Postpneumonectomy Pulmonary Edema*  
Can It Be Predicted Preoperatively?  
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Postpneumonectomy pulmonary edema (PPE) is a rarely reported form of acute lung injury which occurs in up to 4% of all pneumonectomies. The details of two well-documented cases of PPE are described with special emphasis paid to the preoperative lung functions. Both cases illustrated a striking disparity between preserved spirometric lung function and advanced emphysema as detected by quantitative CT emphysema scores and single-breath diffusion of carbon monoxide measurements. Though retrospective in nature, these results suggest a restricted capillary volume plays a critical role in the development of PPE.  
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Key words: acute lung injury; adult respiratory distress syndrome; computed tomography; postpneumonectomy pulmonary edema; pulmonary artery; pulmonary artery occlusion pressure; single-breath diffusion of carbon monoxide

Postpneumonectomy pulmonary edema (PPE) is a form of acute lung injury which follows resectional lung surgery. Though it has been well-described in the thoracic surgery medical literature, its pathogenesis remains unclear.1,3 Some authors attribute it to an increase in pulmonary capillary hydrostatic pressure which results from the combined effects of lung resection and a positive perioperative fluid balance.1,3 Others believe that an increase in pulmonary capillary permeability is the primary mechanism.2 This report contains two well-documented cases of PPE. In both cases, a striking disparity was noted between normal spirometric lung function and advanced emphysema as detected by quantitative CT emphysema scores and, in one of the cases, by single-breath diffusion of carbon monoxide (Dsb) measurements as well. A possible explanation of these findings based on the concept of critical reductions in pulmonary capillary volume (Vc) is proposed.

METHODS
Criteria for the diagnosis of PPE were similar to those of Turnage and Lunn.5 At presentation 2 to 5 days following lung resection, all patients were in acute hypoxicemic respiratory failure. Chest x-ray films demonstrated unilateral infiltrates which progressed from an interstitial to an alveolar pattern. In each case, left ventricular dysfunction (or volume overload) was ruled out by serial cardiac enzymes, pulmonary artery (PA) catheter measurements, and transthoracic or transesophageal echocardiography. At the time of presentation, there was no prevailing clinical or laboratory evidence to suggest pneumonia, sepsis, or aspiration. Preoperative spirometric functions and Dsb measurements were performed on a rolling-seal spirometer (Collins CS modular PFT) utilizing standard techniques suggested by the American Thoracic Society.4 All Dsb measurements were corrected for measured hemoglobin and for carbon monoxide back-diffusion by standard methods.5 Alveolar volume was obtained during the Dsb by helium dilution and then used to correct Dsb for total surface area available for diffusion (Dsb/ alveolar volume). All measurements are expressed in absolute values and as percent predicted based on predicted norms.4,6 All CT scans were obtained at 1-cm intervals from apex to diaphragm at full inspiration using 10-mm collimation. Scans were viewed using appropriate window levels by three different radiologists who were unaware of the clinical history or diagnosis. Each radiologist was asked to quantify the degree of emphysema utilizing a visual scale described by Goddard and associates.7 In this method, each lung slice is visually assessed for areas of low attenuation and vascular disruption. A score of zero represented no abnormality; 1 represented abnormalities involving up to 25% of the lung field; 2, between 25 and 50%; 3, between 50 and 75%; and 4, for near-total involvement. The scores were averaged and expressed as a percentage of the maximum CT score (number of slices × 4) and are shown in Table 1. For this study, a score of 0 to 25 was considered "mild"; a score of 25 to 50 was considered "moderate"; and any score over 50 was thought to be "severe."

REPORT OF CASES

Case 1
A 61-year-old white man with an 80 pack-year history of smoking presented with a persistent cough. An x-ray film of the chest showed an infiltrate of the lower lobe of the left lung with volume loss. A CT scan displayed a left perihilar mass in addition to the postobstructive pneumonia of the lower lobe of the left lung. Also noted were changes consistent with advanced emphysema (Fig 1). Bronchoscopy biopsy specimens were positive for

Abbreviations: Dsb=single-breath diffusion of carbon monoxide; PA=pulmonary artery; PAOP=PA wedge pressure; PAP=PA pressure; PPE=postpneumonectomy pulmonary edema; Vc=capillary volume

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squamous cell carcinoma involving the proximal left lower lobe bronchus. Preoperative pulmonary function testing showed an FVC of 4.09 L (96%), an FEV₁ of 3.30 L/s (110%), an FEV₁/FVC ratio of 81%, and MMEF of 3.02 L/s (103%). Db measurements were not obtained. With the patient breathing room air, blood gas determinations revealed a pH of 7.46, a PCO₂ of 32 mm Hg, and a PaO₂ of 57 mm Hg.

