Cystic fibrohistiocytic tumour of the lung presenting with recurrent pneumothorax: a case report

Christos Kakos1, Savvas Lampridis2, Georgios Geropoulos2, Reena Khiroya3, Achilleas Antonopoulos2, Sofoklis Mitsos2, Nikolaos Panagiotopoulos2

1Department of Cardiothoracic Surgery, Royal Victoria Hospital, Belfast; 2Department of Thoracic Surgery, University College London Hospitals NHS Foundation Trust, London; 3Department of Histopathology, University College London Hospitals NHS Foundation Trust, London, UK

Abstract

Cystic fibrohistiocytic tumour of the lung is a very rare pathological entity that occurs either as a primary pulmonary neoplasm or as a metastasis from skin lesions called cellular fibrous histiocytomas. Herein, we present the case of a 19-year-old man with a history of recurrent pneumothoraces who was managed surgically and was eventually diagnosed with cystic fibrohistiocytic tumour of the lung. Clinicians should include this disease in the differential diagnosis of pulmonary cystic lesions and be aware of its association with cellular fibrous histiocytoma. Reporting of more cases is warranted to further elucidate the natural course of the disease and optimise its management.

Introduction

Cystic fibrohistiocytic tumour of the lung is an extremely rare neoplasm. It commonly represents metastatic disease from cellular fibrous histiocytomas, which are benign cutaneous lesions with low-grade malignant potential [1]. Occasionally, it develops as a primary lung tumour. Herein, we present the case of a young man with pulmonary cystic fibrohistiocytic tumour who presented with recurrent pneumothoraces and received surgical treatment. We subsequently review the pertinent literature to elucidate the epidemiology and establish the management of this rare disease.

Case Report

A 19-year-old man, who had undergone video-assisted thoracoscopic pleurectomy for previous episodes of right-sided pneumothorax, presented to the Emergency Department with a new episode of ipsilateral pneumothorax. His relevant past medical history included asthma. The patient reported removal of a skin lesion from the left shoulder a few years ago. It was benign and cystic in nature, as reported by the patient, but no official histopathology report was found. A chest radiograph demonstrated a large right-sided pneumothorax, which was initially managed with insertion of an intercostal chest drain. A computed tomography (CT) scan of the chest revealed multiple cystic foci within both lungs, the largest of which was associated with the left oblique fissure and measured approximately 16 mm (Figure 1). The cysts were thin-walled and were distributed bilaterally, mainly in the upper and middle zones. Some of these cysts had an irregular outline. No other focal or diffuse pulmonary abnormality or thoracic lymphadenopathy were detected.

The patient underwent repeat video-assisted thoracoscopic excision of the remaining pleura and talc pleurodesis. An immediate postoperative chest radiograph demonstrated a large left-sided pneumothorax, which resolved with insertion of an intercostal chest drain. The patient was discharged on the second postopera-
tive day. A week later, he underwent the same surgical procedure on the left side and was discharged after 48 hours.

The histopathological analysis of the specimens obtained from both lungs revealed multiple, peripherally located, enlarged cystic air spaces. The walls of the cysts were lined by cuboidal epithelial cells, with evidence of squamous metaplasia in some areas. Beneath the surface of the cysts, there was characteristic fibrohistiocytic spindle cell proliferation, which was cytologically bland with no mitotic activity (Figure 2A). Within these areas, there was a rich vascular network. The spindle cells had high nuclear-cytoplasmic ratio, inconspicuous nucleoli and minimal amount of cytoplasm. The spindle cell proliferation was also outspread to the visceral pleura. Immunohistochemical studies showed that these cells were focally positive for CD68 (Figure 2B) and negative for cytokeratins, desmin, smooth muscle actin, CD34, S100 and CD1a.

The patient underwent genetic testing to assist in the final diagnosis of his pathology. Testing for tuberous sclerosis complex 1 & 2 genes (TSC1 & TSC2) to rule out pulmonary lymphangioleiomyomatosis was negative. Similarly, testing for folliculin gene (FLCN), which is responsible for Birt-Hogg-Dubé syndrome, was also negative.

The patient suffered a further episode of right-sided pneumothorax which was managed with repeat video-assisted thoracoscopic talc pleurodesis. The patient is alive after 4 years, remains on regular follow up and has not received any further treatment to date. Serial dermatologic examinations did not reveal further cutaneous lesions. The multiple pulmonary cystic lesions, which were detected on his initial admission, remained stable in subsequent CT imaging.

