Case Report
Ectopic thymic carcinoma in parotid gland: a rare case and review of literature

Peisha Huang², Rongfang Huang¹, Weijin Xiao², Wei Liu¹, Tongmei He³, Weifeng Zhu¹, Chao Li¹,³,⁴

¹Department of Pathology, Fujian Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China; ²Department of Pathology, Fujian Medical University Cancer Hospital and Fujian Cancer Hospital, Fuzhou, China; ³Fujian Provincial Key Laboratory of Translational Cancer Medicine, Fuzhou, China; ⁴Department of Pathology, School of Basic Medical Science, Fujian Medical University, Fuzhou, China

Received September 6, 2018; Accepted September 27, 2018; Epub January 1, 2019; Published January 15, 2019

Abstract: Thymic carcinoma that occurs outside the anterosuperior mediastinum is rare. To date, only five cases of ectopic thymic carcinoma have been reported in the English-language literature. Here, we report a case of 43-year-old Chinese man who suffering from ectopic thymic carcinoma of the parotid gland. Magnetic resonance imaging (MRI) showed a round soft tissue mass in the parotid gland. After enhancement, it showed the edge of the tumor was rough, with irregular shallow lobes. Histological examination (HE) showed tumor cells were invasive, and partially arranged in a lobulated structure. These characteristics were similar to previous English-language literature reports. Immunohistochemical (IHC) examination showed that tumor cells were positive for CD5, CD117 and p63, which confirms this case is ectopic thymic carcinoma. Postoperatively the patient received combined paclitaxel plus carboplatin chemotherapy. Currently, no evidence of metastasis or recurrence has been found in this patient.

Keywords: Parotid gland, ectopic thymic carcinoma, immunohistochemistry

Introduction

In the anterosuperior mediastinum, thymic neoplasms mainly include thymoma and thymic carcinoma. Thymic carcinoma is a malignant epithelium-derived tumor [1]. The most common symptoms are chest pain, also cough, fatigue, fever, loss of appetite, and weight loss. Although thymic carcinoma outside the anterior mediastinum is rare, it most often occurs in the lungs, and less often in the neck, cervical, and parietal pleura. However, this case occurring in the parotid gland is even more rare. As a result of their unexpected location, ectopic thymic carcinomas have not previously been imaged and they are easily misdiagnosed as other common tumors in this area. To date, only a few case reports have been published in the English-language literature [2-6]. Diagnosis of ectopic thymic carcinoma requires morphological and immunohistochemical support [6]. Not long ago, we discovered a case of ectopic thymic carcinoma that occurred in the parotid gland.

Case report

Clinical history

A left parotid tumor measuring 10 × 10 × 10 mm was found coincidentally in an asymptomatic 43-year-old Chinese man 6 months ago. As the tumor gradually enlarged, magnetic resonance imaging showed a round soft tissue mass in the parotid gland, measuring 26 × 24 × 33 mm. After enhancement, it showed uneven and mild to moderate enhancement, and the edge of the tumor was rough, with irregular shallow lobes (Figure 1A, 1B). Specialist examination showed a mass on the left parotid gland, texture hard, ill-defined, acceptable activity, no tenderness. Positron emission tomography-computed tomography (PET-CT) showed no evidence of tumors in other parts of the body, and no abnormalities were found in blood tests and tumor markers. Finally, the patient underwent left total parotidectomy and upper cervical lymph node dissection.
Ectopic thymic carcinoma

Pathological findings

The excised specimens were fixed in formalin and embedded in paraffin and 4 μm thick sections were stained for histological examination. Immunohistochemistry was performed using the Dako Autostainer (Carpentaria, CA, USA) and using the standard Envision method. The primary antibodies were: anti-cytokeratin (MX005; Microm); anti-CD5 (UMAB9; ZSbio); anti-CD117 (YR145; Microm); anti-S-100 (4C-4.9; Microm); anti-synaptophysin (SYN211; Microm); anti-CD56 (123C3.D5; Microm); and anti-p63 (MX013; Microm). The experimental procedure was carried out according to the instructions. For each antibody, using known positive tissue as a positive control.

