Thymic Carcinoma with Adenoid Cystic Carcinomalike Features with Distant Metastases

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Adenoid cystic carcinoma (ACC), which is a subtype of the nonpapillary adenocarcinoma of the thymus, is extremely rare. We report a patient with thymic carcinoma with ACC-like features presented with multiple bone and pulmonary metastases that underwent surgery. The present case firstly demonstrated that thymic carcinoma with ACC-like features could have metastatic potential.

Keywords: thymus, pathology, surgery

Introduction

Thymic carcinomas are defined as thymic epithelial neoplasms, which are classified into 10 histological types. Among these, adenoid cystic carcinoma (ACC), which is a subtype of the nonpapillary adenocarcinoma of the thymus, is extremely rare. To the best of our knowledge, only 6 cases of this rare tumor had been reported so far. We herein report a patient with thymic carcinoma with ACC-like features who presented with multiple bone and pulmonary metastases.

Case Report

A 66-year-old male visited our hospital because of a dry cough. A mediastinal mass was incidentally found on chest X-ray. He had a 4 pack-per-day smoking history which had been ceased 14 years prior. Spirometry revealed a decreased forced expiratory volume (FEV1.0 : 1.29L, FEV1.0% : 52.0%). Computed tomographic (CT) scan demonstrated an anterior mediastinal mass which measured 46 mm in diameter adjacent to the ascending aorta (Fig. 1A). Eight pulmonary nodules up to 8 mm in diameter were also demonstrated in the bilateral lungs. Masses were found in the manubrium and the right fifth rib which measured 25 mm and 15 mm in diameter, respectively (Fig. 1B and 1C). A study of whole-body Fluorine-18-2-fluoro-D-glucose positron emission tomography/CT (FDG-PET/CT) revealed intense focal FDG uptake in the anterior mediastinal mass, the manubrium mass, and the right fifth rib mass [standard uptake value (SUV) max values were 4.6, 2.4, and 1.3 respectively] and no other abnormal FDG uptake.

Based on these radiological findings, a thymic tumor with multiple bone and pulmonary metastases was suspected. A surgical biopsy of the manubrium mass was performed, and the mass was diagnosed to be “non-small cell carcinoma with a cribriform pattern”. Immunohistochemically, the tumor cells were positive for AE1/AE3, and negative for CD56, chromogranin A, p63, SMA, and synaptophysin. The MIB-1 index was less than 10%. Taken together, these findings indicated that the thymic tumor was a low-grade malignant tumor despite its metastatic behavior. Surgery was planned.

The patient was placed in the supine position under general anesthesia.
Resection of the manubrium and bilateral proximal clavicle, the right fifth rib, the thymus and the thymic tumor were accomplished through a median sternotomy. Partial resection of the adherent left upper lobe of the lung was also performed. Complete resection of all of the pulmonary metastases was deemed intolerable due to the patient’s impaired respiratory function (decreased FEV), but one nodule in the right middle lobe was resected for pathological examination. The anterior chest wall was reconstructed using a polytetrafluoroethylene prosthesis and a pedicled left major pectoralis muscle flap. Macroscopically, the cut surface of the tumor showed a well-defined nodular lesion that measured 49 × 44 mm in diameter (Fig. 2A). Microscopically, the tumor was circumscribed by fibrous tissue. Atypical short spindle cells with oval nuclei proliferated showing solid nests with both glandular and cribriform patterns. Small slit-like vessels were occasionally observed among the tumor cells. Hyalinized fibrotic stroma was present between the solid nests of the tumor cells. Mitotic figures were observed 2 to 3 per 10 high power fields (Fig. 2B). Immunohistochemically, the cells in this tumor were positive for AE1/AE3, 34beta E12, p63, EMA (focal), CD10 (partial), and negative for CEA, TTF-1, Laminin, Vimentin, SMA, S-100, Bcl2, CD117, and p53. The pseudo-cysts contained type IV collagen-positive material. The MIB-1 index was 3%. No invasion to the mediastinal pleura nor the lung were observed. The tumors of the manubrium, the right fifth rib, and the right middle lobe of the lung had the same characteristics as the thymic tumor. The final diagnosis was thymic carcinoma with ACC-like features with multiple bone and pulmonary metastases. The patient suffered from transient, left phrenic nerve paralysis postoperatively; however, he had no other symptoms. The patient was discharged and given no adjuvant chemotherapy or radiation. To date, 12 months after the operation, the patient is doing well despite the gradual growth of pulmonary nodules.

Discussion

Thymic carcinomas are defined as thymic epithelial neoplasms, which are classified into 10 different histological types according to the 2004 update of the WHO classification, i.e., (1) squamous cell carcinoma, (2) basaloid carcinoma (BC), (3) mucoepidermoid carcinoma, (4) lymphoepithelioma-like carcinoma, (5) sarcomatoid carcinoma, (6) clear cell carcinoma, (7) papillary adenocarcinoma, (8) nonpapillary adenocarcinoma, (9) carcinoma with translocation, and (10) undifferentiated carcinoma. Within the group of nonpapillary adenocarcinomas, 4 histologic subtypes have been described; mucinous (colloid) carcinoma, carcinoma with glandular differentiation arising in a thymic cyst, hepatoid carcinoma, and ACC.

