

## CASES

## Re-expansion pulmonary edema following thoracentesis

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A 24-year-old man was admitted with a two-day history of shortness of breath and right chest pain. He had an eight-pack-year history of smoking with no significant medical history. He was febrile (temperature 38.6°C), tachycardic, and dyspneic at rest. There was dullness to percussion over the right side of his chest that extended from the midzone to the base; coarse crepitations and bronchial breath sounds were heard above the area of dullness. The rest of his physical examination was unremarkable.

Laboratory examination showed a low hemoglobin level of 103 g/L (normal 135–175) and an elevated leukocyte count of  $18.0 \times 10^9/L$  (normal 3.5–11.0) with 92% neutrophils. His liver and renal profiles were normal. A chest radiograph showed a moderate pleural effusion on the right side (Figure 1A). A computerized tomogram of the chest confirmed a loculated pleural effusion with nodular infiltrates in the right lower and middle lobes, with no masses or lymphadenopathy. After we drained 800 mL of fluid via thoracentesis, a repeat chest radiograph showed no change in the size of the effusion. We made a preliminary diagnosis of pneumonia with empyema and started empirical treatment with piperacillin–tazobactam 4.5 g intravenously every six hours. Analysis of the pleural fluid, with cultures positive for *Streptococcus pneumoniae*, confirmed our clinical diagnosis of empyema. We scheduled a video-assisted thoracoscopic decortication and drainage of the empyema.

Preoperative bronchoscopy excluded endobronchial lesions. Thoracoscopy showed a multiloculated and fibrinous empyema, with entrapment of the right lower lobe. Evacuation of the empyema and decortication through a right lateral thoracotomy resulted in complete re-expansion of the right lung with no parenchymal lung injuries. Two chest tubes were inserted, and the endotracheal tube was successfully removed.

An hour later, the patient had shortness of breath. He was tachycardic and normotensive, a few scattered crepitations were heard on the right side, and the oxygen saturation was 89% (normal 93%–100%). A chest radiograph showed pulmonary vascular congestion over the entire right lung with both chest tubes in situ, consistent with re-expansion pulmonary edema (Figure 1B). We started noninvasive ventilation with bi-level positive airway pressure. Over the next few hours, the patient's condition improved and the ventilation was stopped. The following day, a chest radiograph showed a well-expanded right lung with no evidence of pulmonary congestion (Figure 1C).

### Key points

- Re-expansion pulmonary edema is an uncommon complication following drainage of a pneumothorax or pleural effusion.
- Clinical presentations include cough, chest discomfort and hypoxemia; if the edema is severe, shock and death may ensue. Symptoms are usually noted within 24 hours after thoracentesis.
- Treatment is generally supportive, ranging from oxygen supplementation to noninvasive and invasive ventilation.
- Preventive strategies include the use of low negative pressure ( $< -20$  cm H<sub>2</sub>O) for suction during thoracentesis and limiting drainage of pleural fluid if the patient reports chest discomfort.

### Discussion

The possibility of re-expansion pulmonary edema following drainage of pleural effusion or pneumothorax has been recognized for decades.<sup>1</sup> The reported incidence following drainage of a pleural effusion and pneumothorax has been between 0% and 1% in most studies.<sup>2</sup> These estimates likely reflect widespread under-reporting, since re-expansion pulmonary edema in many instances is clinically mild and detected only using radiography.<sup>3</sup>

