

## Cystic fibrohistiocytic tumor of the lung presenting as a solitary lesion

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### Abstract

Cystic fibrohistiocytic tumor of the lung is a rare neoplasm. In many cases it represents a metastasis from a benign or low-grade fibrohistiocytic tumor of the skin, but occasionally it may be primary. Radiologically it usually occurs as a cystic change of multiple pulmonary nodules, and pneumothorax is the most frequent presenting symptom. We present here a 16-year-old man with recurrent right pneumothorax. The patient had no history of cutaneous fibrohistiocytic lesions. He underwent videothoroscopic right apical segmentectomy, right lower lobe nodulectomy, and pleuroabrasion. Microscopy of the apical segmentectomy showed a cystic fibrohistiocytic tumor, whereas the nodule of the lower lobe was an intraparenchymal lymph node. The patient is alive with no tumor recurrence. The differential diagnosis includes Langerhans cell histiocytosis, lymphangioleiomyomatosis, pleuropulmonary blastoma, and metastatic endometrial stromal sarcoma. This disease usually occurs with multiple pulmonary cysts and cavitation. This case is the first reported presenting as a single lesion.

### Introduction

Cystic fibrohistiocytic tumor of the lung is a rare neoplasm. Its histogenesis is uncertain: it may be a primary disease of the lung, but frequently it represents a metastasis from indolent skin lesions, particularly cellular fibrous histiocytomas.<sup>1,5</sup> To the best of our knowledge, 13 cases have been reported in the English literature since the first description in 1990<sup>6</sup> (Table 1): nine of them had a history of benign or low-grade fibrohistiocytic lesions of the skin, and only four were interpreted as primary. We report here a new case of primary cystic fibrohistiocytic tumor of the lung, the first presenting as a solitary lesion, and review the available literature.

### Case Report

A 16-year-old man presented with recurrent right pneumothorax. After the first episode, the patient underwent high-resolution computed tomography (HRCT) of the chest that showed a single right apical bleb and a single poorly defined subpleural nodule in the right lower lobe. No history of previous cutaneous fibrohistiocytic lesions was reported. Owing to the recurrence of pneumothorax, we performed a videothoroscopic right apical segmentectomy with right lower lobe nodulectomy and pleuroabrasion. Moreover, thoracoscopic examination of the lung showed several small, well-circumscribed, subpleural nodules.

Microscopically, in the apical wedge resection the lung parenchyma showed a small subpleural cyst, which opened into the pleural cavity (Figure 1). The cyst was lined by a single row of benign, cuboidal, alveolar epithelial cells, whereas the wall was composed of a thin rim of mesenchymal tissue (Figure 2). The latter consisted of bland, spindle-to-oval cells with scant cytoplasm, regular nuclear chromatin, and inconspicuous nucleoli. A few mitoses were present. Immunohistochemically, the epithelium lining the cyst was diffusely positive for cytokeratin AE1/AE3 and TTF-1, whereas the mesenchymal cells reacted focally only for estrogen receptors and were negative for progesterone receptors, cytokeratin AE1/AE3, TTF-1, S-100 protein, smooth muscle actin, desmin, CD34, CD68/PG-M1, and HMB-45. KI-67/MIB-1 was low (1%) in the mesenchymal component. A diagnosis of cystic fibrohistiocytic tumor was made. The nodule of the lower lobe was a reactive lymph-node.

A complete clinical work-up including a total-body CT-scan and a dermatological examination was negative for other tumors. No female internal genitals were found, scrotal ultrasonography did not reveal any testicular abnormalities, and a genetic test confirmed a male karyotype. The patient is alive with no evidence of pulmonary recurrence or skin lesions at the latest follow-up, 14 months after surgery.

### Discussion

In our opinion, the peculiar pulmonary lesion we report here, as originally described by Joseph *et al.*,<sup>6</sup> is probably a result of the interstitial proliferation of bland mesenchymal cells, with entrapment of benign alveoli and secondary cystic changes. In the lung, this phenomenon is described in several unusual lesions such as metastatic low-grade sarcomas, pleuropulmonary blastoma, placental transmigration, mesenchymal cystic

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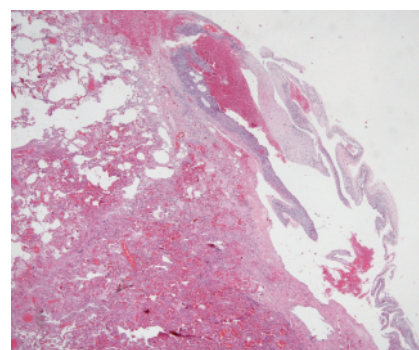


Figure 1. A small pulmonary cyst opening into the pleural cavity. (Hematoxylin and eosin stain; magnification 20X).

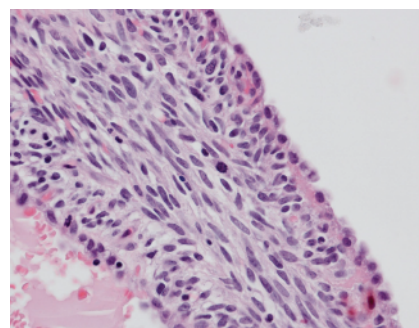


Figure 2. The cyst is lined by a single row of benign-looking cuboidal epithelial cells, whereas the wall is composed of a thin rim of bland spindle-to-oval cells. In the center of the field, a mitotic figure is present. (Hematoxylin and eosin stain; magnification 400X).

