Primary pleomorphic adenoma of the lung with positive staining of TTF-1: a case report and review of literature

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Abstract: Pleomorphic adenoma is a common tumor occurring in the salivary glands of head and neck. But, it is extremely rare in the trachea or lung. Here, we reported a case of primary pleomorphic adenoma of the lung. A 63-year-old man came to our hospital with a tumor in the middle of the trachea nearly obstructing the airway. The histological examination revealed a mixture of epithelial and myxoid-chondroid mesenchymal elements. The tumor tissue was positive for broad-spectrum cytokeratin (CK), CK7, p63, p53, and CK5/6 staining, and focal positive for S-100, EMA, and Vimentin staining. Based on the clinical information, histological features, and the immunohistochemical staining profile, the tumor was diagnosed as a primary pleomorphic adenoma of the lung. Specially, the epithelial cells of this tumor were positive for thyroid transcription factor-1 (TTF-1) staining, which indicated its differentiation toward type II alveolar epithelial cells.

Keywords: Pleomorphic adenoma, TTF-1, salivary gland type tumor, trachea, lung

Introduction

Pleomorphic adenoma is a common tumor occurring in the salivary glands of head and neck. But, it is extremely rare in the trachea or lung. To our knowledge, less than 20 cases of pleomorphic adenoma arising from the lung have been reported in English literature (Table 1) [1-12]. The histological morphology of primary pulmonary pleomorphic adenoma is similar to its counterpart arising from the salivary glands of head and neck. It displays a biphasic cellular composition including epithelial tubules or nests and myoepithelial component embedded in or merging with a myxoid or chondromyxoid stroma [12]. However, the primary pleomorphic adenoma of the lung is very rare, so that its incidence and etiology are unclear. Its feature of immunostaining was also not well known. Here, we reported a special case of primary pleomorphic adenoma of the lung with positive staining of thyroid transcription factor-1 (TTF-1).

Clinical history

A 63-year-old Chinese man went to the First Affiliated Hospital of China Medical University in March 2013 with complaints of trachea neoplasm for seven years and dyspnea for one year. Computed tomography (CT) revealed a circular soft tissue density mass that attached to the front wall of trachea. The tumor mass protruded into the lumen of the trachea, and nearly obstructed the lumen (Figure 1). The bilateral hilar was not enlarged. No enlarged lymph node was found in the mediastinum. The tumor mass was solid, and the tumor size was about 2.1×1.9×1.8 cm. The CT value was about 40 HU. The tumor was resected using fiberoptic bronchoscopy and a diathermy snare without significant bleeding. The patient recovered well, and has no signs of recurrence up to now. The patient had no history of salivary gland neoplasm or prior head and neck surgery. The study was approved by the China Medical University Institutional Review Board for human studies. Written informed consent was got from the patient for use of his clinical records in our study.

Materials and methods

The resected tumor tissue was fixed with 10% neutral-buffered formalin and embedded in
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Table 1. The case reports of pleomorphic adenoma of the lung

