A Case Report of Ectopic Cervical Thymoma: A New Approach for a Preoperative Diagnosis

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Summary: We report an unusual case of ectopic cervical thymoma. A 35-year-old female patient presented with an anterior neck mass that developed over a five-month duration. The patient underwent fine-needle aspiration cytology (FNAC) twice, but the tumor type could not be diagnosed. The surgically removed tumor was white in color and had a smooth surface. According to the postoperative pathological examination, the tumor was diagnosed as a Stage I ectopic cervical thymoma and Type B1 according to the Masaoka staging system and the World Health Organization (WHO) histological staging system, respectively. The patient was in good overall health and remained without tumor recurrence at the time of the 10-month follow-up.

Because it was difficult to make a preoperative definite diagnosis by FNAC for the thymoma, we constructed a cell block from the existing cytological specimen. Immunohistological staining using the cell-block method clearly demonstrated the biphasic cellular population pattern that is a characteristic of thymoma. Therefore, this method may be useful as a preoperative differential diagnostic modality for cervical thymomas.

Key words: ectopic cervical thymoma, surgery, preoperative differential diagnosis, immunohistochemistry, cell-block method

INTRODUCTION

Thymoma is one of the most common tumors in the anterior mediastinum; however, it occurs infrequently in ectopic regions such as the cervix, thyroid, lungs, and pleura1). In the cervical region, thymoma is commonly confused with a thyroid nodule and malignant lymphomas in particular, because it commonly occurs in areas nearer to the thyroid. Here, we report a patient with an ectopic cervical thymoma who was treated with surgical excision.

CASE REPORT

A 35-year-old female patient presented with an anterior neck mass that had developed over a five-
month duration. The patient underwent fine-needle aspiration cytology (FNAC) twice during her first visit to the hospital; however, the tumor type could not be diagnosed. Physical examination of the anterior neck revealed a solid elastic tumor mass measuring approximately 5 × 3 cm with a smooth surface and good mobility. Biochemical examination of the blood, a thyroid function test, a serum parathyroid hormone level, and a soluble interleukin-2 receptor level were all free of abnormal findings. A chest radiograph revealed a cervical tracheal deviation to the left due to compression by the tumor. Enhanced computed tomography showed a large oval neck mass adhering to the right lobe of the thyroid which was slightly enhanced by radiocontrast agents (Figs. 1A and 1B). Cervical ultrasonography demonstrated a solid and sharp-margined hypoechoic nodule with internal heterogeneity measuring approximately 51 × 34 × 34 mm (Fig. 1C). Ultrasound guided FNAC was performed. The cytological smears were composed of numerous small lymphocytes, and did not contain follicular epithelial cells (Fig. 1D). We were unable to perform a definite diagnosis from these cytological findings and thus considered several possibilities, such as a thyroid tumor, parathyroid tumor, neurilemmoma, and malignant lymphoma.

We surgically removed the tumor; it was found to be white in color and had a smooth surface that displaced the thyroid to the superior medial, but did not significantly adhere to the surrounding tissues. The excised specimen was solid (55 × 40 × 27 mm), covered by a thin fibrous capsule, and...
was of a yellowish-white color internally. The interior of the tumor was separated by thin fibrous bands. It was not apparent whether the tumor was connected to the thyroid or the thymus. The tumor was not associated with the recurrent laryngeal nerve or vagus nerve.

Low-power microscopic examination revealed that the tumor was nodular, with a thin fibrous capsule and separated by thin fibrous bands (Fig. 2A). Microscopically, the tumor did not show extracapsular extension or invasion into the surrounding tissue. Morphological examination of the tumor by high-power microscopy revealed a predominance of typical lymphocytes along with polygonal or spindle-shaped epithelial cells (Fig. 2B). Overall, the tumor presented with a biphasic cellular population pattern characteristic of a thymoma. Immunohistological examination revealed that the epithelial cells positively expressed cytokeratin (AE1/AE3) (Fig. 2C), and the lymphocytes expressed CD3 staining as detected by immunohistochemistry.

Fig. 2  (A) Low-power microscopic examination (hematoxylin–eosin 100x) revealed that the tumor is nodular with a thin fibrous capsule and separated by thin fibrous bands. According to the microscopic examination, the tumor was not accompanied by extracapsular extension or invasion. (B) Microscopical examination (hematoxylin–eosin 400x) of the tumor by high-power microscopy revealed a predominance of typical lymphocytes along with polygonal or spindle-shaped epithelial cells. This biphasic cellular population pattern is characteristic of thymomas. (C) The epithelial cells expressed cytokeratin (AE1/AE3), and (D) the lymphocytes were positive for CD3 staining as detected by immunohistochemistry.

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We retrospectively attempted to construct a cell block from the existing cytological specimen. The immunohistological staining of cytokeratin (AE1/AE3) (Fig. 3A) and CD3 (Fig. 3B) using the cell-block method clearly demonstrated the biphasic cellular population pattern, indicating similar findings to those previously shown by the histological examination. Therefore, in the patients with many atypical lymphocytes from tumors located near the thyroid by FNAC, the cell-block method may be useful as a preoperative differential diagnostic modality for cervical thymoma.

