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REVIEW ARTICLE

An uncommon complication of a common clinical scenario: exploring reexpansion pulmonary edema with a case report and literature review

Jared W. Meeker, DO[1,2]*, Amy L. Jaeger, MD[1,2] and William P. Tillis, MD[1,2]

[1]Internal Medicine, University of Illinois College of Medicine at Peoria, Peoria, IL, USA; [2]Illinois Lung & Critical Care Institute, OSF Saint Francis Medical Center, Peoria, IL, USA

Reexpansion pulmonary edema (RPE) is a rare complication that can occur after rapid reinflation of the lung following thoracentesis of a pleural effusion or chest tube drainage of pneumothorax. The severity in clinical presentation can be widely varied from radiographic changes only to rapidly progressive respiratory failure requiring mechanical ventilation. The quick nature of onset and potential for serious decline in a previously stable patient makes it important to prepare, recognize, diagnose, and appropriately manage patients who develop RPE. The standard treatment for RPE consists of supportive care, and there are certain measures that may be taken to reduce the risk, including limiting the amount drained and avoiding excessive negative pleural pressure. Exactly how to prevent RPE remains unclear, however, and varying recommendations exist. This is a case report of RPE after thoracentesis for a pleural effusion and a brief review of literature to date, including potential preventative strategies.

Keywords: *thoracentesis*; *pleural effusion*; *pneumothorax*; *drainage*; *chest tube*; *ventilation*

*Correspondence to: Jared W. Meeker, 3127 N Sheridan Rd., Peoria, IL 61604, USA, Email: jared.w.meeker@gmail.com

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A 60-year-old male with a medical history of end-stage renal disease on hemodialysis, myasthenia gravis in remission, and chronic hepatitis C initially presented to the emergency department with pleuritic chest pain, dyspnea, and a dry cough starting a couple days prior. He had received hemodialysis the day of admission and was at his dry weight. Two view CXR in the emergency department showed a large left pleural effusion and small right pleural effusion (Fig. 1). He had a CT angiography of the chest with and without contrast done as well which revealed filling defects within the right upper and lower segmental and subsegmental pulmonary arteries, representing pulmonary thromboemboli. Bilateral pleural effusions were again demonstrated and a small pericardial effusion was noted. The patient was started on prednisone for suspected pericarditis and a heparin drip for the pulmonary emboli. He underwent dialysis the following morning with 1.5 L removed. Shortly after, he underwent thoracentesis of the large left pleural effusion removing 1.5 L. A post-procedure CXR showed significantly improved left lung aeration and no pneumothorax (Fig. 2). Within 1 min of the thoracentesis, the patient began to decompensate with increasing dyspnea, hypoxia, tachypnea, and cough. He was placed on non-invasive positive-pressure ventilation; however, desaturations persisted between 70 and 80% and he was transferred to the medical intensive-care unit less than 2 h after his procedure. The patient developed diffuse crackles throughout the left lung fields requiring emergent intubation for acute respiratory failure with a series of CXRs demonstrating worsening left lung opacification (Fig. 3). He also became hypotensive requiring central line placement for administration of vasopressors. His left lung remained entirely opacified on CXR 4 h after the thoracentesis (Fig. 4). He was placed on pressure-regulated volume control with a tidal volume of 400 mL, respiratory rate of 14 and required a PEEP of 10 and FiO_2 of 60%. Oxygenation was improved by placing the patient in the right lateral decubitus position. Ventilator settings were weaned to a PEEP of 8 and FiO_2 of 40% in the morning. Over the course of his 20-day hospitalization, he was extubated, oxygen was slowly weaned down, and he was treated for a healthcare-associated pneumonia with IV vancomycin and piperacillin–tazobactam. During the latter portion of his stay, the patient underwent a second thoracentesis for reaccumulation of the left effusion and interestingly, the patient had less severe recurrence of reexpansion pulmonary edema (RPE). Ultimately with