**Table 1. Clinical findings of cystic fibrohistiocytic tumors presenting in the lung.**

Case	Sex	Age (years)	Pulmonary symptoms	Radiological or pathological finding	Previous cutaneous lesion	Follow-up (years)
1	M	38 <sup>7</sup>	Hemoptysis	Bilateral opacities, many nodular and cavitating	None identified	Alive with disease at 2 y
2	M	54 <sup>7</sup>	Hemoptysis	Bilateral small opacities with many nodules	CFH (23 years previously, 2 skin recurrences)	Alive with disease at 4 y
3	M	35 <sup>7</sup>	Not known	Bilateral cystic lung nodules	None identified	Alive with disease at 1 y
4	M	29 <sup>7</sup>	Pneumonia, pneumothorax	Multiple bilateral cavitory lesions	CFH (10 years previously on back)	Not known
5	M	65 <sup>6</sup>	No	Multiple bilateral nodular opacities	None identified	Alive with disease at 2 y
6	M	30 <sup>6</sup>	Dyspnea, pneumothorax	Bilateral nodular opacities	Recurrent DF (5 years previously)	Alive with disease at 20 y
7	M	25 <sup>18</sup>	Hemoptysis	Bilateral diffuse cavities	None identified	Alive with disease at 5 y
8	F	30 <sup>17</sup>	Pneumothorax	Bilateral cystic lesions	DFP (17 years previously)	Not known
9	M	19 <sup>1</sup>	Not known	Cystic lesion on pathology	CFH (1.5 years previously)	Alive and free of disease at 4 y
10	M	40 <sup>1</sup>	Not known	Cystic lesion on pathology	CFH (7 years previously)	Alive with disease at 8 y
11	M	33 <sup>3</sup>	Increasing fatigue	Multiple masses, not cystic	CFH (2 years previously)	Alive with disease
12	M	33 <sup>3</sup>	No	Bilateral multiple cystic lesions	CFH (9 years previously)	Alive with disease at 6 y
13	F	36 <sup>3</sup>	No	Bilateral multiple cystic lesions	CFH (7 years previously)	Alive with disease at 1 y
14	M	16	Pneumothorax	Single nodular opacity, cystic lesion on pathology	None identified	Alive and free of disease at 1 y

M, male; F, female; CFH, cellular fibrous histiocytoma; DF, dermatofibroma; DFP, dermatofibrosarcoma protuberans. Adeapted from Gu et al.<sup>3</sup>

hamartoma, and cystic fibrohistiocytic tumor.

A metastasis from a low-grade sarcoma (particularly from a cutaneous dermatofibrosarcoma protuberans or cellular dermatofibroma)<sup>7</sup> was the most important differential diagnostic consideration in our case, and its exclusion required a careful clinical work-up. Metastasis from endometrial stromal sarcoma<sup>8</sup> and benign metastasizing leiomyoma are other lesions that occasionally can present as pulmonary cysts, but they were not considerations in our case owing to the sex of the patient. Type I pleuropulmonary blastoma<sup>9</sup> generally involves small children, presents as a large mass, and has the histological and immunohistochemical characteristics of rhabdomyosarcoma; all these features were absent in our case. Placental transmogrification<sup>10</sup> is a rare condition bearing a superficial resemblance to placental villi. It is morphologically very different from our case. The differential diagnosis also includes Langerhans cell histiocytosis<sup>11</sup> and lymphangioleiomyomatosis,<sup>12</sup> but both of them can easily be differentiated from our case based on clinico-radiological, histological, and immunohistochemical data.

In 1986, Mark reported five patients (one pediatric and four adults) with peculiar pulmonary cysts and nodules, and he named the lesion mesenchymal cystic hamartoma.<sup>13</sup> The entity remains controversial; the pediatric patient subsequently died of disease and the lesion was reinterpreted as pleuropulmonary blastoma,<sup>14</sup> whereas an adult female was found to have a uterine stromal sarcoma and the pulmonary lesion was reinterpreted as a metasta-

sis from the latter.<sup>15</sup> A few more cases of mesenchymal cystic hamartoma have subsequently been reported in the literature.<sup>16</sup> A few years later, a group from the Mayo Clinic reported two cases under the term "multiple cystic fibrohistiocytic tumors of the lung."<sup>16</sup> One of the two turned out to be a metastasis from a cutaneous fibrohistiocytic tumor.<sup>17</sup> Few cases of cystic fibrohistiocytic tumors have since been reported.<sup>7</sup> Even if the exact relationship between mesenchymal cystic hamartoma and cystic fibrohistiocytic tumors remains controversial, there is clearly a significant overlap and probably the two entities are, in reality, just one.

In our case, the nature of the mesenchymal cells remains elusive. Although the histological and the immunohistochemical features suggest an immature mesenchymal phenotype, the focal immunohistochemical expression of estrogen receptors is intriguing, and further studies are necessary to elucidate the issue. The clinical behavior of cystic fibrohistiocytic tumors is uncertain (Table 1). The case we report is a small and single cyst of the lung, that we consider a benign or low-grade lesion; therefore, we believe that a careful follow-up is rational and prudent. The patient is alive with no tumor recurrence 24 months after surgery.

In summary, we report here the first case of primary cystic fibrohistiocytic tumor of the lung presenting as a single lesion. Cystic fibrohistiocytic tumors of the lung are very rare, the majority of them probably representing metastases from benign or low-grade fibrohistiocytic tumors of the skin, but occasionally they are

primary or the primary site remains occult. Whenever a cyst lined by a benign alveolar epithelium with a thin rim of mesenchymal tissue, even if it is bland, is found in the lung, a pleuropulmonary blastoma (in childhood) and a metastasis from a low-grade malignancy (in adulthood) have to be considered and strictly excluded.

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