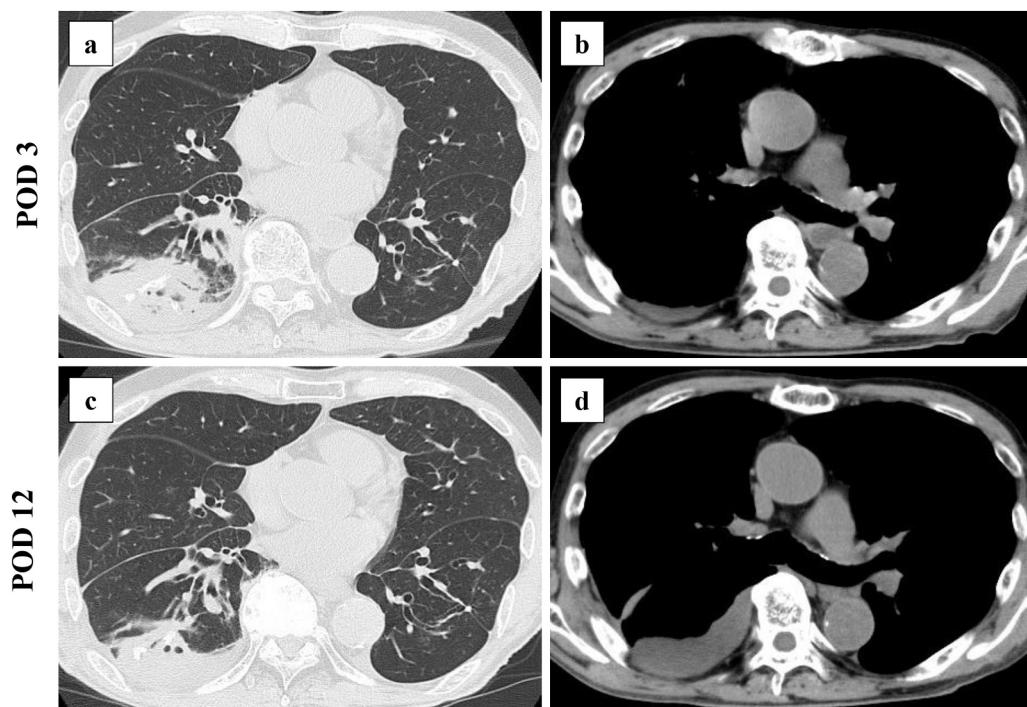
### 3. Discussion

EPE is defined as an eosinophil count of  $\geq 10\%$  in pleural effusion [9]. EPEs account for approximately 10% of exudative pleural effusions [10], and are mainly caused by malignant tumors, infections, autoimmune diseases, drugs, pulmonary embolism, and chest trauma [10]. The main symptoms of EPE are fever, cough, shortness of breath, and chest pain [11]. In this case, the patient had prolonged fever and was diagnosed with fibrin glue-induced EPE by DLST. Although drug-induced EPEs often improve after discontinuation of the causative drug [12], the effectiveness of systemic or intrathoracic administration of corticosteroids has also been reported [13,14]. In the past case of fibrin glue-induced EPE, the symptoms reportedly improved only with thoracic drainage as in this case [7]. In general, fibrin glue is absorbed and excreted from the body in approximately 3 weeks [15]. Therefore, it is

POD	Before surgery	0	1	2	3	7	11	12	14	15	16	18	20	30	34	134	
		CEZ	CTRX				TAZ/PIPC										
<b>Drug administration</b>																	
		Tramadol, Acetaminophen				Tramadol, Acetaminophen				Tramadol, Acetaminophen							
Body temperature (°C)	36.3	36.5	37.5	37.8	37.6	37.5	38.8	37.1	37.0	36.7	37.9	37.0	36.8	36.6	36.6		
SpO <sub>2</sub> (%) on room air	99	99	98	96	95	98	95	97	98	96	94	96	97	98	98		
CRP (mg/dL)	0.09		2.88		26.24	8.62	2.35	7.10	13.69		12.14	23.34	10.21	1.45		0.09	
WBC (/μL)	8510		11660		14400	9130	11020	10970	13160		13820	11640	9170	9110		6330	
Eosinophils (/μL)	894		513		893	1013	1256	1393	1935		1271	2095	1614	1503		791	
(%)	10.5		4.4		6.2	11.1	11.4	12.7	14.7		9.2	18.0	17.6	16.5		12.5	
						<b>POD 3</b>	<b>POD 11</b>	<b>POD 22</b>	<b>POD 134</b>								