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Location</th>
<th>Size</th>
<th>Clinical presentation</th>
<th>Management</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>36</td>
<td>Left lower lobe</td>
<td>NA</td>
<td>Incidental</td>
<td>Lobectomy</td>
<td>Wang JS, et al. 1994</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>63</td>
<td>Left lower lobe</td>
<td>3.3 cm</td>
<td>Vomiting, abdominal pain</td>
<td>Fine needle aspiration</td>
<td>Kanchustambham, et al. 2017</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>47</td>
<td>Left mainstem bronchus</td>
<td>2.5 cm</td>
<td>Cough, chest pain</td>
<td>Pneumonectomy</td>
<td>Moran, et al. 1994</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>67</td>
<td>Right middle lobe</td>
<td>NA</td>
<td>Incidental</td>
<td>Lobectomy</td>
<td>Noda M, et al. 2002</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>18</td>
<td>Right middle lobe</td>
<td>NA</td>
<td>Incidental</td>
<td>Lobectomy</td>
<td>Tanigaki T, et al. 2002</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>56</td>
<td>Right middle lobe</td>
<td>2 cm</td>
<td>Incidental</td>
<td>Lobectomy</td>
<td>Ang KL, et al. 2003</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>22</td>
<td>Right lower lobe</td>
<td>2 cm</td>
<td>Incidental</td>
<td>Lobectomy</td>
<td>Carretta, et al. 2004</td>
</tr>
<tr>
<td>8</td>
<td>Female</td>
<td>25</td>
<td>Left lung periphery</td>
<td>2.5 cm</td>
<td>Incidental</td>
<td>Wedge resection/VATS</td>
<td>Jin HY, et al. 2007</td>
</tr>
<tr>
<td>9</td>
<td>Male</td>
<td>65</td>
<td>Right main bronchus</td>
<td>1.3 cm</td>
<td>Cough</td>
<td>Rigid bronchoscopy</td>
<td>Fitchett, et al. 2008</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>8</td>
<td>Distal trachea and right main bronchus</td>
<td>NA</td>
<td>Respiratory distress</td>
<td>Right carinal resection, pneumonectomy</td>
<td>Baghai-Wadji M, et al. 2006</td>
</tr>
<tr>
<td>11</td>
<td>Male</td>
<td>38</td>
<td>Right lobe</td>
<td>10 cm</td>
<td>Post-traumatic after bull injury to the chest</td>
<td>Surgical excision</td>
<td>Pozgain, et al. 2016</td>
</tr>
</tbody>
</table>

NA = not available.
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**Figure 1.** The image of computed tomography examination. Computed tomography revealed that a circular soft tissue density mass attached to the front wall of trachea and protruded into the lumen of the trachea (arrow).

paraffin blocks. Tissue blocks were cut into 4-μm sections. The histological evaluation was performed on hematoxylin and eosin stained sections. The tumor tissue sections were immunostained with primary antibodies against broad-spectrum cytokeratin (CK), CK7, CK5/6, epithelial membrane antigen (EMA), p63, p53, TTF-1, S-100, vimentin, SMA and Ki67. All of these antibodies were purchased from Maixin, Fuzhou, China. After incubation with primary antibody, the detection of antibodies was accomplished using the streptavidin-peroxidase method.

**Results**

**Gross features**

Gross pathologic examination revealed that the tumor was round, about 2.0 cm in diameter. The cut surface of the tumor was rubbery, soft, and gray-white with no apparent hemorrhagic or necrotic foci.

**Microscopic features**

The tumor displayed different growth patterns, including glandular or tubular structure, solid cell nests, and myxoid or chondroid areas (**Figure 2**). The proportion of each component is different. The neoplastic epithelial cells included myoepithelial cells, glandular epithelial cells, and squamous cells. In the component of glandular or tubular structure, the tumor cells arranged as two layers. The inner layer was lined by cuboidal or low columnar epithelial cells with eosinophilic cytoplasm. The outer layer was surrounded polygonal, spindle or stellate myoepithelial cells with clear or light staining cytoplasm. Myxoid or chondromyxoid areas were mixed with epithelial cell nests. Some spindle shape myoepithelioid cells embedded in or merged with the myxoid or chondromyxoid components. A small part of cells showed squamous cell differentiation and keratinization. All of the tumor cells were mild, and without cellular atypia or mitotic figures.

**Immunohistochemistry**

Immunostaining showed that broad-spectrum CK was strongly positive in almost all the neoplastic epithelial cells. TTF-1 was strongly positive in the nuclei of glandular epithelial cells, and also positive in part of the abluminal cells. CK7 and EMA were positive in the glandular epithelial cells. P63 was positive in all of the myoepithelial cells, S-100 and Vimentin were positive in part of the myoepithelial cells. The percentage of cells that stained positively for Ki67 was about 5% (**Figure 3**).

