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CASE REPORT

Primary Mucinous Adenocarcinoma of the Thymus: A Case Report and Literature Review

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THYMIC carcinoma is a rare malignant tumor, but the most common malignant tumor of the anterior mediastinum. According to the latest World Health Organization (WHO) classification, primary thymic carcinoma has a variety of histological types, mainly including squamous cell, basaloid, mucoepidermoid, lymphoepithelioma-like, sarcomatoid, clear cell and neuroendocrine carcinomas, and papillary adenocarcinoma.¹⁻⁴ Thymic mucinous adenocarcinoma was discovered in recent years, and only 10 cases were reported. In this paper, we described a case of thymic mucinous adenocarcinoma, the histopathological findings and immunohistochemical results.

CASE DESCRIPTION

A 44-year-old woman presented with a right anterior

mediastinum lesion for a month detected in a physical examination. The woman was admitted to National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences, for further diagnosis and treatment. The patient felt mild chest pain and cough, but no other symptoms. Also, she had no special medical history. Chest X-ray and CT scan indicated the lesion located in the anterior mediastinum. After a comprehensive physical examination, there was no primary neoplasm identified elsewhere. The patient underwent a complete resection of the mediastinal neoplasm, and we made the surgical margin as clean as possible.

Pathological examination revealed mucinous adenocarcinoma. One month later after the surgery, she received chemotherapy. However, she died of multiple bone metastases 13 months after the surgery.

Macroscopically, the anterior mediastinal mass was round, hard, and tan-to-white, with a maximum diameter of 5 cm (Fig. 1A). The cut surface was white to yellowish-white in color, translucent, containing solid, gelatinous or mucinous areas.

Histologically, the tumor cells showed as small nests, acinar and cribriform structures floating in pools of extracellular mucin (Fig. 1B). The solid areas consisted predominantly of nests and islands of malignant cells separated by desmoplastic stroma. The tumor cells were mostly cuboidal to columnar with varying amounts of cytoplasmic mucin (Fig. 1C). In one of the sections, a large cyst with columnar epithelia, in the vicinity of the tumor, was also identified (Fig. 1D). Small remnants of thymic tissue were seen around the cysts.

Immunohistochemically, most tumor cells were positive for cytokeratin (CK) 20 (Fig. 2A, ZhongBin, diluted, EP23), caudal type homeobox transcription factor 2 (CDX-2) (Fig. 2B, ZhongBin, diluted, EP25), AE1/AE3 (Dako, 1:120, AE1/AE3), and CD117 (Dako, 1:600, Polyclonal), but negative for thyroid transcription factor-1 (TTF-1) (ZhongBin, diluted, SPT24), Napsin-A (MaiXin, diluted, Polyclonal), and Vimentin (MaiXin, diluted, V9).

Figure 1. Cut sections of the resected thymus revealed a well-demarcated (arrow), solid, and partly myxoid mass (arrow, A).

The tumor cells showed as small nests, acinar and cribriform structures floating in pools of extracellular mucin (arrow, B, $\times 20$ HE). The solid areas consisted predominantly of nests and islands of malignant cells (arrow) separated by desmoplastic stroma (C, $\times 20$ HE). A large cyst with columnar epithelia (arrow) was identified in part area (D, $\times 20$ HE).

Figure 2. Most tumor cells showed diffuse light brown cytoplasmic staining (arrow) for cytokeratin 20 (A) and diffuse brown nucleus staining (arrow) for caudal type homeobox transcription factor 2 (B). SP $\times 20$

DISCUSSION

Thymic carcinoma is extremely rare among thymic epithelial tumors, and the variety of histological types has brought great challenges to both clinicians and pathologists.²⁻³ Most reported primary carcinomas in the thymus are squamous cell carcinomas or its variants. Primary adenocarcinoma of the thymus is the rarest. Since it was first reported by Choi *et al* in 2003, only ten cases have been documented.⁴⁻⁶

Comprehensive imaging examinations and clinical pathology research need to be done, in order to make a correct diagnosis of primary thymic mucinous adenocarcinoma. Clinically, the lesion has to be located in the anterior mediastinum without primary tumors in other parts of the body. Histopathologically, the diagnosis of primary thymic adenocarcinoma should be supported by the observation of malignant transformation of benign epithelial cells of thymic cysts. In our case, thymic cysts can often be found around the adenocarcinoma.

Because primary thymic adenocarcinoma is so rare, it is necessary to exclude other kinds of primary thymic tumors with abundant mucin, such as thymic carcinoid tumor or mucoepidermoid carcinoma.⁶ The carcinoid tumor is rich in mucin and has the characteristics of conventional neuroendocrine tissues, such as an organoid pattern, and positive results for neuroendocrine markers. For a tumor to be diagnosed as mucoepidermoid carcinoma, histologically both squamous and mucin-producing components should be included.⁷⁻⁸ But these findings were not found in our case.

Thymus primary mucinous adenocarcinoma is a diagnosis of exclusion. Among thymic malignancies, metastatic adenocarcinoma is very common.³ Therefore, it is important to distinguish between a metastasis and a primary thymic adenocarcinoma. In addition, the respiratory and upper alimentary tracts are the most common primary sites where adenocarcinomas migrate to the thymus, although other sites of origin have also been reported,⁹⁻¹⁰ such as breast or ovary.

The lung is one of the most common primary sites of metastatic mediastinal carcinomas, as reported by Hess *et al*.¹⁰ TTF-1 and Napsin-A can be the important markers of lung adenocarcinoma. And 77%-100% of all the pulmonary mucinous adenocarcinoma cases express these biomarkers.⁴ In this case of our report, both markers were negative. In addition, after the comprehensive physical examination, primary tumor was not found in the lungs. Based on this, we believe the possibility of pulmonary origin of this tumor is considerably low.

Besides, in this case, the tumor showed diffuse and

strong reactivity to CK20 and CDX2, which is similar to gastrointestinal adenocarcinomas. Therefore, it is a very necessary to perform the imaging and endoscopic examinations. In fact, all of them turned out to be negative. Based on these findings, we speculate that the possibility of gastrointestinal origin of this tumor is also extremely low.

So far, no specific immunohistological markers for thymus-derived tumors have been found. CD5, a lymphocytic biomarker, has been reported useful in differentiating thymic from nonthymic carcinoma.⁶ And it is expressed in approximately 70% of all cases of thymic adenocarcinoma. However, Kapur *et al*¹¹ considered that CD5 does not play a decisive role in the diagnosis of primary thymic adenocarcinoma. In the present case, the tumor was negative for CD5, which highlighted the diagnostic dilemma.

The prognosis is difficult to determine on the basis of a small number of cases. Our patient with thymic mucinous adenocarcinoma died 13 months after diagnosis because of bone metastasis.⁹ Although no autopsy was carried out, the diagnosis of primary thymic mucous adenocarcinoma is supported by the results of imaging, endoscopic examination and immunohistochemical data. It appears that thymic mucinous adenocarcinoma maybe have more aggressively than the non-mucinous adenocarcinomas.

In conclusion, primary mucinous adenocarcinomas of the thymus are very rare. The diagnosis requires comprehensive clinical examination, imaging and pathological research.

Conflict of Interest Statement

The authors have no conflict of interest to disclose.

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