**DISCUSSION**

In 1941, Bowman reported the first instance of ectopic cervical thymoma. Ectopic cervical thymoma is a relatively rare tumor that arises from ectopic thymic tissue anywhere along the embryological course of thymic descent from the embryonic pharyngeal wall to the anterior mediastinum. The incidence of mediastinal thymoma is equally present in males and females. However, 90% of patients with cervical thymoma are females, and it occurs more commonly in a ratio of 2:1 on the left side of the neck. Nagato performed a detailed analysis of 37 subjects with cervical thymoma, and concluded that the most frequent initial symptom was swelling of the neck; two patients with hoarseness had an invasive type thymoma. Despite the absence of symptoms, several cases of tracheal deviation were discovered by chest radiography during medical examination. Myasthenia gravis occurs in 47% patients with mediastinal thymoma. On the other hand, cervical thymomas were not associated with myasthenia gravis. The present patient did not present with myasthenia gravis either before or after surgery.

The Masaoka staging system and WHO histological classification system are widely used, and reflect the oncological and biological behaviors of mediastinal thymomas. The Masaoka staging system is based on the degree of invasiveness into the capsule and surrounding organs. This system categorizes tumors without capsular invasion as Stage I; tumors with capsular invasion or surrounding fatty tissue and mediastinal pleura as Stage II; tumors with invasion into the pericardium, large vessels, or lung as Stage III; pleural or pericardial dissemination as Stage IVa; and distant metastases as Stage IVb. The twenty-year survival rates of each clinical stage in the mediastinal thymomas are 89% in Stage I, 91% in Stage II, 49% in Stage III, and 0% in Stage IV. Complete surgical tumor re-
section is the first choice of treatment for patients with thymoma, and postoperative radiation thera-
py with or without chemotherapy is widely used in patients with invasive thymoma, especially for
those in Stages II and III\(^6,10\). Irradiation of the entire mediastinal field was found to be effective in
preventing mediastinal recurrence in patients with completely resected thymomas\(^10\). In patients
with Stage I thymoma, postoperative irradiation is not recommended because of the low incidence of
recurrence, even without radiation therapy\(^10\). We decided not to administer adjuvant therapy to our
patient because we diagnosed the thymoma as Stage I without capsular invasion by a postoperative
histological examination. However, the incidence of recurrence was found to be 19% in patients with
peritumoral adherence, even if they were Stage I patients\(^11\). In contrast, those patients without peri-
tumoral adherence did not relapse after surgery\(^11\). Therefore, for optimal treatment, both intraopera-
tive and histological findings are important in gauging the necessity for additional postoperative radi-
ation therapy.

The WHO histological classification system is based on both the morphology of the epithelial cells
and the relative ratio of lymphocytes and epithelial cells\(^4\). This system categorizes a tumor compris-
ing of neoplastic epithelial cells and nuclei with a spindle or ovoid shape as Type A, and that with
dendritic or plump appearances as Type B. Tumors with both these morphologies are categorized as
Type AB. Furthermore, Type B tumors are subdivided into three subtypes: Type B1 resembles the
normal thymus with predominant lymphocytes, Type B3 has a predominance of epithelial cells, and
Type B2 is intermediate between B1 and B3. The incidence of invasion into surrounding tissues in-
creases, and the 20-year patient survival rates decreases, in the following order of tumor types: A to
AB to B1 to B2 to B3. Both the WHO histological classification system and the Masao ka staging
system have proven to be significant independent prognostic indicators by a multivariate analysis\(^4\).

A characteristic finding of FNAC for thymomas is a biphasic cellular population pattern composed
of both epithelial and lymphocytic cells, which reflect the histological features of thymomas\(^1\). How-
ever, a preoperative diagnosis of cervical thymoma is difficult\(^12\). It is frequently misdiagnosed as ma-
lignant lymphoma\(^13\) because thymomas are extremely rare in the cervical region and malignant lymph-
omas commonly occur in the thyroid. In the present case, based on the observations by FNAC,
we initially suspected follicular lymphoma or follicular hyperplasia. In contrast, we established an ac-
curate diagnosis of Type B1 thymoma by histopathological examination of the excised specimen,
which showed infiltration by atypical small lymphocytes with CD3 positivity as well as by a few poly-
gerous or spindle-shaped epithelial cells with immunohistochemical cytokeratin AE1/AE3 staining.
As described above, the immunohistochemical staining of both epithelial and lymphocytic markers
were useful in the differential diagnosis of thymoma. It is important to not only assess lymphocytic
markers but also epithelial markers to avoid misdiagnosing thymoma as a malignant lymphoma\(^13\).
Despite reviewing the cytological specimen, we were unable to diagnose the tumor as an epithelial
tumor such as a thymoma because it contained only a small number of irregular epithelial cells which
can be confirmed only by immunohistochemistry.

Several investigation techniques such as MRI\(^14\), scintigraphy with thallium-201\(^15\) or technet-
ium-99\(^16\), and flow cytometric immunophenotyping\(^5\) are used for the differential diagnosis of cervi-
cal thymoma. However, these techniques should not be performed if it is not already suspected to be
cervical thymoma. A definite preoperative diagnosis in cases without the characteristic biphasic cel-
lar population pattern appearing on the FNAC for the cervical thymoma is especially difficult be-
cause of the unusual location and its rarity in cervical lesions. Therefore, we attempted to construct
a cell block from the existing cytological specimen. Compared to FNAC using only Papanicolaou staining, immunohistological staining using the cell-block method clearly demonstrated the biphasic cellular population pattern, thus corroborating the findings previously obtained by a histological examination. In the patients with many scarce atypical lymphocytes from tumors located near the thyroid by FNAC, the cell-block method may be a useful preoperative differential diagnostic modality for cervical thymoma.

REFERENCES