Case Report
Thymic adenocarcinoma associated with thymic cyst: a case report and review of literature

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Abstract: Thymic adenocarcinoma of the mediastinum is extremely rare. Only 12 cases adenocarcinoma associated with a thymic cyst have been reported in the literature. In this report, we describe a case of a thymic adenocarcinoma associated with thymic cyst. A 70-year-old man, presented with two months of chest tightness, breath shortness and chest pain. The contrast enhanced CT scan of chest revealed a round, cystic mass in right anterior mediastinum. Microscopic examination revealed that the lining consisted of flat to cuboidal and columnar epithelium and adenocarcinoma infiltrated into the thymic tissue and the soft tissue around the wall of cyst. Based on clinical history, imaging studies, pathological findings and absence of extramediastinal tumor, a diagnosis of thymic adenocarcinoma associated with thymic cyst was established. The patient was alive without any sign of recurrence 7 months after the operation.

Keywords: Thymic cyst, thymic carcinoma, pathology

Introduction
Thymic adenocarcinoma is a rare type of thymic carcinoma. Carcinoma associated with thymic cysts is extremely rare [1]. Only 12 cases adenocarcinoma associated with a thymic cyst have been reported in the literature [1-12]. In the current case, we report a case of thymic adenocarcinoma associated with a thymic cyst. We also describe the pathologic features and discuss the pathologic diagnostic procedure and follow-up in this case. Here, we report our case with a review of literatures.

Case report
A 70-year-old man, presented with two months of chest tightness, breath shortness and chest pain, was admitted to our hospital. He gave a history of hypertension but without other notable medical history. Physical examination showed blood pressure 144/87 mmHg and body temperature 37.2°C. Laboratory investigation gave the following results: The level of prostate specific antigen (PSA) was high at 12.12 ng/ml (normal <4). The serum level of carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), carbohydrate antigen 15-3 (CA15-3), carbohydrate antigen 125 (CA-125), neuron-specific enolase (NSE) is normal. The liver function and kidney function were all in the normal ranges.

The contrast enhanced CT scan of chest revealed a round, cystic mass in right anterior mediastinum (Figure 1A). The patient underwent excision of the mass under general anesthesia. At surgery the mass was found to be globular, smooth surface, well circumscribed and situated below the right lobe of the thymus (Figure 1B). There was no attachment to the pericardium. The mass was excised and sent for histopathological examination.

The excised mass was measured 7 cm×4 cm×3 cm and cystic. The cyst had smooth walls and was filled with gelatinous mucinous (Figure 1C). The wall of the cyst was collagenous and smooth muscle, with areas of vascular dilation, congestion, hemorrhage, and hyperplasia of the thymus. The lining consisted of flat to cuboidal and pseudostratified columnar epithelium.
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(Figure 2A). Some of the sections were seen thymic tissue around the wall of the cyst (Figure 2B). A neoplasm revealed island like or flaky infiltration into the soft tissue around the wall of cyst, some of which was also seen in the thymic tissue (Figure 2C, 2D). The neoplastic cells were arranged to form irregularly dilated and branched glandular spaces, which was positive for periodic acid Schiff (PAS) staining. These cells were oval to spindle-shaped, exhibiting pleomorphism and mitosis. Immunohistochemical staining showed that the neoplastic cells were positive for CK, CK7, CK20, CDX-2, Villin, P53 and the smooth muscle was positive for SMA (Figure 3). The Ki-67 index was about 20%-30%. Staining was negative for thyroid...
transcription factor-1 (TTF-1), vimentin, CD5, calretinin and P63. Based on clinical history, imaging studies, absence of extramediastinal tumor and pathological findings, a diagnosis of thymic adenocarcinoma associated with thymic cyst was established.

There were no postoperative complications. No further operation and adjuvant chemotherapy was required. The tumor exhibited no signs of recurrence or metastatic spread after 7 months of follow-up.

Discussion

There have been rare reports about thymic adenocarcinomas associated with thymic cyst in the anterior mediastinum [1]. Review of the literature demonstrates that the median age of these 12 thymic adenocarcinomas with thymic cyst patients is 50 years, with a predominance in females (2:1) (Table 1). Most patients commonly present with compressive symptoms such as cough, dyspnea, and dysphagia since these tumors can compress or invade local...

Figure 2. Microscopic findings. (A) The lining consisted of flat to columnar epithelium. (B) Thymic tissue was seen around the wall of the cyst. (C) A neoplasm revealed island like infiltration into the soft tissue around the wall of cyst, (D) some of which was also seen in the thymic tissue.
mediastinal structures. These tumors range in size from 4 to 14.5 cm in maximum dimension. Histological subtypes can be the papillary, mucinous and others [4].

Two main theories have been trying to explain the pathogenesis of thymic carcinomas associated with thymic cyst. Some researchers favor a malignant transformation of the lining epithelium of a preexisting thymic cyst. In some cases they find the focal nests of uniform cells are continuous with the cyst lining and extend into the muscular wall, which reveal that thymic carcinoma is derived from epithelium of thymic cyst [13, 14]. On the other hand, some theories postulate that the cystic changes are an exaggerated hyperplastic response of the thymic epithelium to certain tumor antigens leading to cystic dilatation of Hassall corpuscles in thymic carcinomas associated with thymic cyst cases [15].

