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Case Report

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

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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, immunohistochemisty

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.

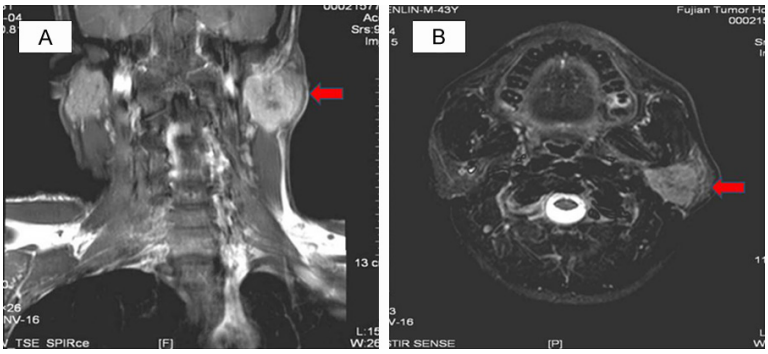

Figure 1. A, B. MRI of the parotid gland demonstrated a round soft tissue mass. After enhancement, it showed the edge of the tumor was rough, with irregular shallow lobes.

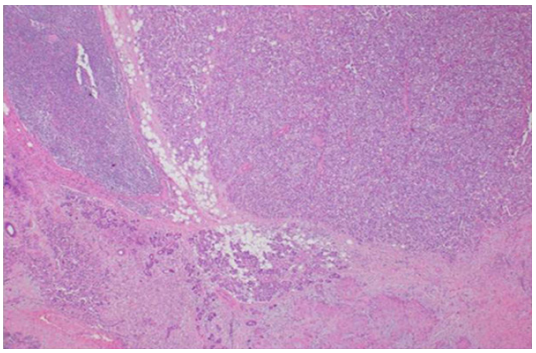

Figure 2. Microscopic image showing tumor cells are invasive, and partially arranged in a lobulated structure (HE; original magnification × 20).

Pathological findings

The excised specimens were fixed in formalin and embedded in paraffinand 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;

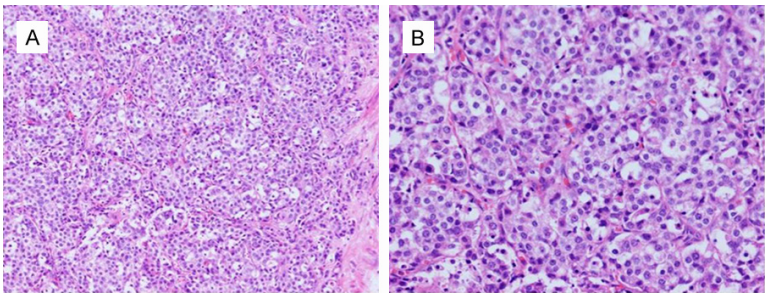

Figure 3. A. Microscopic findings: tumor cells arranged in nests (HE; original magnification × 100); B. Higher magnification showed that the tumors were composed of epithelioid cells, with round nuclei, eosinophilic, partially transparent cytoplasm, and readily visible nucleoli (HE; original magnification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

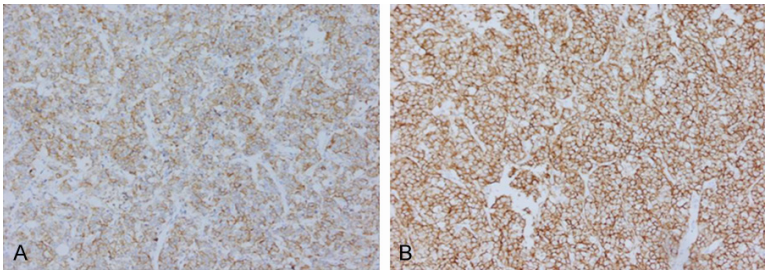

Figure 4. A. Atypical epithelioid cells showing strong membranous immunoreactivity for CD5 (original magnification × 100). B. Atypical epithelioid cells showing strong membranous immunoreactivity for CD117 (original magnification × 200).

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 case 4, immunohistochemical examination showed the tumor cells positive for vimentin, and CAM5.2 Negative results included napsin A, thyroid transcription factor-1 (TTF1), CD5, calretinin, synaptophysin, chromogranin A, and CD56. These findings suggested that mesothelioma and lung carcinoma could be ruled out. Otherwise, it is mentioned in the English-language literature that undifferentiated thymic carcinomas can be negative for CD5 and CD117 [12]. Based on these histologic findings, immunohistochemistry, and review of the literature, the final diagnosis was undifferentiated ectopic thymic carcinoma [5]. Diagnosis is made difficult because some pathologists lack awareness of thymoma or thymic carcinoma, and these types of tumors lack typical features [6]. Correct diagnosis is also challenging because the tumor is located in such an unusual site and has several histologic patterns. 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 synatophysin, 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].