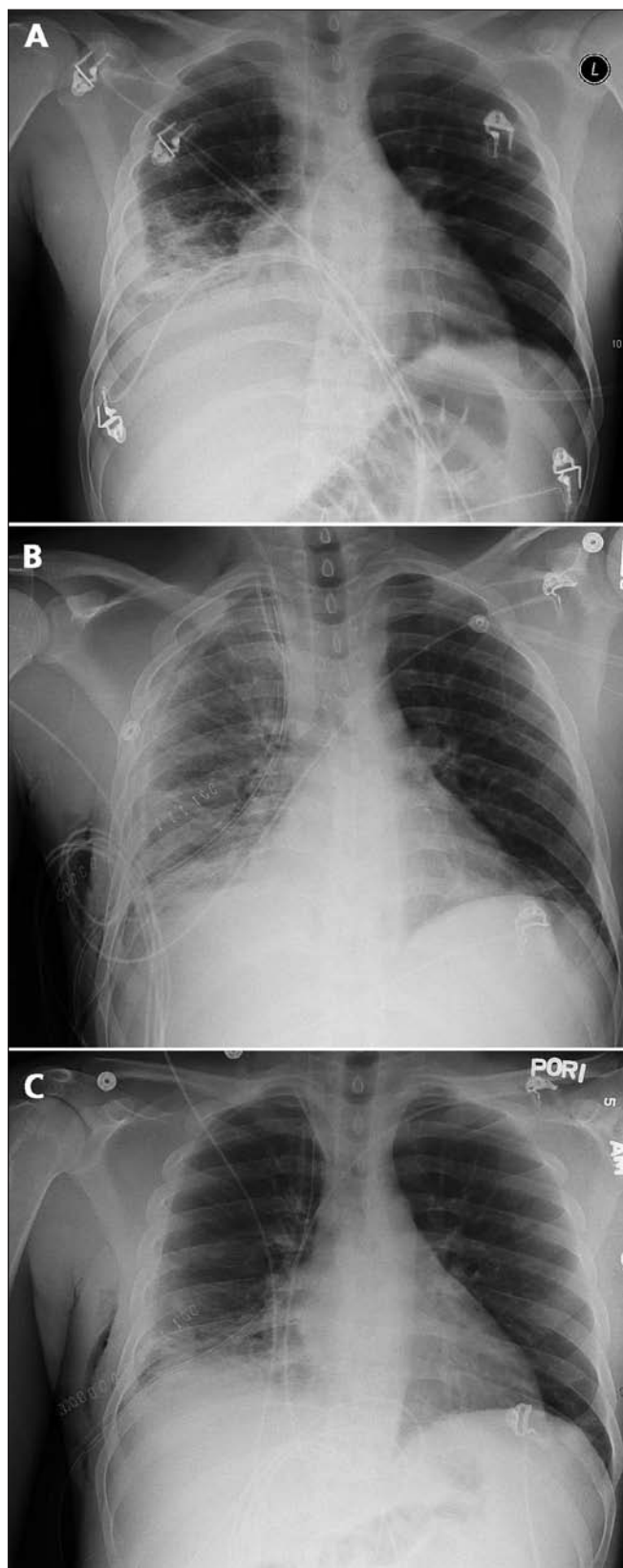
### Clinical features

Symptoms of re-expansion pulmonary edema include chest discomfort, persistent severe cough, production of frothy sputum and dyspnea. The onset of symptoms is usually within 24 hours, with 64% of patients having onset within 1–2 hours after lung re-expansion.<sup>3</sup> The cardinal signs are tachypnea, tachycardia, and crackles on the affected side of the lung as well as hypoxemia, which may be refractory to oxygen therapy. The edema generally affects the entire re-expanded lung. Occasionally, it may affect a single lobe or the contralateral lung, or it may be a bilateral process.<sup>3</sup> A chest radiograph is usually diagnostic.