The tumor measured 26 × 24 × 33 mm. At low magnification, HE showed tumor cells are invasively growing, and partially arranged in a lobulated structure (Figure 2). The tumor cells were arranged in nests, organ (Figure 3A). Higher magnification showed that the tumors were composed of epithelioid cells, with round nuclei, eosinophilic, partially transparent cytoplasm, and readily visible nucleoli (Figure 3B).

Immunohistochemical analysis of paraffin-embedded sections showed that the tumor cells were positive for CD5 and CD117 (Figure 4A, 4B), which were specific for diagnosis of ectopic thymic carcinoma [7]. The tumor cells were also strong positive for cytokeratin, and p63.

Discussion

In the anterosuperior mediastinum, thymic neoplasms mainly include thymoma and thymic carcinoma [1]. Thymic carcinoma is a malignant epithelial tumor and tends to be aggressive, and most of them occur in middle age and in men. Thymic carcinoma that occurs outside the anterior mediastinum is rare. To date, only five cases of ectopic thymic carcinoma have been reported in the English-language literature: (i) Hsu et al, showed a case of cervical ectopic thymic squamous cell carcinoma with a microcarcinoma in the remnant mediastinal thymus [2]; (ii) Calderon et al, described a case of ectopic thymic carcinoma in the intrapericardial [3]; (iii) Yao et al, summarized a case of ectopic thymic squamous carcinoma in the neck [4]; (iv) Matsuoka et al, found a case of ectopic undifferentiated thymic carcinoma in the intrathoracic [5]; and (v) Haoshuai et al, discovered a case of ectopic thymic carcinoma in the right parietal pleura [6]. Not long ago, we discovered a case of ectopic thymic carcinoma that occurred in the parotid gland, which is extremely rare. As far as I know, these are the only six cases that have been discovered. All the characteristics of these cases are shown in Table 1. Generally speaking, all of these patients are adults. aged 24-83 years (median 53.5 years, with five >40 years). There were five men and one woman. Here, we describe a series of 6 ectopic thymic carcinoma, including the cervical (one), intrapericardial (one), neck (one), intrathoracic (one), right parietal pleural (one), and parotid gland (one).

The lesions ranged from 1.5 to 55 mm in size with an average size of 28.25 mm. HE revealed that cases 1, 2, 5 and 6 had classic histology;
Ectopic thymic carcinoma

Figure 3. A. Microscopic findings: tumor cells arranged in nests (HE; original magnification × 100); B. Higher magnification showed that the tumors were composed of epithelioid cells, with round nuclei, eosinophilic, partially transparent cytoplasm, and readily visible nucleoli (HE; original magnification × 200).

Figure 4. A. Atypical epithelioid cells showing strong membranous immunoreactivity for CD5 (original magnification × 100). B. Atypical epithelioid cells showing strong membranous immunoreactivity for CD117 (original magnification × 200).

case 3 had nests with focal squamoid differentiation; and case 4 had spindle and sarcomatous cells with multinucleated giant cells. Only case 3 had thymic tissue near the tumor. The results of immunohistochemical staining are summarized in Table 1. Cases 1, 3, 5 and 6 were positive for CD5 staining, cases 3 and 6 were positive for CD117; and cases 3, 5 and 6 were positive for p63. In case 2, immunohistochemistry results for CD5, CD117 and p63 were not available, as usual for biopsy specimens diagnosed with ectopic thymic carcinoma. In our case, HE showed tumor cells were invasively growing, and partially arranged in a lobulated structure which suggested that the tumor cells originated from the thymus.

According to the tumor site, histologic morphology and biological behavior, the differential diagnosis should include seminoma, clear cell sarcoma, neuroendocrine tumor and ectopic thymic carcinoma. Immunohistochemical negative expression of SALL4 and PLAP suggested that seminoma could be ruled out. Clear cell sarcoma would be positive for S-100 and HMB-45, thus excluding this diagnosis. Last but not least, immunohistochemistry negative for synaptophysin, chromogranin A and CD56 and positive for CD5, CD117 and p63, confirmed that this case is not neuroendocrine tumor but thymic carcinoma. The World Health Organization (WHO) classification [7] and the International Thymic Malignancy Interest Group [9] believe that positivity for CD5 and CD117 provides strong evidence for the diagnosis of thymic cancer based on morphology. Taking into account various factors, a final diagnosis of ectopic thymic carcinoma was reached.