**Discussion**

Based on clinical information, histological features, and the immunohistochemical staining profile described above, the tumor was diagnosed as a primary pleomorphic adenoma of the lung. Pleomorphic adenoma is a common tumor in the salivary glands of the head and neck, especially the parotid gland. Pleomorphic adenoma arising in regions other than the head and neck are very rare. Few reports have documented its presence in other regions, such as lung and lower eyelid [11, 13]. To date, less than 20 cases of pleomorphic adenoma of the lung have been reported in the literature (Table 1) [1-12]. Previous reports and ours have summarized the features of pleomorphic adenoma of the lung. This tumor often occurs in middle and old age patients (≥40 years old). The occurrence of this tumor does not differ by gender. Macroscopically, these tumors are typically well-circumscribed, and ranging from 1.5 to 16 cm in size. The cut surface can appear grayish white, soft, rubbery, and myxoid. Most tumors are associated with a major or
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This tumor is similar to its counterpart in salivary glands of the head and neck. Similar to the tumors in salivary glands, tongues of tumor tissue outside their fibrous capsules were also observed in pulmonary pleomorphic adenoma. So, their incomplete excision may be a potential source of recurrent disease [6].

Primary pleomorphic adenoma may be confused with other primary or metastatic tumors of lung. First, metastatic pleomorphic adenoma from salivary gland of the head and neck should be excluded by detailed clinical examination and evaluation. The immunostaining of pleomorphic adenoma displays the positivity of broad-spectrum CK, CK7, EMA, P63, S100 and vimentin, which is helpful for the diagnosis of a “mixed tumor” composed by epithelial and myoepithelial cells. Other differential diagnoses include hamartoma, pulmonary blastomas and carcinosarcoma. Hamartomas typically have well-developed chondroid elements, which was uncommon in pulmonary pleomorphic adenoma. Pulmonary blastomas and carcinosarco-

Figure 2. The histological features of the primary pleomorphic adenoma of the lung. A. The myoepithelial cells and glandular epithelial cells were arranged in cords, flakes or tubular structure. Hyaline basement membrane-like material was observed in the stroma. (H&E ×200). B. Squamous cell metaplasia was observed in some region (arrow). (H&E ×200). C. Chondromyxoid areas were mixed with epithelial cell nests. (H&E ×100).

Figure 3. The immunohistochemical staining of the primary pleomorphic adenoma of the lung. (A) The immunohistochemical staining of CK was positive in almost all the neoplastic epithelial cells (×200). (B) P63 was positive in all of the myoepithelial cells, but negative in glandular epithelial cells (×200). (C) TTF-1 was strongly positive in the nuclei of glandular epithelial cells, and also positive in part of the abluminal cells (red arrow) (×200). (D) Showed the expression of TTF-1 in the same field with (B). TTF-1 was strongly positive in the nuclei of glandular epithelial cells (red arrow), but negative in abluminal myoepithelial cells (black arrow) (×200).
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mas are malignant tumors with apparent atypia and invasiveness, and they have sarcomatous elements [14].

The present case showed typical structure of pleomorphic adenoma. The diagnosis was not difficult. But, the specific character of this case was that the tumor epithelial cells were positive for TTF-1 staining. TTF-1 was used as a marker for pulmonary or thyroid epithelial cells. The salivary gland-type tumors of the lung, including pleomorphic adenoma, were originated from the bronchial glands, and were thought negative for TTF-1. So, TTF-1 was considered as a useful marker in the differential diagnosis of salivary gland-type tumors and tumors originated from pulmonary epithelial cells, such as pulmonary adenomas, adenocarcinomas, and adenosquamous carcinomas. But, our case indicated that TTF-1 also can positive in pleomorphic adenoma. Matsumoto et al. reported a similar case in a 74-year-old man, previously [15]. TTF-1 positive staining was also reported in mucoepidermoid carcinoma and epithelial-myoepithelial tumors [16-18]. So, using TTF-1 as a marker of differential diagnosis should be careful. When a pulmonary tumor shows positive for TTF-1, the salivary gland-type tumor cannot be excluded from the differential diagnostic panel. On the other hand, the positive staining of TTF-1 indicates the epithelial cells of a salivary gland-type tumor exhibits differentiation toward type II alveolar epithelial cells, which supports its pulmonary origin.

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Disclosure of conflict of interest

None.

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