Following resection of the lower lobe of the left lung, a completion pneumonectomy was performed due to a positive tumor margin. During the first 24 h, the patient had a net positive fluid balance of 4,500 mL. Thereafter, fluid balance was maintained with intermittent doses of intravenously administered furosemide. On postoperative day 2, crackles were heard in the base of the right lung, but the chest x-ray film showed no new infiltrates. On postoperative day 5, the patient was noted to be dyspneic with a resting tachycardia and a pulse oximetry saturation of only 60% while receiving nasal cannula oxygen at a rate of 4 L/min. A cardiac examination revealed prominent neck veins, a right ventricular S₂, and a murmur consistent with tricuspid regurgitation. Following a “low” probability ventilation-perfusion scan, the patient was transferred to the ICU. A chest x-ray film showed a new interstitial infiltrate developing in the right lower lung field along with left-sided postoperative changes (Fig 2). He was intubated and mechanically ventilated with an FiO₂ of 80%.

A PA catheter was inserted and revealed the presence of mild PA hypertension with a PA systolic/PA diastolic pressure of 44/15 mm Hg and a mean PA pressure (PAP) of 25 mm Hg. The PA wedge pressure (PAOP) was 4 mm Hg, the central venous pressure was 4 mm Hg, the cardiac output was 4.6 L/min, and the calculated systemic vascular resistance and pulmonary vascular resistance were 1,530 and 365 dyne-s · cm⁻⁵, respectively. On the next day, a transesophageal echocardiogram disclosed normal left ventricular function along with right atrial and right ventricular enlargement. Cardiac enzyme levels were not indicative of acute injury. Though all tracheal aspirates and blood cultures were negative for bacterial pathogens, empiric treatment with intravenously administered antibiotics (ceftriaxone disodium and aztreonam) was begun. Two days later, the infiltrates had become more alveolar and spread to involve the entire right lung field. By postoperative day 14, the patient’s PAP was 54/20 mm Hg with a calculated pulmonary vascular resistance of nearly 900 dyne · s/ cm⁻⁵. He was transferred to a referral hospital for consideration of nitric oxide therapy but died shortly after transfer. No autopsy was obtained.

**Case 2**

A 69-year-old Asian man with a 100 pack-year history of smoking and a long-standing seizure disorder was admitted to the hospital for evaluation of hemoptysis. A chest x-ray film showed a lobulated 4 × 7-cm mass of the upper lobe of the right lung. A CT scan of the chest confirmed the findings just mentioned and additionally revealed a small 1 × 1-cm nodule of the lower lobe of the right lung. No mediastinal adenopathy was detected. Lung windows disclosed changes consistent with advanced emphysema.

**Table 1—Emphysema Score as a Percentage of Maximum Possible CT Score**

<table>
<thead>
<tr>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Observer 3</th>
<th>Mean Score and SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>36.93</td>
<td>36.36</td>
<td>42.05</td>
</tr>
<tr>
<td>Patient 2</td>
<td>49.43</td>
<td>39.20</td>
<td>47.73</td>
</tr>
</tbody>
</table>

*N* is too small for valid interobserver analysis.

**Figure 1.** (Case 1). Preoperative CT scan showing moderately advanced emphysema despite normal spirometry.

**Figure 2.** Chest x-ray film of patient 1 at presentation showing postoperative changes (left) and developing reticulonodular infiltrate of the right lung.

**Figure 3.** CT scan of patient 2 showing extensive emphysematous changes. Spirometric function was normal.
inciting cause or trigger unique to pneumonectomy patients. Other investigators believe volume overload contributes to the development of PPE. The present study does not support this theory. Though patient 1 in this series did have a positive fluid balance during the 1st postoperative day, he did not present clinically or radiographically until 4 days later. Hemodynamic measurements, cardiac enzyme levels, echocardiography, and, in case 2, postmortem examination all failed to demonstrate any evidence of volume overload or left ventricular failure.

