

## Analysis of edema fluids and histologic features of the lung in reexpansion pulmonary edema during video-assisted thoracoscopic surgery

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**R**eexpansion pulmonary edema (PE) is a rare complication of general thoracic surgery; however, it may lead to severe hypoxemia with a mortality as high as 20%.<sup>1</sup> The exact mechanisms of development and resolution of reexpansion PE remain undefined. We present here 2 cases of reexpansion PE in which edema fluids drained from endobronchial tubes during video-assisted thoracic surgery (VATS) for

pneumothoraces. We examined edema fluids and histologic characteristics of the lung and provide evidence of acute inflammatory response and active Na<sup>+</sup> transport in the process of rapid development and resolution of reexpansion PE.

### Clinical Summary

**PATIENT 1.** A 52-year-old man had shortness of breath for 10 days. The chest x-ray film showed a collapsed left lung with a giant bulla. The left upper lobe remained completely collapsed after overnight chest drainage. A double-lumen endobronchial tube was inserted, and both lungs were ventilated at a maximal airway pressure of 20 cm H<sub>2</sub>O. Approximately 1 hour after the start of mechanical ventilation, yellowish and clear fluid drained from the left lung over 30 minutes (20 mL in total). Pulse oximetry was consistently at 100% with the patient breathing 50% oxygen. Once the drainage of fluid subsided, the giant bulla was resected by VATS. A lung tissue sample was also resected from the edematous lingual segment. A postoperative chest x-ray film showed parenchymal infiltration only in the reexpanded lung lobe (Figure 1). A chest x-ray film on the third postoperative day showed resolution of pulmonary edema.

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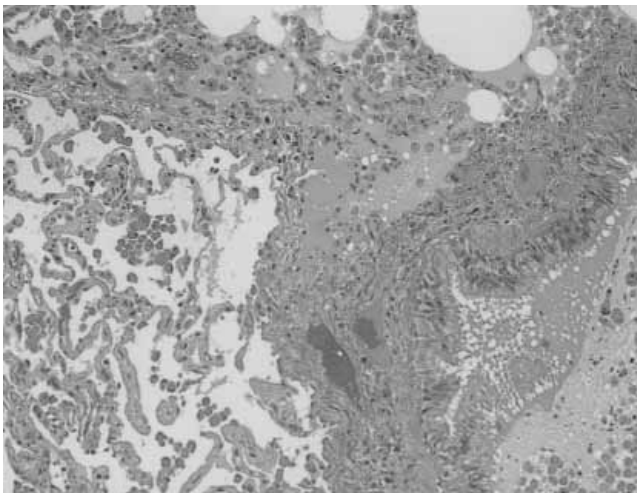
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**Figure 1.** Postoperative chest x-ray films of case 1. Very fine parenchymal infiltration was seen only in the reexpanded lung lobe.



**Figure 2.** Histologic features of the lung in case 2. The alveolar spaces were mostly fluid-free and only fine protein debris was found. Small airways were filled with protein-rich fluids. (Hematoxylin and eosin; original magnification  $\times 200$ .)

**PATIENT 2.** A 30-year-old man had sustained pain in the right side of the chest and shortness of breath for more than a week. A chest x-ray film showed a collapsed right lung with a small bulla in the upper lobe. Overnight chest drainage revealed continuous air leakage, and the right upper lobe remained collapsed. A double-lumen endobronchial tube was inserted, and both lungs were ventilated at a maximal airway pressure of 20 cm H<sub>2</sub>O. Approximately

**TABLE 1.** Laboratory data of tracheal aspirates

	Patient 1 (fluid/serum)	Patient 2 (fluid/serum)
Total protein (g/dL)	6.4/6.1	8.1/6.4
Albumin (g/dL)	4.4/3.8	5.3/3.6
Na <sup>+</sup> (mmol/L)	142/142	138/143
K <sup>+</sup> (mmol/L)	5.5/4.3	7.8/3.8
Cl <sup>-</sup> (mmol/L)	110/105	102/109
Lactate dehydrogenase (U/L)	730/280	2773/409
Interleukin 6 (pg/mL)	3100/3.9	12,300/15.6
Interleukin 8 (pg/mL)	773/<12.5	1260/<12.5
GM-CSF* (pg/mL)	Not measured	30/8
Granulocyte elastase ( $\mu$ g/mL)	Not measured	2760/107

\*Granulocyte macrophages-colony stimulating factor.