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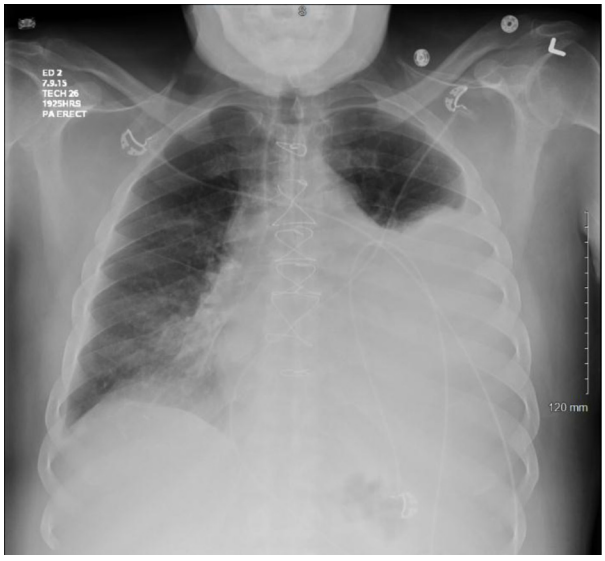

Fig. 1. PA erect CXR prior to thoracentesis reveals large left pleural effusion.

supportive care, the patient was able to discharge home significantly improved.

Discussion

RPE is a rare but potentially fatal complication, often after thoracentesis of pleural fluid as described in this case. While the effects are well described and recognizable, the etiology remains unclear.

Epidemiology

The prevalence is quite rare, generally cited as less than 1% of cases. The range reported in the literature varies significantly, however, ranging from 0.3 to 32.5% (1, 2). This is likely due to differences in definition (clinical vs. radiographic), small sample sizes, and different patient

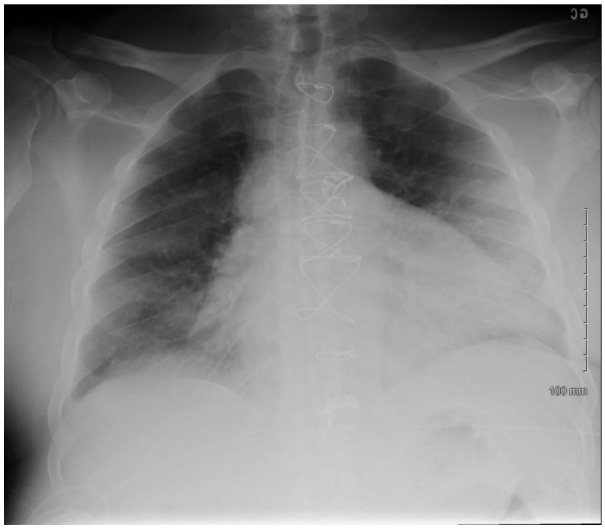

Fig. 2. AP semi-erect taken 30 min after thoracentesis with significant improvement.

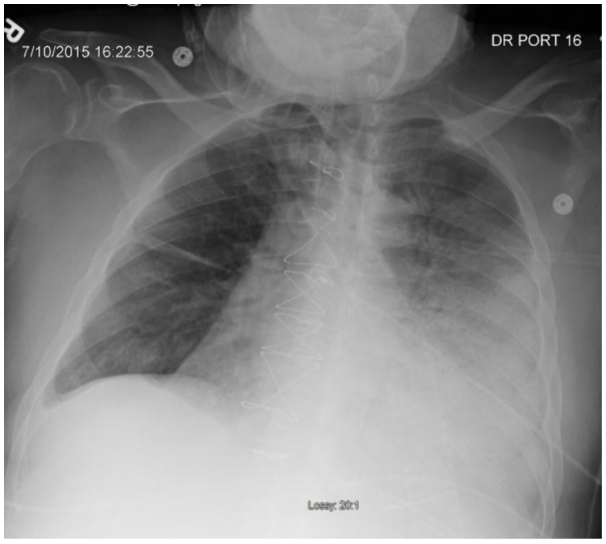

Fig. 3. AP upright 2 h after thoracentesis with early evidence of reexpansion pulmonary edema.