For over 50 years, investigators have hypothesized that PPE results from critical reductions in pulmonary (Vc). Because of a large unused pulmonary vascular reserve, lung resection is normally tolerated without an increase in mean PAP. Once this reserve is depleted, further resection would lead to increased blood flow to the remaining lung and an increase in PAP if pulmonary vascular resistance remains unchanged. Given a normal PAOP, the pulmonary capillary hydrostatic pressure (Pc) will rise as shown in equation 1:

\[
Pc = PAOP + 0.4 \times \frac{PAP - PAOP}{4}
\]

Such an increase will lead to distention of the remaining capillary bed and move the mean capillary pressure point toward the venous end. The net effect of increasing pulmonary capillary hydrostatic pressure and capillary surface area is an increase in fluid flux and hydrostatic edema if other compensatory mechanisms, such as the lymphatic pump, are overwhelmed. In support of this concept, Zeldin and colleagues convincingly demonstrated PPE in 6 of 13 dogs following right-sided pneumonectomy and 1 of 2 volume infusions. According to their hemodynamic calculations, blood flow to the remaining lung increased five- to six-fold as a result of both volume loading and pneumonectomy. Staub suggested such an increased blood flow and flow velocity may physically injure capillary endothelium, allowing protein-rich fluid to enter the interstitium and the alveolar space.

The two cases reported in this communication indirectly support the role of critical reductions in Vc in the pathogenesis of PPE. Despite normal spirometry, each patient had advanced emphysema as determined by CT emphysema scores (Table 1). Using the visual CT scoring method of Goldklard and associates, all three radiologists scored each patient as having moderately advanced emphysema. Patient 2 in this series had a significantly reduced Dsb which, in the absence of other causes, is also consistent with emphysema. One may suspect that both these measurements reflect advanced emphysema with corresponding reductions in Vc.

Direct measurement of Vc requires a series of Dsb measurements to be obtained at different oxygen concentrations utilizing the method of Roughton and Forster. Unfortunately, such measurements are not routinely available. Even so, it is commonly assumed that Vc is reduced in proportion to the degree of emphysema since emphysema involves destruction of alveolar walls and septa that contain pulmonary capillaries. This idea is supported by the work of Morrison and associates who measured Vc and Dsb in 110 patients undergoing lung resection and

### Discussion

PPE is a poorly understood form of acute lung injury which followed resectional lung surgery. In an autopsy review by Turnage and Lunn, ARDS was demonstrated histologically in 15 or 17 PPE patients. This finding is nonspecific, however, and does not indicate a particular
found both measures were proportionately reduced and correlated (negatively) with the presence of histologic emphysema. Morrison and coworkers\textsuperscript{13} also found a high positive correlation between CT emphysema score and pathologic emphysema, a finding that has been documented by others.\textsuperscript{14,15}

Since \( V_c \) was not measured directly in this study, the proposed link between PPE and \( V_c \) is speculative. If possible, a larger prospective study is needed to ascertain if there is a true relationship between measured \( V_c \) and PPE. Measuring \( V_c \) preoperatively may not be unreasonable in evaluating advanced emphysema patients with preserved spirometric function. Such patients with "non-obstructive emphysema"\textsuperscript{16} who undergo aggressive lung resection may be at increased risk for PPE.

REFERENCES

Hypersensitivity Pneumonitis Due to Humidifier Disease*

Seek and Ye Shall Find

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Study Objectives: This study reports a classic case of hypersensitivity pneumonitis (HP) with classic histologic changes in lung tissue and the research used to identify the causative antigens.

Design: A patient with clinical, radiographic, pulmonary function abnormalities and a lung biopsy consistent with HP had no identifiable antigen exposure.

Setting: Evaluation of the patient’s activities provided no suggestion of antigen exposure. Her home was evaluated. It was found that her humidifier ran continually without being cleaned but water was added periodically.

Conclusion: Removal of the humidifier, cleaning of the house, and a course of prednisone resulted in the return of the patient to a normal state.

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Key words: allergic bronchopulmonary aspergillosis; Aspergillus fumigatus; double gel diffusion; fungal antigens; humidifier disease; hypersensitivity pneumonitis; Ouchterlony technique

Abbreviations: ABPA=allergic bronchopulmonary aspergillosis; HP= hypersensitivity pneumonitis

Hypersensitivity pneumonitis (HP) is also referred to as extrinsic allergic alveolitis. It is the result of inhalation of antigens and occurs in both atopic and nonatopic individuals. HP is an important disease since it may result in acute or chronic illness. Investigative work by leaders in the field defined diseases and suggested diagnostic methods.\textsuperscript{1,2} In patients with chronic HP, unless the diagnosis is

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