Discussion

Cystic fibrohistiocytic tumour of the lung is a very rare neoplasm. Morphological and immunohistochemical evidence suggest that this tumour usually derives from cutaneous cellular fibrous histiocytomas (dermatofibromas) [2-6]. However, there is a small number of cases of cystic fibrohistiocytic tumour of the lung where

Figure 1. Axial computed tomographic images of the chest demonstrating multiple parenchymal cysts in both lungs (red arrows).

Figure 2. A) H&E staining (1000x magnification): Cystic space surrounded by bland spindle cell proliferation. B) Immunohistochemical stain for CD68 (1100x magnification): CD68 shows focal positive staining within the spindle cell areas.
no skin lesion was identified [1,2,7-9]. These cases can be interpreted as primary pulmonary neoplasms or as cases where the primary skin lesion is occult [1].

Cystic fibrohistiocytic tumour of the lung was first by Holden et al. in 1982 [8]. Since then, 15 more cases, including ours, have been published (Table 1). Only lesions that were cystic in histology have been included in the table. The mean age of presentation was 33 years (range, 16–65 years), with a male predominance (3:1). The main clinical manifestations included pneumothorax (40%) and haemoptysis (20%), symptoms identified in other cystic lung diseases. The remaining 40% of the patients had no symptoms from the respiratory system, and the tumour was diagnosed incidentally or in the context of surveillance following resection of cutaneous fibrous histiocytoma. On CT scan of the chest, cystic fibrohistiocytic tumours usually appeared as bilateral multiple cystic foci or nodular opacities. In one case, however, the tumour presented as a solitary pulmonary nodule [7]. The overall prognosis was excellent; of 13 patients, all were alive at a median follow-up of 2 years (interquartile range, 1.45 years).

The diagnosis of cystic fibrohistiocytic tumour of the lung is confirmed with histopathological and immunohistochemical studies. Macroscopically, this neoplasm usually presents as multiple enlarged cystic nodules in the pulmonary parenchyma. Microscopically, these lesions are lined by cuboidal and squamous epithelial cells, while the intervening stroma shows characteristic proliferation of cytologically bland spindle cells mixed with histocytes, lymphocytes and plasma cells. The lesions are characterized by rich vasculature without evidence of necrosis or lymphovascular invasion. The immunohistochemical labelling is also typical, as the epithelial cells are TTF1+, which suggests origin from the alveolar parenchyma. Moreover, the spindle cells are usually CD68+, while the cystic lesions are not stained for CD34, S100, desmin, smooth muscle actin, cytokeratins, EMA, factor VIII or CD1a [1,5,7].

The differential diagnosis includes Langerhans cell granulomatosis, lymphangioleiomyomatosis, pleuropulmonary blastoma, metastatic low-grade sarcoma, mesenchymal cystic amartoma, benign uterine leiomyoma and uterine sarcoma [6,9]. Radiologically, the differential diagnosis could also include cystic amyloidosis and gastrointestinal malignancies. Clinical features, morphological characteristics and immunohistochemical analysis can help differentiate between these entities.

Cellular fibrous histiocytomas belong to a greater family of neoplasms called cutaneous fibrohistiocytic tumours, which share

Table 1. Demographic and clinical characteristics of published cases of cystic fibrohistiocytic tumour of the lung presenting as cystic pulmonary lesions.