populations. Different etiologies of RPE tend to give different numbers when studied together as well. Taira et al. only studied 40 patients retrospectively, and they all had spontaneous pneumothorax prior to RPE. That particular study found RPE in 13 of the 40, or 32.5%, and concluded that the incidence may be higher than previously reported. Also, strict CT-based criteria for diagnosis were used that were more sensitive than radiographic or clinical criteria (2). Feller-Kopman et al. conducted a prospective study of 185 individuals with varying amounts of pleural fluid removed by thoracentesis with an incidence of clinical RPE at 0.5% and radiographic RPE at 2.2% (3). Yoon et al.

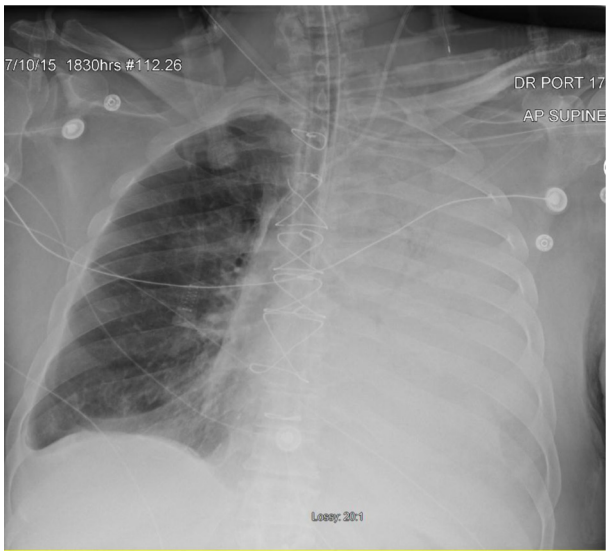

Fig. 4. AP supine 4 h after thoracentesis with evidence of florid reexpansion pulmonary edema requiring intubation and left internal jugular central venous catheter placement for vasopressor support.

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again cited the incidence higher in a population with spontaneous pneumothorax at 16% (4). As the higher numbers tend to be based on radiographic data, a more accurate and useful assessment would be that clinically significant RPE is an occurrence of less than 1%.

The mortality rate is often cited at 20%; however, that number appears to have come from one study of 53 patients and is likely an overestimation (5). More recent studies have found it to be much lower (2, 4). With such low prevalence, prognosis is difficult to estimate.

Although the pathophysiology at this time is not fully elucidated, there are risk factors to be aware of. Taira et al. found the presence of pleural effusion in conjunction with a pneumothorax increased risk but duration of symptoms, size of pneumothorax, and location had minimal effect (2). In the 185 patients studied prospectively by Feller-Kopman et al. in 2007, they found RPE was independent of the volume removed, pleural pressures, and pleural elastance; instead recommending that large pleural effusions be drained completely (3). Yoon et al. showed in a retrospective study of 306 patients that RPE was more common in patients with diabetes and tension pneumothorax, and found those with RPE tended to have a larger pneumothorax than those without (4). Another study of 146 cases of spontaneous pneumothorax found the rate of RPE to be higher in persons aged 20–39 than in those over 40 and again correlated with size of pneumothorax (6). After a review of 233 papers, Echevarria and colleagues determined that the patients at highest risk are those with large pneumothoraces, young patients, those with lung collapse for more than 1 week, and those needing 3 L of fluid drained (7).

Pathophysiology

Several underlying mechanisms have been postulated as follows. Excessive negative pleural pressures have long been thought of as a major contributor to RPE. Several authors have suggested avoiding pleural pressures less than -20 cm H_2O for this reason. This was first based on animal models (8, 9). Other authors since have found it less important or that RPE may be completely independent of the pleural pressure (3, 10).

