Case Report

Pulmonary microcystic fibromyxoma: a rare benign myxoid tumor in the lung

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Abstract: Primary pulmonary microcystic fibromyxoma is very rare. We describe a case of 68-year-old female who had a 4 months history of thorax suffocation and dyspnea. Computed tomography revealed a well-circumscribed nodule with a diameter of approximately 2.2 cm in the right upper lobe. After extensive workup, she received a right upper lobe wedge resection. Pathologically, microcystic architecture with myxoid stroma was revealed in the well-circumscribed tumor. The tumor cells were spindled to stellate, with innocuous appearance. Immunohistochemical staining showed strong expression of vimentin and CD99 in the tumor cells, but no expression of epithelial markers and other mesenchymal markers for distinctive differentiation. Genetically no EWSR1 or SS18 rearrangements were detected by fluorescence in situ hybridization. Eventually this case was diagnosed as primary pulmonary microcystic fibromyxoma. No tumor recurrence or metastasis was observed during 25 months follow-up.

Keywords: Myxoma, lung, microcystic, pathology

Introduction

Myxoma is a benign tumor that frequently occurs in the heart, especially the left atrium [1]. Primary myxoma of the lung is very rare [2-5]. Morphologically, myxoma is characterized by abundant extracellular mucoid (myxoid) matrix. Various sized mucoid filled cystic spaces can be found in myxoma, but the diffuse microcystic architecture is uncommon. Herein, we present a 68-year-old woman who had a rare benign pulmonary myxoid tumor showing prominent microcystic architecture. According to the literature, this tumor belongs to a kind of rare myxoma, pulmonary microcystic fibromyxoma. Up to now, only four cases have been reported in literatures [2, 3]. The study was approved by the Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. Written informed consent was obtained from the patient.

Case report

A 68-year-old female with a four months history of thorax suffocation and dyspnea was admitted to our hospital. Chest X-ray showed an abnormal shadow in the right upper lung area (Figure 1A) and computed tomographic (CT) scan demonstrated a well-circumscribed 2.2 cm peripheral lung nodule in the right upper lobe suspected of being a primary lung tumor (Figure 1B, 1C). A careful physical examination and selected laboratory tests were performed on this patient, and there was no other particular finding. Cytological examination under bronchofiberscopy did not demonstrate any malignancy but inflammation. No other intrathoracic abnormalities were found. A right thoracotomy was undertaken in order to establish the patient’s diagnosis. The surgeon confirmed the presence of a peripherally tumor with a diameter of approximately 2.3 cm in the upper lobe. The frozen section of tumor specimens revealed it to be a benign tumor. Therefore, a right upper lobe wedge resection was performed at last and the tumor was removed for pathological examination.

Materials and methods

The samples were fixed in 10% buffered formalin, embedded in paraffin, sectioned conven-
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**Table 1.** Antibodies and dilutions used in this study

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Dilution</th>
<th>Vendor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancytokeratin</td>
<td>1:20</td>
<td>Dako</td>
</tr>
<tr>
<td>Cytokeratin 5/6</td>
<td>1:200</td>
<td>ZYMED</td>
</tr>
<tr>
<td>Cytokeratin 7</td>
<td>1:200</td>
<td>Dako</td>
</tr>
<tr>
<td>TTF-1</td>
<td>1:200</td>
<td>Dako</td>
</tr>
<tr>
<td>Vimentin</td>
<td>1:200</td>
<td>Dako</td>
</tr>
<tr>
<td>S-100</td>
<td>1:1000</td>
<td>Dako</td>
</tr>
<tr>
<td>Smooth muscle actin</td>
<td>1:400</td>
<td>Dako</td>
</tr>
<tr>
<td>CD31</td>
<td>1:100</td>
<td>Dako</td>
</tr>
<tr>
<td>CD34</td>
<td>1:100</td>
<td>Dako</td>
</tr>
<tr>
<td>CD99</td>
<td>1:50</td>
<td>Dako</td>
</tr>
<tr>
<td>Calretinin</td>
<td>prediluted</td>
<td>Biogenex</td>
</tr>
<tr>
<td>D2-40</td>
<td>1:100</td>
<td>Dako</td>
</tr>
<tr>
<td>HMB45</td>
<td>1:100</td>
<td>Dako</td>
</tr>
<tr>
<td>Melan-A</td>
<td>1:25</td>
<td>Dako</td>
</tr>
<tr>
<td>Ki67</td>
<td>1:30</td>
<td>Novocastra</td>
</tr>
</tbody>
</table>