Thymic carcinoma is a malignant tumor of epithelial origin [8]. The most common pathological type is thymic squamous cell carcinoma with a five-year survival rate of approximately 30% [4]. Thymic carcinoma is a malignant tumor and tends to be aggressive. Early detection, diagnosis and treatment can improve survival rate and improve prognosis [11].
## Ectopic thymic carcinoma

### Table 1. Characteristics of reported cases of ectopic thymic carcinoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Age (years)</th>
<th>Clinical presentation</th>
<th>Location</th>
<th>Size (mm)</th>
<th>Histology features</th>
<th>Thymus tissue</th>
<th>Capsular invasion</th>
<th>CD5 IHC</th>
<th>CD117 IHC</th>
<th>p63 IHC</th>
<th>Treatment</th>
<th>Follow up (months)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hsu et al [2]</td>
<td>49</td>
<td>Hoarseness</td>
<td>Cervical</td>
<td>1.5</td>
<td>Classic</td>
<td>None</td>
<td>NO</td>
<td>Positive</td>
<td>NA</td>
<td>NA</td>
<td>CR RT CH</td>
<td>26</td>
<td>Alive</td>
</tr>
<tr>
<td>2</td>
<td>Calderon et al [3]</td>
<td>73</td>
<td>Cough, dyspnea and anorexia</td>
<td>Intrapericardial</td>
<td>UK</td>
<td>Classic</td>
<td>None</td>
<td>NO</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>CR</td>
<td>Died*</td>
<td>Died</td>
</tr>
<tr>
<td>4</td>
<td>Maosuoka et al [5]</td>
<td>83</td>
<td>Asymptomatic</td>
<td>Intrathoracic</td>
<td>55</td>
<td>Spindle*</td>
<td>None</td>
<td>NO</td>
<td>Negative</td>
<td>NA</td>
<td>NA</td>
<td>CR</td>
<td>24</td>
<td>Alive</td>
</tr>
<tr>
<td>6</td>
<td>Present study</td>
<td>43</td>
<td>Asymptomatic</td>
<td>Parotid gland</td>
<td>26</td>
<td>Classic</td>
<td>None</td>
<td>Surface of tissue</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>CR CH</td>
<td>10</td>
<td>Alive</td>
</tr>
</tbody>
</table>

*The patient underwent surgical excision of the tumor and died of right ventricular rupture during the procedure. *Nests with focal squamoid differentiation; *spindle and sarcomatous cells with multinucleated giant cells. CH, chemotherapy; CR, complete resection; NA, not available; NED, no evidence of disease; RT, radiotherapy; UK, unknown.
Ectopic thymic carcinoma

Nowadays, the treatment recognized by the medical community is to completely remove the tumor and assist with chemotherapy and radiotherapy [10]. Treatment of ectopic thymic carcinoma is similar to thymic cancer. The results of treatment strategy are summarized in Table 1. After resection of ectopic thymic carcinoma, cases 1 and 3 had chemotherapy and radiotherapy, case 5 was treated with radiotherapy, and case 6 had chemotherapy. Furthermore, case 4 did not receive adjuvant therapy owing to advanced age and case 2 the patient who died of right ventricular rupture during surgery. After complete removal of the ectopic tumor, no evidence of metastasis or recurrence has been found in these patients during 6 to 24 months.

In conclusion, correct diagnosis of ectopic thymic carcinoma is challenging because it is a rare tumor found in such an unusual location, with varying histologic patterns. Therefore, pathologists need to combine morphology and immunohistochemistry to make a correct diagnosis.

Acknowledgements

This research was supported by Fujian Provincial Health Technology Project (Grant number: 2017-CX-10).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Chao Li, Department of Pathology, Fujian Cancer Hospital and Fujian Medical University Cancer Hospital; Fujian Provincial Key Laboratory of Translational Cancer Medicine; Department of Pathology, School of Basic Medical Science, Fujian Medical University, 420 Fuma Rd, Jinan District, Fuzhou 350014, China. E-mail: lichao3501@163.com

References