Although most patients completely recover within five to seven days, severe re-expansion pulmonary edema can lead to

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**Figure 1:** (A) Chest radiograph of a 24-year-old man with pneumonia showing pleural effusion on the right side. (B) Pulmonary edema after surgical decortication and drainage of the pleural effusion. (C) Resolution of the pulmonary edema 24 hours later.

sequestration of large quantities of fluid in the lung, which may result in shock and possibly death.<sup>3,4</sup>

Proposed risk factors include age between 20 and 40 years,<sup>5</sup> duration of collapse greater than 72 hours, the application of high negative pressures during thoracic drainage ( $> 20$  cm H<sub>2</sub>O), and rapid lung expansion with drainage of large volumes of pleural fluid ( $> 1.5$  L).<sup>3</sup>

### Pathophysiology

Although the pathophysiology of re-expansion pulmonary edema is multifactorial and poorly understood, new investigations are uncovering possible mechanisms. One of the more promising theories suggests that the root of the condition is increased permeability of the pulmonary capillaries as a result of inflammation. Ventilation and reperfusion of a previously collapsed lung may lead to an inflammatory response, with production of reactive oxygen species and superoxide radicals, a sequence of events that ultimately results in increased capillary permeability. Inflammatory mediators, including interleukin 8, leukotriene B<sub>4</sub> and monocyte chemoattractant activating factor, are pivotal in this inflammatory response.<sup>4</sup> Another recent study identified a signaling pathway of the small guanosine triphosphate-binding protein Rho and its target protein ROCK (Rho-associated coiled-coil-forming protein kinase) as a possible mechanism. The activation of Rho via the action of its target protein causes phosphorylation of myosin light chains, actomyosin contraction and dysfunction of the endothelial barrier cells.<sup>6</sup>

Alternatively, research suggests that mechanisms such as increased pulmonary hydrostatic pressure caused by enhanced venous return, pressure-induced mechanical disruption of the alveolar capillaries, decreased levels of functional surfactant, increased pressure across the capillary–alveolar membrane from bronchial obstruction and altered lymphatic clearance may also lead to re-expansion pulmonary edema in some patients.<sup>3</sup>

Although our patient had a pre-established empyema and lung collapse, the contribution of thoracotomy and decortication cannot be overlooked given the rapid onset of symptoms of re-expansion pulmonary edema (within one hour after surgery). Evidence linking endoscopic and open thoracotomy to the development of re-expansion pulmonary edema is limited to a few reports.<sup>7</sup> We speculate that in our patient, the surgical stress during thoracotomy may have induced a clinical or subclinical pulmonary inflammation, which in turn may have provided a “second hit” mechanism for the development of the pulmonary edema. Further reason to consider this possibility is evidence that one-lung ventilation during unilateral thoracotomy, as was done in our patient, has been shown to change the partitioning of blood flow between the nondependent and dependent lungs.<sup>8</sup>

### Treatment

Prompt recognition is paramount in ensuring successful treatment of re-expansion pulmonary edema. Management is generally supportive but varies by severity of the condition. Whereas oxygen supplementation may prove adequate in patients with mild symptoms, those with severe symp-

toms require endotracheal intubation and mechanical ventilation.<sup>3</sup> In patients with worsening symptoms, the use of noninvasive ventilation with bi-level positive airway pressure may help to circumvent the need for endotracheal intubation.<sup>9</sup> Having the patient lie on his or her unaffected side is therapeutic in unilateral pulmonary edema.<sup>6</sup> Evidence supporting the use of diuretics, bronchodilators, prostaglandin analogues (e.g., misoprostil), ibuprofen and steroids remains anecdotal.<sup>9</sup>

### Prevention

Preventive strategies include the use of low negative pressure (< -20 cm H<sub>2</sub>O) for suction during tube thoracostomy and limiting drainage to about 1 to 1.5 L of pleural fluid.<sup>9</sup> Recent evidence suggests that large-volumes can be safely drained as long as pleural pressures are monitored.<sup>1,10</sup> If the patient reports vague chest pressure during thoracentesis, this may indicate a precipitous drop in intrapleural pressure, and the thoracentesis should be stopped. Pleural manometry is being increasingly advocated for the drainage of large pleural effusions.<sup>10</sup>

This article has been peer reviewed.

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ATIVAN is contraindicated in patients with myasthenia gravis or acute narrow angle glaucoma, and in those with known hypersensitivity to benzodiazepines.

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