Gross examination revealed the neoplasm to be a well-circumscribed mass measuring 2.3 cm×2.2 cm×2.0 cm without an obvious fibrous capsule. It was soft and unassociated with airways or vessels. The cut surface was grey and mucoid. Microscopically, the tumor was composed of distinctive microcysts containing abundant myxoid matrix, which resembled the appearance of pulmonary alveolar adenoma, but the lining cells were absent in microcyst wall (Figure 2A-C). Bland spindled and stellate-shaped cells were observed between micro-
cysts (Figure 2D). No mitosis or necrosis was present in the lesion. Small amount of lymphocytes, plasma cells and other chronic inflammatory cells could be found in cystic spaces. Lymphocyte infiltration can also be observed in peripheral lung stroma and peribronchial tissue.

Immunohistochemistry

Immunohistochemical examination of the tumor cells revealed vimentin and CD99 positive, and epithelial marker (Pancytokeratin, cytokeratin 5/6 and cytokeratin 7) negative, consistent with the mesenchymal origination (Figure 3A-C). While those markers indicative of certain differentiations, such as S-100, smooth muscle actin, CD31, CD34, calretinin, WT-1, D2-40, HMB45 and Melan-A were all negative in the tumor cells. The Ki-67 labelling index was low (<0.1%) (Figure 3D).

EWSR1 and SS18 FISH

Next genetical analysis was performed on this tumor. At least 200 cells were counted for the presence of rearranged signals under a multi-filtered fluorescence microscope. A split signal pattern was considered positive for EWSR1 or SS18 rearrangement if the distance between the green and the red signals was greater than the diameter of any one signal. However, this case showed two fusion signals or very close green and red signals, which were negative for a rearrangement of the EWSR1 and SS18 gene loci (Figure 4A, 4B).

Discussion

Myxoid tumors occurring in the lung are rare. If there is a myxoid tumor in the lung, a careful clinical work-up should be taken to exclude metastases. The most common metastatic
myxoid tumor in the lung is metastatic sarcomas, in particular extraskeletal myxoid chondrosarcoma [6]. Occasionally, benign myxoid tumor, such as myxoma, can also metastasize to the lung. Cardiac myxomas that metastasize or embolize to the brain, arteries, bones, soft tissue and lung had been reported [1]. Concerning to primary myxoid tumors of the lung, variants of salivary gland-type mixed tumors and the myxoid variant of pulmonary...
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Hamartoma are first taken into consideration [7, 8]. Besides, primary pulmonary myoid sarcoma had also been reported [9, 10]. Primary pulmonary myxoma is extremely rare. Up to now, only 10 cases have been reported with 2 lesions in trachea and 8 in pulmonary parenchyma [2-5]. The mean age of the patients was 54.8 years (range, 26-73 years), and male-to-female ratio was 1 to 1. The mean size of primary pulmonary myxoma was 1.59 cm (range, 0.5-2.5 cm).

In the current case, the complete physical examination only revealed a solitary nodule with distinct border in the lung and no neoplasia in other sites, which indicate a primary pulmonary tumor. Morphologically, the lesion is well circumscribed with myxoid stroma and conspicuous cystic change. No necrosis was observed. The spindle or stellate tumor cells showed little nuclear pleomorphism and very low mitotic activity, thus malignant myxoid tumors seems less likely. Due to absence of chondroid and salivary differentiation, myxoid variant of chondroid hamartoma and salivary tumor could be excluded, and pulmonary myxoma was taken into consideration due to myxoid change of the tumor. While the impressive cystic change of the lesion remind us a kind of rare myxoma-pulmonary microcystic fibromyxoma, which is a descriptive diagnosis first proposed by Shilo K et al. in 2006 [2].