However, because of the limited number of reported cases, the precise etiology, pathogenesis, and prognosis factor of this tumor are largely unknown. The present case showed adenocarcinoma in fibrous tissue around the wall of cyst and in the thymus tissue. However, there was no clear evidence to see malignant transformation between neoplasms and the lin-
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Table 1. Clinicopathologic features of patients with thymic adenocarcinoma associated with thymic cyst

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Sex</th>
<th>Age</th>
<th>Size</th>
<th>Tumor type</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Babu MK [3]</td>
<td>1994</td>
<td>M</td>
<td>50</td>
<td>7×4×3 cm</td>
<td>Conventional</td>
<td>Alive after 4 months</td>
</tr>
<tr>
<td>Choi WW [4]</td>
<td>2003</td>
<td>M</td>
<td>15</td>
<td>8×5×4 cm</td>
<td>Mucinous adenocarcinoma</td>
<td>Died after 26 months</td>
</tr>
<tr>
<td>Zaitlin N [5]</td>
<td>2003</td>
<td>F</td>
<td>51</td>
<td>9×7 cm</td>
<td>Papillary adenocarcinoma</td>
<td>Died after 26 months</td>
</tr>
<tr>
<td>Kşpur P [6]</td>
<td>2006</td>
<td>M</td>
<td>41</td>
<td>10.5×8 cm</td>
<td>Mucinous adenocarcinoma</td>
<td>Died after 26 months</td>
</tr>
<tr>
<td>Ra SH [7]</td>
<td>2007</td>
<td>F</td>
<td>82</td>
<td>14.5×7 cm</td>
<td>Mucinous adenocarcinoma</td>
<td>Died after 26 months</td>
</tr>
<tr>
<td>Morresi-Hauf A</td>
<td>2008</td>
<td>F</td>
<td>38</td>
<td>6×4×2.5 cm</td>
<td>Adenocarcinoma</td>
<td>Died after 26 months</td>
</tr>
<tr>
<td>Morikawa H [9]</td>
<td>2010</td>
<td>F</td>
<td>68</td>
<td>4 cm</td>
<td>Papillary adenocarcinoma</td>
<td>Alive after 15 months</td>
</tr>
<tr>
<td>Ishiwata T [10]</td>
<td>2010</td>
<td>M</td>
<td>54</td>
<td>Diffused</td>
<td>Papillotubular adenocarcinoma</td>
<td>Passed away after 56 days</td>
</tr>
<tr>
<td>Abdul-Ghafar J</td>
<td>2012</td>
<td>F</td>
<td>36</td>
<td>5.6×4.4 cm</td>
<td>Mucinous Adenocarcinoma</td>
<td>Died after 15 months</td>
</tr>
<tr>
<td>Maghbool M [1]</td>
<td>2013</td>
<td>F</td>
<td>28</td>
<td>—</td>
<td>Mucinous adenocarcinoma</td>
<td>Passed away due to surgical complications</td>
</tr>
<tr>
<td>Current case</td>
<td>2014</td>
<td>M</td>
<td>70</td>
<td>7×4×3 cm</td>
<td>Adenocarcinoma</td>
<td>Alive after 6 months</td>
</tr>
</tbody>
</table>

It is also important to exclude the metastatic tumors and other possibilities. Immunohistochemical staining could be a useful method. For example, the tumor derived from the lung or thyroid by evaluating TTF-1, from pleura by evaluating calretinin, from breast by the staining of estrogen receptor (ER), progesterone receptor (PR) and Gross Cystic Disease Fluid Protein-15 (GCDFP15). Germ cell tumor and adenocarcinomas originating in the internal organs or in a foregut cyst also need to be considered. In addition to pathological finding and immunohistochemical investigation, clinical and radiological evaluations are also essential to exclude the presence of a primary tumor outside the thymus for an accurate diagnosis [9].

Sometimes, it could be difficult for the differential diagnosis between thymic cysts and bronchogenic cysts. Thymic cyst revealed a fibrous cyst wall with focal residual thymic tissue. The cyst wall was lined by a monolayer of cuboidal to columnar mucinous epithelial cells. The lining epithelium could be replaced by fibrin, hemorrhage, and cholesterol clefts. While a bronchogenic cyst was usually with cartilage plates, smooth muscle bundles and ciliated respiratory epithelial lining and/or seromucinous glands [14]. However, these confirmatory elements were mentioned in only 43% of cases. So the diagnosis of the thymic cyst also needs the aid of the imaging findings, typical mediastinal location and clinical data.

The treatment and prognosis for thymic adenocarcinoma associated with thymic cyst have not been mentioned because of the limited number of cases. Some cases reported that complete resection is the best treatment and a significant prognostic factor for thymic carcinoma. Yim had reported complete thymectomy and thymic cystectomy by video-assisted thoracoscopic surgery (VATS), which was considered to be a simple approach [18]. Zaitlin et al. also had used VAST for excision of thymic cyst [5]. However, they suggest it is important not to spill the content of the cyst because it contains tumor cells during the resection of tumors associated with thymic cysts.

Sometimes, it could be difficult for an accurate diagnosis of thymic adenocarcinoma associated with thymic cysts because of the limited number of cases. In addition to pathological finding, immunohistochemical investigation, clinical and imaging studies are also essential to exclude the presence of a primary tumor outside the thymus. This study demonstrates the importance of a comprehensive pathological work-up and the pathological diagnostic procedure.

Disclosure of conflict of interest

None.

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