1 hour after starting mechanical ventilation, yellowish and clear fluid (10 mL in total) drained from the right lung for 30 minutes. Pulse oximetry was consistently at 100% with the patient breathing 50% oxygen. Once fluid drainage subsided, a bulla at the edematous right upper lobe was resected by VATS. A postoperative chest x-ray film showed parenchymal infiltration only in the reexpanded lung lobe. A chest x-ray film revealed clearing of the edema on the second postoperative day.

Total protein and albumin concentrations in edema fluids were higher than those in serum, whereas Na<sup>+</sup> and Cl<sup>-</sup> concentrations were similar. Levels of inflammatory cytokines such as interleukin 8 were also markedly elevated in the face of the almost normal levels in serum (Table 1). The cell count in edema fluid of patient 1 was 250 cells/mm<sup>3</sup>, with 49% neutrophils, 9% lymphocytes, and 42% macrophages.

Light microscopic examination of the resected lung tissues showed markedly dilated lymphatic vessels in the pleura and perivascular area. However, the alveolar spaces were mostly fluid-free and only fine protein debris was found. Protein-rich fluids existed in small airways (Figure 2).

## Discussion

High protein concentration in edema fluids indicates that our 2 cases of reexpansion PE were examples of high-permeability edema. In addition, neutrophils and high levels of inflammatory cytokines in the fluids suggest that an acute inflammatory response took place in the reexpanded lung.<sup>2</sup> Inflammatory cytokines such as interleukin 8 activate neutrophils and alter permeability of the alveolar-capillary barrier. However, we found total protein and albumin at higher concentrations than those in serum, suggesting that lung edema fluids had been condensed before collection. This is different from our previous observation in reexpansion PE during thoracotomy, which was performed to remove gigantic intrathoracic sarcomas.<sup>2</sup> We found high protein concentration in lung edema fluids; however, the fluid/blood concentration ratio did not exceed 1.<sup>2</sup> Inasmuch as there were no differences in Na<sup>+</sup> or Cl<sup>-</sup> concentrations between edema fluids and serum, it is very unlikely that the fluids simply evaporated in the endobronchial tube. Rather, lung edema fluids might be absorbed in part from the alveolar spaces. Histologic studies of the lung in both cases showed interstitial

edema, whereas the alveolar spaces were mostly fluid-free when the small airways were filled with protein-rich edema fluids.

Fluid absorption from the alveolar spaces may depend in part on active Na<sup>+</sup> transport of the alveolar epithelium.<sup>3</sup> Resected human lungs are known to display active Na<sup>+</sup> transport with alveolar fluid clearance at a rate of 12% in 4 hours.<sup>4</sup> Active Na<sup>+</sup> transport produces fluid movement from the alveolar spaces into the interstitium and lymphatic vessels. Sieving of larger molecules at the alveolar epithelium may then increase albumin concentration in the air space without significant changes in electrolyte concentrations. Assuming that albumin concentrations in the air space were equal to serum at the onset of reexpansion PE, lung edema fluids were roughly calculated to be concentrated to 1:1.16 (86%) and 1:1.47 (68%) in volume over 90 minutes, giving 9% and 21% per hour clearance of alveolar fluid in patients 1 and 2, respectively. The faster clearance rate in our cases of reexpansion PE may be explained by the presence of blood flow and mechanical ventilation. The latter may increase the alveolar surface area and accel-

ate fluid movement across the alveolar epithelium. Continuous positive airway pressure is reported to be beneficial in the treatment of reexpansion PE.<sup>5</sup>

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