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Radiological/histopathological findings</th>
<th>Primary tumour</th>
<th>Cutaneous lesions</th>
<th>Respiratory symptoms</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holden [8]</td>
<td>1982</td>
<td>25</td>
<td>M</td>
<td>Bilateral diffuse thin-walled cavities</td>
<td>Yes</td>
<td>No</td>
<td>Haemoptysis</td>
<td>Alive at 5 years</td>
</tr>
<tr>
<td>Joseph [2]</td>
<td>1990</td>
<td>65</td>
<td>M</td>
<td>Bilateral multiple nodular lesions, cystic on microscopy</td>
<td>Yes</td>
<td>No</td>
<td>None ( incidental finding on routine CXR)</td>
<td>Alive at 2 years</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>M</td>
<td></td>
<td>Bilateral multiple cystic lesions</td>
<td>No</td>
<td>No</td>
<td>Pneumothorax</td>
<td>Alive at 20 years</td>
</tr>
<tr>
<td>Colome-Grimmer [3]</td>
<td>1996</td>
<td>18</td>
<td>M</td>
<td>Bilateral lung lesions, cystic on microscopy</td>
<td>No</td>
<td>CFH 1.5 years ago</td>
<td>None (FU post removal of CFH)</td>
<td>Alive at 4 years</td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>M</td>
<td></td>
<td>Bilateral lung lesions, cystic on microscopy</td>
<td>No</td>
<td>CFH 1 year ago</td>
<td>None (FU post removal of CFH)</td>
<td>Alive at 8 years</td>
</tr>
<tr>
<td>Osborn [1]</td>
<td>2003</td>
<td>38</td>
<td>M</td>
<td>Bilateral nodular and cavitating opacities</td>
<td>Yes</td>
<td>No</td>
<td>Haemoptysis</td>
<td>Alive at 2 years</td>
</tr>
<tr>
<td></td>
<td>54</td>
<td>M</td>
<td></td>
<td>Bilateral nodular and cavitating opacities</td>
<td>No</td>
<td>No</td>
<td>Haemoptysis</td>
<td>Alive at 4 years</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>M</td>
<td></td>
<td>Bilateral multiple cystic lesions</td>
<td>No</td>
<td>No</td>
<td>NK</td>
<td>Alive at 1 year</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>M</td>
<td></td>
<td>Bilateral multiple cavitary lesions</td>
<td>No</td>
<td>No</td>
<td>Pneumothorax pneumonia,</td>
<td>NK</td>
</tr>
<tr>
<td>DiGiovine [9]</td>
<td>2004</td>
<td>35</td>
<td>F</td>
<td>Unilateral multiple cystic lesions</td>
<td>Yes</td>
<td>No</td>
<td>Chest pain, dyspnoea, pneumothorax</td>
<td>Alive at 1 year</td>
</tr>
<tr>
<td>Gu [5]</td>
<td>2007</td>
<td>36</td>
<td>F</td>
<td>Bilateral multiple cystic lesions</td>
<td>No</td>
<td>CFH 7 years ago</td>
<td>None ( incidental finding)</td>
<td>Alive at 1 year</td>
</tr>
<tr>
<td>Paci [7]</td>
<td>2010</td>
<td>16</td>
<td>M</td>
<td>Single cystic lesion</td>
<td>Yes</td>
<td>No</td>
<td>Pneumothorax</td>
<td>Alive at 2 years</td>
</tr>
<tr>
<td>Present study</td>
<td>2020</td>
<td>19</td>
<td>M</td>
<td>Bilateral multiple cystic lesions</td>
<td>No</td>
<td>Yes, unknown histology</td>
<td>Pneumothorax</td>
<td>Alive at 4 years</td>
</tr>
</tbody>
</table>

CFH, cellular fibrous histiocytoma; CXR, chest radiograph; FU, follow-up; NK, not reported; NR, not known.
similar clinical, morphological and molecular characteristics [10]. The literature suggests that these tumours tend to metastasise either locally or systemically and usually have an indolent course [1-3,5,6,11]. However, a more aggressive clinical behaviour cannot be ruled out by the histopathological characteristics of these neoplasms. All of the above render their diagnosis challenging leading to potential underreporting of this entity. Therefore, it is deemed necessary to establish frequent and close follow-up of patients with cutaneous fibrohistiocytic tumours who underwent surgical resection even with negative margins [11]. Adjuvant chemotherapy has been associated with poor results; however, little evidence exists regarding its use [6,12].

**Conclusions**

Cystic fibrohistiocytic tumour of the lung is a rare proliferative disease and represents an infrequent cause of spontaneous pneumothorax. When treating patients with pulmonary cystic lesions, clinicians must include this disease in the differential diagnosis. Moreover, they should be knowledgeable of its association with cutaneous cellular fibrous histiocytoma. The rarity of pulmonary cystic fibrohistiocytic tumours in combination with the lack of well-defined diagnostic criteria have probably led to underreporting of this neoplasm. Reporting of more cases along with longer patient follow-up are needed to further understand the natural course of the disease and optimise its management.

**References**