A paper describing two cases of RPE showed marked increases in polymorphonuclear neutrophils (PMNs) and PMN-elastase with elevated fluid to plasma protein concentration. Thromboxane B2 and 6-keto-PGF1-alpha concentrations were elevated as well. This suggested inflammatory mechanisms leading to microvascular permeability (11). Interleukin (IL)-8 and leukotriene B-4 have been observed in edema fluid (as well as PMN-elastase again and P-selectin) (12). Experimental rabbit models for RPE showed up-regulation of pro-inflammatory cytokines as well but no significant difference in capillary permeability (13).

As opposed to prior studies that had suggested a mechanism based primarily on increased capillary permeability (11, 12, 14–16), Sue et al. found using edema to plasma protein ratios in a retrospective analysis that hydrostatic mechanisms may play a more significant role (17). Sohara asserts histological abnormalities of the pulmonary microvasculature result from a collapsed lung in the order of days, as well as mechanical stress during reexpansion, are the mechanisms driving RPE (18). These histologic changes may be mediated by inflammatory cytokines as previously suggested as well as oxidative stress.

Experimental studies in rats were able to demonstrate, with statistical significance, higher levels of a marker for oxidative stress, malondialdehyde (MDA), in the experimental groups (19). Additional studies on rats also suggest tissue reperfusion, hypoxia, and free radical damage by lipid peroxidation in a collapsed lung as a mechanism for injury and edema (16). It is likely these all contribute in varying degrees depending on the particular clinical scenario.

Clinical presentation

RPE may be a radiographic finding only in mild cases. When clinically significant, signs and symptoms may include a new cough generally lasting more than 20 min, dyspnea, tachypnea, hypoxia, tachycardia, chest pain, or hemodynamic instability (3, 10, 20, 21). Most patients are symptomatic within an hour after pleural drainage, although it can occur at any point within 24 h (10, 21). CT findings most commonly include ipsilateral ground-glass opacities, septal thickening, consolidation, and persistent areas of atelectasis (22). Edema most commonly occurs in the ipsilateral lung, but can present in the contralateral lung or bilaterally (22, 23).

Treatment

Currently, the mainstay treatment for RPE is supportive care with supplemental oxygen and diuretics. Steroids and hemodynamic support are sometimes used in severe cases, although rare (2, 18, 24). Other clinicians recommend positioning the patient in lateral decubitus with the affected side down with noninvasive positive pressure or orotracheal intubation with mechanical ventilation if the RPE is more severe (10). There have been a few case studies demonstrating successful outcomes of severe RPE with alternative treatment methods. One case study by Cho demonstrated a very severe case of RPE requiring a double-lumen endobronchial tube with asynchronous differential lung ventilation for 48 h before ventilation profusion mismatch was restored (25). Pretreatment with IL-8 neutralizing antibody to combat overproduction of IL-8 during lung collapse and reexpansion has shown promise in rabbits (15). Similarly alpha-lipoic acid (ALA) has been suggested as a treatment option by reduction of oxidative stress, demonstrated in rat models (19). Although these small animal studies are promising, they have limited clinical utility thus far in clinical medicine. Most cases require only minimal supportive care. As severe RPE is exceedingly rare, more emphasis has been placed

on prevention. Avoidance of pleural pressures less than -20 cm H_2O and removing less than 1.8 L are often cited methods (3, 10, 26), though the data is limited.

Conclusion

This is a classic case of RPE and demonstrates the potential for its sudden onset and severity. The condition does appear to be more benign than previously thought, and clinically significant episodes are rare. In severe cases such as this one, proper support with mechanical ventilation, diuretics, and hemodynamic support are pillars of treatment. Our particular patient benefited significantly from lateral decubitus position ventilation with the affected side up. How to best prevent RPE is still up for debate. Many studies investigating the pathophysiology and preventative techniques are too small to have adequate power. There are some general guiding principles that appear to help minimize risk, including the avoidance of extreme negative pleural pressures, limiting the amount taken off at one time, stopping with symptoms like chest pain and cough, and recognizing patients at higher risk. Irrespective of the cutoffs used, this rare complication can be managed effectively with supportive care most of the time. Further research, especially larger studies, may be beneficial in understanding and further minimizing the risks associated with RPE.

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Conflict of interest and funding

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