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 \textit{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).

Discussion

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

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. 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. A chest radiograph is usually diagnostic.

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

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 H₂O) for suction during thoracentesis and limiting drainage of pleural fluid if the patient reports chest discomfort.

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Proposed risk factors include age between 20 and 40 years, duration of collapse greater than 72 hours, the application of high negative pressures during thoracic drainage (> 20 cm H2O), and rapid lung expansion with drainage of large volumes of pleural fluid (> 1.5 L).

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 B4 and monocyte chemotactic activating factor, are pivotal in this inflammatory response. 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.

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.

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. 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.

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-
Practice

toms require endotracheal intubation and mechanical ventilation. 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.10 Having the patient lie on his or her unaffected side is therapeutic in unilateral pulmonary edema. Evidence supporting the use of diuretics, bronchodilators, prostaglandin analogues (e.g., misoprostil), ibuprofen and steroids remains anecdotal.9

Prevention

Preventive strategies include the use of low negative pressure (<-20 cm H2O) for suction during tube thoracostomy and limiting drainage to about 1 to 1.5 L of pleural fluid.9 Recent evidence suggests that large-volumes can be safely drained as long as pleural pressures are monitored.1,10 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.10

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REFERENCES

1. Feller-Kopman D, Berkowitz D, Boiselle P, et al. Large-volume thoracentesis and the risk of reexpansion pulmonary edema. *Ann Thorac Surg* 2007;84:1656-61.
2. Echevarria C, Twomey D, Dunning J, et al. Does re-expansion pulmonary oedema exist? *Interact Cardiovasc Thorac Surg* 2008;7:485-9.
3. Mahfood S, Hix WR, Aaron BL, et al. Reexpansion pulmonary edema. *Ann Thorac Surg* 1998;54:340-5.
4. Sherman SC. Reexpansion pulmonary edema: a case report and review of the current literature. *J Emerg Med* 2003;24:23-7.
5. Matsura Y, Nomimura T, Murakami H, et al. Clinical analysis of reexpansion pulmonary edema. *Chest* 1991;100:1562-6.
6. Sawafuji M, Ishizaka A, Kohno M, et al. Role of Rho-kinase in reexpansion pulmonary edema in rabbits. *Am J Physiol Lung Cell Mol Physiol* 2005;289:L946-53.
7. Suzuki S, Niikawa H, Shibuya J, et al. Analysis of edema fluids and histologic features of the lung in reexpansion pulmonary edema during video-assisted thoracoscopic surgery. *J Thorac Cardiovasc Surg* 2002;123:387-47.
8. Barbierakis N, Samanidis G, Palouzas D, et al. Re-expansion pulmonary edema following video-assisted thoracic surgery for recurrent malignant pleural effusion. *Interact Cardiovasc Thorac Surg* 2008;7:532-4.
9. Iqbal M, Multz AS, Rossiff LJ, et al. Reexpansion pulmonary edema after VATS successfully treated with continuous positive airway pressure. *Ann Thorac Surg* 2000;70:669-71.
10. Feller-Kopman D, Parker MJ, Schwartzstein RM. Assessment of pleural pressure in the evaluation of pleural effusions. *Chest* 2009;135:201-9.

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ATIVAN is useful for the short-term relief of manifestations of excessive anxiety in patients with anxiety neurosis. It is also useful as an adjunct for the relief of excessive anxiety that might be present prior to surgical interventions. Anxiety and tension associated with the stresses of everyday life usually do not require treatment with anxiolytic drugs.

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

Severe anaphylactic/anaphylactoid reactions have been reported with the use of benzodiazepines. Cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses of benzodiazepines. Some patients taking benzodiazepines have had additional symptoms such as dyspnea, throat closing or nausea and vomiting. Some patients have required medical therapy in the emergency department. If angioedema involves the tongue, glottis, or larynx, airway obstruction may occur and be fatal. Patients who develop angioedema after treatment with a benzodiazepine should not be rechallenged with the drug.

ATIVAN is not recommended for use in depressive neurosis or in psychotic reactions. Because of the lack of sufficient clinical experience, lorazepam is not recommended for use in patients less than 18 years of age. Since ATIVAN has a central nervous system depressant effect, patients should be advised against the simultaneous use of other CNS depressant drugs. Patients should also be cautioned not to take alcohol during the administration of lorazepam because of the potentiation of effects that may occur. ATIVAN should not be used during pregnancy. Since lorazepam is also a benzodiazepine derivative, its administration is rarely justified in women of childbearing potential. ATIVAN should not be administered to breast-feeding women, unless the expected benefit to the mother outweighs the potential risk to the infant.

Use of benzodiazepines, including lorazepam, may lead to potentially fatal respiratory depression. Excessive sedation has been observed with lorazepam at standard therapeutic doses. The most frequently reported adverse reaction to ATIVAN was drowsiness. See prescribing information for complete adverse reaction information.

The lowest effective dose of ATIVAN should be prescribed for the shortest duration possible. The risk of withdrawal and rebound phenomena is greater after abrupt discontinuation; therefore, the drug should be discontinued gradually. Withdrawal symptoms (e.g., rebound insomnia) can appear following cessation of recommended doses after as little as one week of therapy. Abrupt discontinuation of lorazepam should be avoided and a gradual, dose-tapering schedule followed after extended therapy. ATIVAN should not be administered to individuals prone to drug abuse. Lorazepam may have abuse potential, especially in patients with a history of drug and/or alcohol abuse.