Primary Spontaneous Pneumothorax: Looking Beyond the Usual

Primary spontaneous pneumothorax (PSP) refers to a pneumothorax that occurs in patients without underlying pulmonary disease. Emergency physicians are often the first group of health care providers for patients presenting with a PSP. The currently recommended course of management for these patients involves conservative management either with observation (for small pneumothoraces) or with simple aspiration/small bore chest tube placement (for larger/more symptomatic pneumothoraces).\(^1,2\) Consideration of chest computed tomography (CT) scanning to evaluate for the presence of underlying pulmonary disorders and pleurodesis to prevent future events are not recommended while managing patients with the first episode of PSP.\(^1\)

It has been suggested by multiple prior studies that patients presumed to have PSP often have underlying undiagnosed pulmonary abnormalities such as emphysema-like changes and subpleural blebs/bullae that predispose them to the development of spontaneous pneumothorax.\(^3,4\) However, there are other sets of diseases, such as diffuse cystic lung diseases (DCLDs), that predispose patients to the development of recurrent spontaneous pneumothoraces. DCLDs represent a pathophysiologically heterogeneous group of disorders that share a common phenotype of multiple thin-walled, air-filled pulmonary cysts.\(^5\) These cysts are prone to rupture and frequently lead to the development of spontaneous pneumothorax.\(^6\)

Among DCLDs, the most common diseases that can present with a spontaneous pneumothorax include lymphangioleiomyomatosis (LAM), Birt-Hogg-Dubé syndrome (BHD), and pulmonary Langerhans cell histiocytosis (PLCH). LAM is a female-predominant, metastasizing smooth muscle cell neoplasm that occurs due to mutations in the tuberous sclerosis complex genes.\(^5\) BHD is an autosomal dominant disease caused by mutations in the tumor suppressor gene (FLCN) that leads to the development of hair follicle tumors, kidney tumors, and pulmonary cysts.\(^7\) PLCH is a cigarette smoke–induced pulmonary disorder that has recently been characterized as an inflammatory neoplasm due to the detection of mutations in the MAP kinase pathway.\(^5\)

Spontaneous pneumothorax is a common mode of presentation for patients with LAM, BHD, and PLCH. Although the prevalence of pneumothorax varies among the three disorders, all three diseases share a common demographic with PSP with regards to the age at presentation and in contrast to PSP have a very high risk of recurrent pneumothoraces (Table 1).\(^8-11\)

Due to the high burden of recurrent pneumothoraces in these disorders, pleurodesis is recommended follow-

<table>
<thead>
<tr>
<th>Condition</th>
<th>Median Age of First Pneumothorax (Years)</th>
<th>Recurrence Rate, if Managed Conservatively (%)</th>
<th>Recurrence Rate Following Pleurodesis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSP</td>
<td>15-34</td>
<td>30</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>LAM</td>
<td>35</td>
<td>71</td>
<td>32</td>
</tr>
<tr>
<td>BHD</td>
<td>37</td>
<td>73</td>
<td>35</td>
</tr>
<tr>
<td>PLCH</td>
<td>29</td>
<td>56</td>
<td>0-20</td>
</tr>
</tbody>
</table>

The median age at presentation with a spontaneous pneumothorax in patients with LAM, BHD, and PLCH is similar to the typical demographics of patients with PSP.\(^8-10,13\) However, the rate of recurrence is substantially higher in patients with DCLDs compared to patients with a PSP. Thus pleurodesis should be offered following the first episode of spontaneous pneumothorax to patients with DCLDs.\(^5,8,10-12,19\)

BHD = Birt-Hogg-Dubé syndrome; DCLD = diffuse cystic lung disease; LAM = lymphangioleiomyomatosis; PLCH = pulmonary Langerhans cell histiocytosis; PSP = primary spontaneous pneumothorax.

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ing the first spontaneous pneumothorax rather than waiting for a recurrent event as is typically done for patients with PSP.\textsuperscript{1,6,8,10,12}

Primary spontaneous pneumothorax is most commonly seen in young individuals with the typical age at presentation ranging between 15 and 34 years.\textsuperscript{13} Similarly, the median age of development of spontaneous pneumothorax in patients with LAM, BHD, and PLCH is 35, 37, and 29 years, respectively,\textsuperscript{8–10} thus highlighting the extensive overlap in the patient demographics of these conditions. In fact, LAM, BHD, and PLCH can be the underlying etiology in approximately 10% of the patients presenting with an apparent PSP.\textsuperscript{14} For example, two small studies conducted in China and Holland have shown that BHD is the underlying etiology of pneumothorax in 5% to 10% of patients presenting with an apparent PSP.\textsuperscript{15,16} Similarly, LAM has been estimated to be the underlying etiology of pneumothorax in greater than 5% of nonsmoking, reproductive-age females presenting with a spontaneous pneumothorax.\textsuperscript{17}

All three of these DCLDs (LAM, BHD, and PLCH) have a distinct pattern of cysts on high-resolution CT (HRCT) scan of the chest that can aid in the correct diagnosis (Figure 1). In fact a critical review of the cystic pattern on chest HRCT by an expert radiologist can lead to accurate diagnosis in greater than 80% of these cases.\textsuperscript{18} However, chest CT scan to evaluate for the presence of underlying etiologies is not recommended for patients presenting with an apparent PSP.\textsuperscript{1} A recent study has shown that a strategy of obtaining chest HRCT to screen for the presence of LAM, BHD, and PLCH in patients presenting with an apparent PSP is remarkably cost-effective. The marginal cost-effectiveness ratio for the CT screening strategy was $1,427 per quality-adjusted life-year (QALY) gained, which is significantly below the commonly accepted threshold of $50,000 per QALY. This strategy stayed cost-effective as long as the prevalence of DCLDs among patients presenting with an apparent PSP was less than 0.01%. This study did not take into account other benefits that can be accrued from a timely diagnosis of these disorders, such as appropriate targeted treatment (in patients with LAM), screening for renal tumors and asymptomatic family members (in patients with BHD), and appropriate counseling for smoking cessation (in patients with PLCH).\textsuperscript{14}

In light of the above-mentioned evidence, it is time to rethink the evaluation and management of patients presenting with an apparent PSP. In this age of personalized medicine and targeted treatment, it is imperative that we do not lump patients into nonspecific

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**Figure 1.** High-resolution chest CT scan images showing the characteristic cyst features seen in patients with LAM, BHD, and PLCH. (A and B) Smooth, round, uniform, thin-walled cysts distributed in a diffuse distribution in both lungs in two patients with LAM. (C) Round-elliptiform cysts seen in a basilar-predominant location with a predilection for the subpleural regions in a patient with BHD. (D) Upper-lobe predominant cysts of varying shapes and sizes with varying wall thickness and associated peribronchiolar nodules in a patient with PLCH. BHD = Birt-Hogg-Dubé syndrome; CT = computed tomography; LAM = lymphangioleiomyomatosis; PLCH = pulmonary Langerhans cell histiocytosis.
categories of primary and secondary spontaneous pneumothoraces, but rather it is our duty to identify the specific etiology of pneumothorax and provide disease-specific management recommendations. Emergency physicians, often the stewards of managing patients with PSP are best placed to implement this paradigm shift in our understanding, evaluation, and management of patients with PSP and lead the way in appropriate CT screening, timely diagnosis, and early consideration of pleurodesis in patients with DCLDs presenting with a spontaneous pneumothorax.

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References