Ectopic Hamartomatous Thymoma: A Case Report and Literature Review

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Ectopic hamartomatous thymoma is a rare benign tumor located at supraclavicular/suprasternal area and is speculated with a branchial anlage origin. There are usually 3 components in the tumor: spindle cells, epithelial cells, and adipose tissue, although proportion of each varies from case to case. The tumor cells present with a unique immunophenotype, with strong positivity for AE1/AE3, CD34, CD10, and variable staining for Bcl-2 and SMA. Here we report such a case in a 61-year-old male, with a compatible morphology and immunopattern for this entity.


Key Words: Ectopic hamartomatous thymoma, branchial anlage, AE1/AE3, CD34, CD10, Bcl-2, SMA

INTRODUCTION

Ectopic hamartomatous thymoma (EHT) is a rare benign neoplasm, which is almost exclusively developed in the lower neck area of adult male, including supraclavicular/suprasternal area. This tumor usually presents as a subcutaneous slow growing mass with no significant symptoms. Microscopically, the tumor is composed of an admixture of spindle cells, epithelial cell clusters, and mature adipose tissue. This entity was first described by Smith et al. in 1982, followed by Rosai et al in 1984.1,2 These authors speculated that the origin of the tumor was ectopic thymus. However, over the years, the origin has still been a matter of debate. Alternative assumptions include developmental abnormality of the 3rd or 4th branchial pouches, the cervical sinus of His, or the ultimobranchial body.1,3 Recently, branchial anlage mixed tumor is favored by a few soft tissue pathologists.4

Up to date, there are only about 60 cases having been reported.1,6 Because of its rarity, many pathologists are not aware of this entity and have mis-diagnosed it as leiomyoma/leiomyosarcoma, dermatofibrosarcoma protuberans, biphasic synovial sarcoma, or malignant peripheral nerve sheath tumor, etc. Therefore, it’s crucial to recognize this benign entity to avoid over-diagnosis/over-treatment. Here we report such a case in a 61-year-old white male, presenting as a solid mass in his left sternoclavicular joint region.

CASE REPORT

Patient was a 61-year-old white male with no significant previous medical history. He was referred by his primary care doctor for evaluation of a superficial nodule in the sternoclavicular joint area. The patient stated that it had been present there for years. He reported that it had increased in size over the past year and was painful upon palpation. He denied trauma to the area. Physical examination revealed a tender on palpation, mobile, 4x 2.5 cm mass. MRI scan revealed a well-defined 2.3 cm x 2.1 cm left supraclavicular faintly enhancing proteinaceous mass of uncertain etiology. It was located at the sternal attachment of the left sternocleidomastoid muscle, however was not clear whether it was arising from the muscle or the adjacent fibrous/adipose tissue. There was no inflammatory change in the surrounding soft tissue. Radiologic differentials included a sebaceous cyst, or a myxoid tumor. The mass was surgically removed. The patient recovered without event.

An ovoid mass was received by pathology department. Cut surface was tan-yellow and homogenous. Tissue sections showed prominent spindle cell proliferation forming fascicles, mixed with mature adipose tissue (Figure 1A, 1B). Focal epithelioid cells were also identified (Figure 1C). The epithelial component grew in complex clusters. There were no significant atypia, mitosis, or necrosis in all the components. Immunostaining revealed both spindle and epithelial cells were positive for AE1/AE3 (Figure 1D), P63 (Figure 2A), CD34 (Figure 2B), CD10 (Figure 2C), Bcl-2 (Figure 2D), weak SMA (Figure 2E), CK8/18, CK5/6, calponin, P40, but negative for GFAP, desmin, CD117, or Sox10 (data not shown). The Ki-67 proliferative index is very low (< 1%) (Figure 2F). Considering the location of the

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lesion, the microscopic and immunophenotype, the tumor was classified as an EHT (branchial anlage mixed tumor).

Expert soft tissue pathologists were consulted, who concurred the diagnosis.