Table 1. Characteristics of reported cases of ectopic thymic carcinoma

Case	Author	Age (years)	Clinical presentation	Location	Size (mm)	Histology features	Thymus tissue	Capsular invasion	CD5 IHC	CD117 IHC	p63 IHC	Treatment	Follow up (months)	Outcome
1	Hsu et al [2]	49	Hoarseness	Cervical	1.5	Classic	None	NO	Positive	NA	NA	CR RT CH	26	Alive
2	Calderon et al [3]	73	Cough, dyspnea and anorexia	Intrapericardial	UK	Classic	None	NO	NA	NA	NA	CR	Died[a]	Died
3	Yao et al [4]	24	Difficulty swallowing, neck soreness	Neck	55	Nests[b]	Thymus tissue	NO	Positive	Positive	Positive	CR RT CH	6	Alive
4	Maosuoka et al [5]	83	Asymptomatic	Intrathoracic	55	Spindle[c]	None	NO	Negative	NA	NA	CR	24	Alive
5	Haoshuai et al [6]	73	Asymptomatic	Right parietal pleural	47	Classic	None	Surface of the lung	Positive	NA	Positive	CR RT	17	Alive
6	Present study	43	Asymptomatic	Parotid gland	26	Classic	None	Surface of tissue	Positive	Positive	Positive	CR CH	10	Alive

[a]The patient underwent surgical excision of the tumor and died of right ventricular rupture during the procedure. [b]Nests with focal squamoid differentiation; [c]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.

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 that 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.

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Disclosure of conflict of interest

None.

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References

[1] Weissferdt A, Moran CA. The spectrum of ectopic thymomas. Virchows Arch 2016; 469: 245-254.

[2] Hsu IL, Wu MH, Lai WW, Lin MY, Chang JM, Yen YT, Tseng YL. Cervical ectopic thymoma. J Thorac Cardiovasc Surg 2007; 133: 1658-1659.

[3] Calderon AM, Merchan JA, Rozo JC, Guerrero CI, Treistman B, Sulak LE, Cheong BY, Rodríguez G, Mesa A. Intrapericardial primary thymic carcinoma in a 73-year-old man. Tex Heart Inst J 2008; 35: 458-461.

[4] Yao WT, Chen CH, Lee JJ, Chen BF, Liu TP. Ectopic thymic carcinoma in the neck. Ann Thorac Surg 2010; 90: 666-668.

[5] Matsuoka K, Murata Y, Ueda M, Miyamoto Y. Ectopic thymic carcinoma presenting as an intrathoracic mass. Asian Cardiovasc Thorac Ann 2016; 24: 480-483.

[6] Zhu H, Lei Y, Zou J, Su C, Zeng B, Li Y, Luo H. Ectopic right parietal pleural thymic carcinoma: a rare case and review of the literature. J Thorac Dis 2017; 9: 609-613.

[7] Marx A, Chan JK, Coindre JM, Detterbeck F, Girard N, Harris NL, Jaffe ES, Kurrer MO, Marom EM, Moreira AL, Mukai K, Orazi A, Ströbel P. The 2015 world health organization classifcation of tumors of the thymus: continuity and changes. J Thorac Oncol 2015; 10: 1383-1395.

[8] Eng TY, Fuller CD, Jagirdar J, Bains Y, Thomas CR Jr. Thymic carcinoma: state of the art review. Int J Radiat Oncol Biol Phys 2004; 59: 654-664.

[9] Marx A, Ströbel P, Badve SS, Chalabreysse L, Chan JK, Chen G, de Leval L, Detterbeck F, Girard N, Huang J, Kurrer MO, Lauriola L, Marino M, Matsuno Y, Molina TJ, Mukai K, Nicholson AG, Nonaka D, Rieker R, Rosai J, Ruffini E, Travis WD. Itmig consensus statement on the use of the who histological classifcation of thymoma and thymic carcinoma: refned defnitions, histological criteria, and reporting. J Thorac Oncol 2014; 9: 596-611.

[10] Ahmad U, Yao X, Detterbeck F, Huang J, Antonicelli A, Filosso PL, Ruffini E, Travis W, Jones DR, Zhan Y, Lucchi M, Rimner A. Thymic carcinoma outcomes and prognosis: results of an international analysis. J Thorac Cardiovasc Surg 2015; 149: 95-100.

[11] Hsu HC, Huang EY, Wang CJ, Sun LM, Chen HC. Postoperative radiotherapy in thymic carcinoma: treatment results and prognostic factors. Int J Radiat Oncol Biol Phys 2002; 52: 801-805.

[12] Thomas de Montpreville V, Ghigna MR, Lacroix L, Besse B, Broet P, Dartevelle P, Fadel E, Dorfmuller P. Thymic carcinomas: clinicopathologic study of 37 cases from a single institution. Virchow Arch 2013; 462: 307-313.