Pulmonary microcystic fibromyxoma is very rare. Shilo K et al. only revealed 3 cases of microcystic fibromyxoma in the past 20 years in their consultation center. The tumors are presented as incidental solitary peripheral lung nodules on radiographic examination, and were well circumscribed with distinctive microcystic architecture and myxoid stroma. These distinctive morphological changes are exactly consistent with our finding. In their report, innocuous tumor cells showed no epithelial, chondroid, neural, myofibroblastic, lipomatous or vascular differentiation on immunohistochemical studies. The prominent microcystic morphology and abundant stromal matrix containing collagen fibers made the descriptive diagnosis of “microcystic fibromyxoma” reasonable.

In this study, we also performed immunohistochemical staining to explore the direction of certain differentiations. A panel of immunohistochemical markers was applied in this case (Table 1). The innocuous tumor cells were completely negative for endothelial markers and strong positive for vimentin, which indicated us a mesenchymal tumor. Similar with the previous report, these tumor cells were all negative for those mesenchymal differentiation markers. The only difference is that CD99 was strongly positive in the tumor cells of our case. However, CD99 has poor tissue specificity and was hard to confirm the origination of this tumor.

Molecular diagnostics can serve as a useful diagnostic ancillary tool, especially in sarcomas. For the first time we analyzed the molecular perspective on this solitary pulmonary tumor. The EWSR1 gene at chromosome 22q12 is a promiscuous fusion partner involved in plenty of sarcomas characterized by gene fusions, including the Ewing family of tumors, desmoplastic small round cell tumor, extraskel-etal myxoid chondrosarcoma, angiomatoid fibrous histiocytoma, myxoid liposarcoma, and primary pulmonary myxoid sarcoma [11]. Recently years, rare cases of benign tumor, such as hemangioma and myoepithelial tumor have been reported with new fusion of the EWSR1 and other genes [12, 13]. Rearrange-ment of the SS18, which is presumed to be highly specific for synovial sarcoma, was also found in aneurysmal bone cyst [14]. In this tumor, no rearrangements of EWSR1 or SS18 were detected, which help us to exclude the possibilities of corresponding sarcomas. However, more thoroughly genetic analyses need to be performed to clarify the genetic mechanism responsible for the occurrence of this kind of myxoma.

Considering its distinctive microcystic architecture, ultimately, we diagnosed this case as “primary pulmonary microcystic fibromyxoma”. In fact, microcystic feature is not only present in myxoma, but also appears in other tumors, such as the stromal tumor of ovary [15] and meningioma [16]. However, this characteristic in myxoma was very rare, only 5 cases had been reported [2, 3, 17]. And except 1 case occurring in mandible, the other 4 cases were all found in lung. This incidence rate of microcystic architecture in primary pulmonary myxoma is not low. According to the current data, 5 cases in 9 primary myxomas of pulmonary parenchyma had this feature. Given the rarity of pulmonary microcystic myxoma, the correla-
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Clinically, pulmonary microcystic fibromyxoma are usually found incidentally. Patients usually have no symptoms and the tumor was found probably for the advances in chest imaging techniques occurring within recent years [2]. But in our case, the patient presented with thorax suffocation and dyspnea. These symptoms might be partly resulted from secondary inflammation confirmed by cytological and histological examination. Due to its innocuousness, myxoma generally has good prognosis. Among 11 reported cases of pulmonary myxoma, metastasis had not yet been described, which is different from atrial myxomas showing malignant biological behavior though the histologic appearance was innocuous. The real causes of their susceptibility to embolize to distant organs are still unknown, but echocardiographic features, the composition or amount of the myxomatous matrix and MMP expression had been considered in related studies [7]. As a variant of myxoma, microcystic fibromyxoma was unassociated with airways or vessels, therefore had little chance to embolize to other organs. The disease-free survival of pulmonary microcystic fibromyxoma after surgical resection was long, with a mean follow-up of 48 months as Shilo K et al. reported. In this study, the patient had an uneventful postoperative recovery after surgery, and during the 25-month follow-up, she has survived without remarkable findings.

In conclusion, pulmonary microcystic fibromyxoma is a myxoma with diffuse microcystic architecture. Completely resection is essential for pulmonary microcystic fibromyxoma. While considering the biological behavior of myxoma occurring in atrial, it should also be paid close attention once the location is close to airways or vessels, and extracellular matrix is decreased.

Disclosure of conflict of interest

None.

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References

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