![Figure 1. Histology and immunostaining for AE1/AE3 of the tumor cells. A. The tumor contains spindle cells (left) and mature fat (right). 50X; B. Spindle cell component, 400X; C. Epithelial cell component, 400X; D. The tumor cells are positive for AE1/AE3, 200X.](image)

**DISCUSSION**

EHT is a rare benign neoplasm that occurs in the supraclavicular/suprasternal area. This entity was first described by Smith et al. in 1982 as “mixed tumors exhibiting adipose, fibroblastic and epithelial components”, and was named EHT by Rosai et al. in 1984.\(^1\)\(^2\) Since then, only about 60 cases have been reported, and among them, 2 cases of adenocarcinoma arising from EHT have been reported.\(^7\)

In a recent review, Jing et al. summarized this tumor as 1) slow growing, 2) predominantly affecting middle aged adults with male predominance, 3) commonly located at the subcutaneous tissue of the supraclavicular, suprasternal, and sternoclavicular areas, 4) histologically admixture of spindle cells, epithelial elements, and mature adipose tissue, and 5) immunopositivity for AE1/AE3, CD34, CK5/6, Bcl-2 (partial), and SMA (partial) in both spindle and epithelial components.\(^8\) Of note, the proportion of tumor components of epithelial cells, spindle cells or adipocytes vary greatly, ranging from evenly present to one component predominant.\(^6\) In our case, only a small focus of epithelial cells and a small amount of fatty tissue were identified after meticulous search. The immunophenotype also displays diversity. Except strong reactivity for AE1/AE3 and CD34, the intensity and scope of Bcl-2 and SMA range from focal/weak to extensive/strong.\(^3\)\(^4\)

In our case Bcl-2 is strong/ extensive, and SMA is weak/ extensive for epithelial and spindle cells.

Rosai et al. in 1984 postulated that the tumor was likely originated from the 3\(^{rd}\) branchial pouch derivatives that had failed to migrate to the mediastinum (hence the name of ectopic hamartomatous thymoma).\(^2\) Fetsch et al presented a new hypothesis in 2004, based on their observation that there was no definitive thymic tissue in this entity and there is no EHT analogues found in the mediastinum. They proposed that EHT was likely represented a mixed tumor originated from branchial anlage of the cervical sinus of His (hence the name of branchial anlage mixed tumor).\(^4\) Finally, Weissferdt
et al. argued that the components of EHT corresponded to nonfunctional or precursor-type of thymic epithelium and developed as a neoplastic process arising within a developmental defect/thymic anlage remnants (hence the name of thymic anlage tumor). Overall, the origin of this entity is still not settled. Further research is needed to clarify this matter.

Figure 2. Immunopattern for the tumor cells. A. The tumor cells are positive for P63, 200X; B. The tumor cells are positive for CD34, 200X; C. The tumor cells are positive for CD10, 200X; D. The tumor cells are positive for BCL-2, 200X; E. The tumor cells are weakly positive for SMA, 200X; and F. The tumor cells have very low Ki-67 proliferative index, 200X.

The differential diagnosis for this entity is garden variety, mainly dependent on which component is predominant in the tumor. For example, if the EHT is rich for fat and squamoid epithelial cells, a branchial cleft cyst would be a good differential (this entity is rich in lymphoid infiltration/aggregates, and epithelial cells are negative for CD34). If presence with both spindle and epithelial cells, a biphasic synovial sarcoma should always be ruled out. In biphasic synovial sarcoma, although the epithelial cells are positive for cytokeratin, the spindle cells are negative for cytokeratin and CD34. In addition, the spindle cells are positive for CD99, and show cytologic atypia and increased
mitosis, all of which are not shown in EHT. Finally, synovial sarcoma carries t(x;18) translocation, which is lack in EHT, but is confirmatory for synovial sarcoma. If spindle cells predominant in EHT, differentials should include dermatofibrosarcoma protuberans (DFSP) and other spindle cell sarcomas (leiomyosarcoma, fibrosarcoma, etc.). DFSP happens in the shoulder/neck area, with a dermal/subcutaneous localization. In addition, the spindle cells are also CD34+, and might trap subcutaneous fat in the tumor. But differential features include cytologic atypia and increased mitosis in DFSP, negative for AE1/AE3 in the spindly tumor cells, and increased Ki-67 proliferative index. Regarding other spindle cell sarcomas, they generally show cytologic atypia, increased mitotic figures and Ki-67 proliferative index, and negative for AE1/AE3 or CD34. Overall, a meticulous search for epithelial and adipose components, appreciation of the bland appearing cytology of the spindle cells, immunopositivity for AE1/AE3 and CD34, and localization of the mass at front low neck, are the key differential features for a diagnosis of EHT.

CONCLUSION

Here we described a rare case of EHT in a 61-year-old patient. This benign entity features 3 components in the tumor and shows a unique immunopattern including positive for AE1/AE3 and CD34. The origin of this tumor is still controversial, although most of the experts suspect it is from branchial pouch 3 or 4 area.

CONFLICT OF INTEREST

The authors have no conflict of interest.

REFERENCES