**Fig. 2.** Postoperative clinical course.

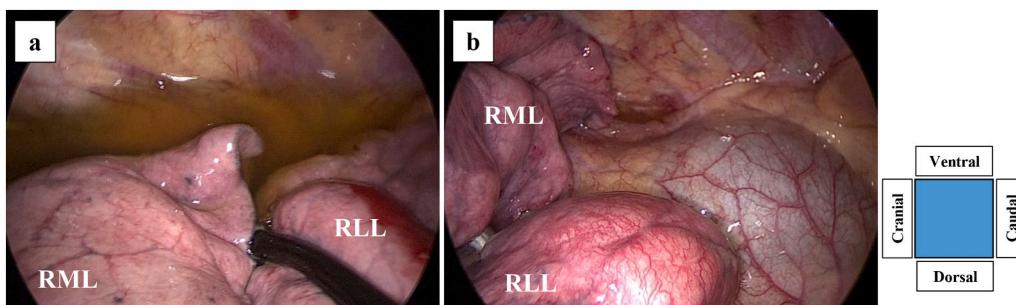
CEZ, cefazolin; CRP, C-reactive protein; CTRX, ceftriaxone; POD, postoperative day; SpO<sub>2</sub>, percutaneous oxygen saturation; TAZ/PIPC, tazobactam/piperacillin; WBC, white blood cell.



considered that the passage of time contributed to the improvement of EPE as well as thoracic drainage.

Empyema develops in 0.9% patients after lung cancer surgery [16]. If

pleural effusion on the surgical side, with fever or an elevated inflammatory cell number, is observed in the early postoperative period after pulmonary resection, empyema should be considered first and foremost.



**Fig. 4.** Thoracoscopic imaging findings.

(a, b) The pleural effusion is not purulent and there is no fibrin formation in the thoracic cavity: the case is not empyema.

**Table 1**  
Pleural effusion data.

Collection day	Postoperative day	12	15
Collection method		Thoracentesis	Thoracoscopy
Leukocyte fraction (%)			
Neutrophils	15	19	
Lymphocytes	40	63	
Monocytes	25	7	
Eosinophils	21	11	
Bacterial culture		Negative	Negative
Cytology		N/A	Negative

**Table 2**  
DLST stimulation index (%).

	POD 20	POD 48
Fibrin glue (Beriplast P®)	180 <sup>a</sup>	110
Polyglycolic acid sheet (Neovail sheet®)	120	100

DLST; drug lymphocyte stimulation test, POD; postoperative day.

<sup>a</sup> ≥180% is considered positive.

In this case, although antibacterial drugs were administered for possible empyema, the inflammatory cell number was further elevated, and culture of pleural effusion showed no bacteria. Thoracoscopy was performed because it was considered necessary to observe the thoracic cavity. As a result, empyema was ruled out, and the unnecessary antibacterial drug treatment was discontinued.

Patients with idiopathic eosinophilia are sometimes reported to develop EPE [17,18]. In this case, the patient's comorbidity was secondary eosinophilia, and the use of fibrin glue may have induced the development of EPE. One limitation of this study is that the background of patients who are likely to develop fibrin glue-induced EPE, is unknown. Therefore, it is recommended that data on such cases be accumulated in the future.

#### 4. Conclusion

In cases of pleural effusion on the surgical side, with an increase in inflammatory cells, it is advisable to consider the possibility of fibrin glue-induced EPE, as well as empyema. It is recommended that the leukocyte fraction be examined, if pleural effusion is collected for postoperative pleural effusion.

#### Ethical approval

Ethical approval was not required for our paper because case reports are exempt from ethical approval at our institute.

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#### Author contribution

Nobutaka Kawamoto performed the operation, acquired the data, and drafted the manuscript.

Riki Okita conducted the entire study.

Masanori Okada, Kosuke Ito and Katsutoshi Hirazawa attended to the patient postoperatively.

Hidetoshi Inokawa supervised the writing of the manuscript.

All authors read and approved the final manuscript.

#### Guarantor

Nobutaka Kawamoto

#### Research registration number

We believe this case report does not fall into a research category that requires registration. Therefore, we have not registered it in a publicly accessible database.

#### Declaration of competing interest

All authors have no conflicts of interest.

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