ACC is usually a tumor of the salivary glands. ACC-
like tumors are rarely detected at unusual sites such as the breast, lung and prostate.\(^2\)–\(^4\) Thymic tumors with ACC-like features are even rarer. To determine whether a thymic tumor is primary or secondary, it is necessary to rule out the presence of tumors of the salivary glands and breasts, lungs, or prostate. In the present case, because these tumors were excluded by whole-body FDG-PET/CT and a chest CT, the thymic tumor was determined to be the primary tumor. The histologic features of this rare tumor were similar to its counterpart in the salivary gland. Immunohistochemical studies are generally performed to exclude the presence of a combined thymic epithelial tumor, including neuroendocrine or squamous cell carcinomas. The differential diagnosis includes thymic carcinoma with hyaline stromal material\(^5\) and BC. BC, a variant of squamous cell carcinoma, resembles the solid type of ACC. Most cases of BC are composed of small, hyperchromatic nuclei that form solid lobules, adenomatoid arrangements and cords.\(^6,7\) However, the tumor cells were normochromatic in the present case. In addition, BC usually has an apparent focus of squamous cell carcinoma\(^5\)\(^6\)\(^7\) while a squamous cell carcinomatous component was completely absent in the present case. Based on these findings, we diagnosed the patient with a thymic tumor with ACC-like features.

To the best of our knowledge, only 6 patients with thymic tumors with ACC-like features have been reported so far (Table 1).\(^\text{5-10}\) The ages of all 7 patients, including the present case (4 males and 3 females) ranged from 37 to 77 (median 65) years. The reported symptoms were cough, dyspnea, chest pain, fever, and weight loss. The diameters of the tumor ranged from 2 cm to 14 cm. Involvement of the pericardium has been reported, however, no patients with nodal involvement nor distant metastasis have been reported in the past. The present case is the first patient with thymic carcinoma with ACC-like features that presented with distant metastases. Four of the seven patients underwent surgery alone, and three patients were treated with combined therapy (combination of surgery and radiation or chemotherapy). There is little information on long-term patient outcome after treatment. In the series by Di Tommaso and colleagues,\(^8\) 1 patient was alive at 22 months, 1 patient died of myeloid leukemia 5 years later, and 2 were lost to follow-up. The patient reported by Coulibaly and colleagues\(^9\) was alive at 7 months after diagnosis.

We believe that the basic surgical principle for thymic tumors, i.e., \textit{en bloc} resection with negative margins if curative resection is possible can be applied to thymic tumors with ACC-like features. On the other hand, the role of systemic chemotherapy for metastatic ACC remains controversial. According to a review by Laurie and colleagues,\(^11\) the evidence in support of the efficacy of any systemic therapy for metastatic ACC is limited, and they stated that systemic therapy should be reserved for patients with disease-related symptoms or rapidly progressive disease. In the present case, surgery was planned despite the presence of distant metastases. The reasons why we performed surgery were as follows. (1) The risk of surgery was deemed tolerable. (2) The significance of incomplete resection of low grade malignant thymic tumors remains unclear. (3) The response rate of chemotherapy for adenoid cystic carcinoma is generally less than 30%,\(^1\) and there is currently no effective chemotherapy regimen for adenoid cystic carcinoma. (4) Surgery has advantages in that it can prevent pathological fractures of the bone.
due to bone metastases, and provides a total biopsy of the thymic tumor. We informed the patient about the advantages and disadvantages, risks, benefits and alternatives to surgery, and he desired to undergo surgery. In the present case, complete resection of all of the pulmonary metastases in our patient was deemed intolerable due to his impaired respiratory function. It was considered that chemotherapy should be performed if disease-related symptoms or enlargement of the pulmonary metastases were observed.

In conclusion, the present case demonstrated that thymic carcinoma with ACC-like features has metastatic potential, although the indications for surgery remain debatable.

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Disclosure Statement

None of the authors has any financial or other potential conflicts of interest.

References

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Table 1  Summary of reported cases of thymic tumors with ACC-like features

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age/ Sex</th>
<th>Size (cm)</th>
<th>Distant metastasis</th>
<th>Treatment</th>
<th>Outcome</th>
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<td>Di Tommaso</td>
<td>2007</td>
<td>65/ M</td>
<td>5</td>
<td>No</td>
<td>S</td>
<td>Lost follow up</td>
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<td></td>
<td>2007</td>
<td>63/ F</td>
<td>2.5 × 2</td>
<td>No</td>
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<td>Lost follow up</td>
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<td>69/ M</td>
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<td>S,R</td>
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<tr>
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<td>77/ M</td>
<td>13 × 10</td>
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<td>S</td>
<td>Alive without disease; 22mo</td>
</tr>
<tr>
<td>Coulibaly</td>
<td>2008</td>
<td>37/ F</td>
<td>large</td>
<td>No</td>
<td>S,C,R</td>
<td>Alive without disease; 7mo</td>
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<td>Banki</td>
<td>2010</td>
<td>65/ F</td>
<td>14 × 8.8</td>
<td>No</td>
<td>S</td>
<td>Alive without disease; 30mo</td>
</tr>
<tr>
<td>Our Case</td>
<td>2011</td>
<td>66/ M</td>
<td>4.9 × 4.4</td>
<td>Yes</td>
<td>S</td>
<td>Alive with disease; 12mo</td>
</tr>
</tbody>
</table>

ACC: adenoid cystic carcinoma; C: chemotherapy; F: female; M: male; R: radiotherapy; S: surgery