

# Ectopic Hamartomatous Thymoma

## – A Case Report along with a Review of the Literature Concerning the Histogenesis and New Nomenclature –

Sang Hee Seok · Dong Hyun Lee<sup>1</sup>  
Su Hwan Kang<sup>1</sup> · Young Kyung Bae

Departments of Pathology and <sup>1</sup>Surgery,  
Yeungnam University College of Medicine,  
Daegu, Korea

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**Corresponding Author**

Young Kyung Bae, M.D.  
Department of Pathology, Yeungnam University,  
College of Medicine, 317-1 Daemyung-dong, Nam-gu,  
Daegu 705-717, Korea  
Tel: 053-620-3336  
Fax: 053-622-8432  
E-mail: ykbae@ynu.ac.kr

Ectopic hamartomatous thymoma (EHT) is a rare and distinctive benign neoplasm of the lower neck. We here report on a case of EHT arising in the suprasternal area of 47-year-old male patient. The well-circumscribed mass measured 7 × 6 × 4 cm and it predominantly had a solid gray-white cut surface. Microscopically, the tumor consisted of spindle cells, epithelial nests, and mature adipose tissue. The epithelial component was arranged in anastomosing cords, solid nests and variable-sized cysts that were lined by squamous or cuboidal epithelium. The spindle cells revealed the myoepithelial immunohistochemical phenotype. There was no obvious thymic differentiation nor was any normal thymic tissue observed in our case. We think that EHT needs to be reclassified with using different nomenclature to designate its origin and histology. Further, pathologists and clinicians should be aware of the existence of this tumor in the lower neck so as not to mistake it for high-grade sarcoma or spindle cell carcinoma.

**Key Words :** Thymoma; Hamartoma; Branchial arch; Mixed tumor; Immunohistochemistry

Ectopic hamartomatous thymoma (EHT) is a distinctive benign neoplasm of the lower neck. It usually occurs in the supraclavicular, suprasternal, and presternal areas and it has been known to arise from thymic tissue that is ectopically arrested at the cervical portion during migration in embryonic period.<sup>1-3</sup> Although it was firstly described as “unusual subcutaneous mixed tumor exhibiting adipose, fibroblastic, and epithelial components” or as “spindle cell thymic anlage tumor”, Rosai *et al.* introduced the designation “ectopic hamartomatous thymoma” in the sense that the tumor represents a haphazard admixture of all the components of the thymic gland (hamartoma) and the bulk of the mass is made up of morphologically abnormal cells (neoplasm).<sup>1,2</sup> To date, about 47 cases, including two Korean cases<sup>4,5</sup> have been published worldwide.<sup>3,6,7</sup> However the histogenesis and nomenclature of this tumor are now being challenged since the term “branchial anlage mixed tumor” was introduced.<sup>6</sup> We present here an additional case of EHT in order to increase the awareness of this rare entity. A brief discussion about the tumor’s histogenesis and differential diagnosis is included.

### CASE REPORT

A 47-year-old male was admitted to the hospital due to a slowly growing mass that was present in the suprasternal area for several years (Fig. 1A). On the ultrasonogram, the mass was located subcutaneously between the medial margin of the right sternocleidomastoid muscle and the medial side of the left clavicle, and the mass showed heterogeneous echogenicity. The laboratory data showed no abnormalities. The excised mass was well-circumscribed and it measured 7 × 6 × 4 cm. The cut surface was predominantly solid gray-white and it was interrupted by islands of adipose tissue and various sized small cysts (Fig. 1B).

Microscopically, the tumor consisted of spindle cells, epithelial nests and mature adipose tissue. These cellular elements were haphazardly disposed in varying proportions in different areas (Fig. 2A). The predominant component was plump, spindle cells arranged in fascicular, storiform and basket weave-like patterns. The plump, spindle cells were bland-looking and they displayed fine chromatin pattern with small or inconspicuous nucleoli and

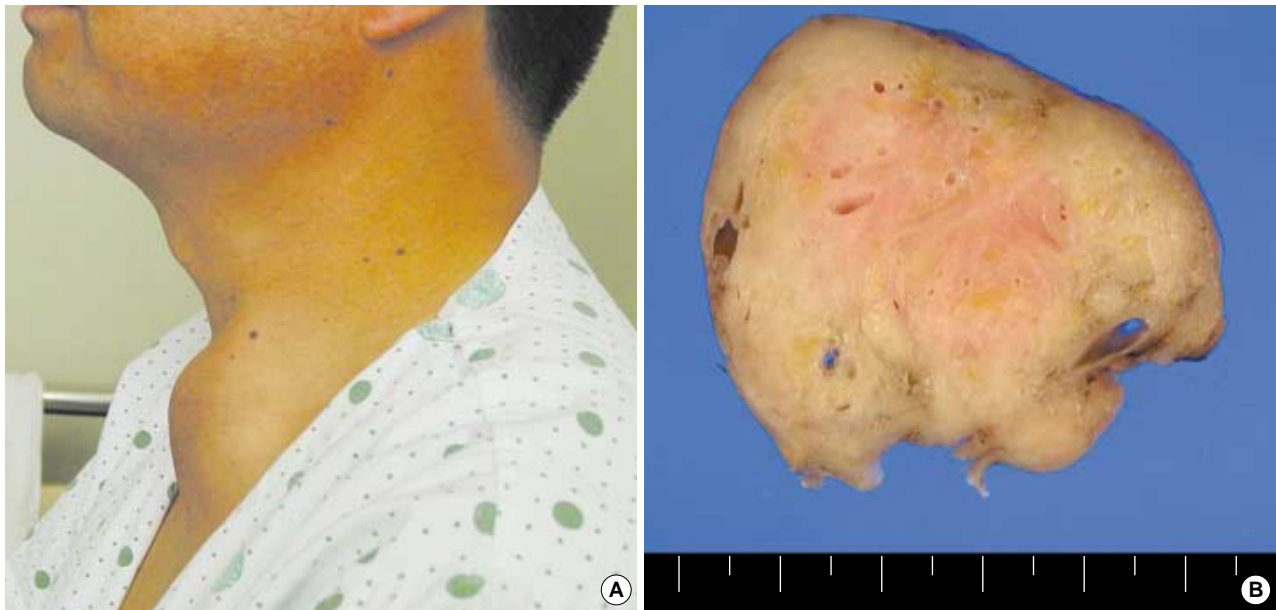


Fig. 1. (A) The patient has a protruding mass from the suprasternal area of anterior neck. (B) The cut surface of the mass shows gray-white, solid tumor with scattered, small cystic spaces and yellow foci of adipose tissue.

ill-defined, eosinophilic cytoplasm. There were also delicate, fibroblast-like spindle cells between the bundles of plump, spindle cells and around the epithelial nests and islands of adipose tissue (Fig. 2B). The epithelial component was arranged in anastomosing cords, solid islands of mature squamous epithelium and variable-sized cysts lined by squamous epithelium, or in small glands lined by cuboidal epithelium (Fig. 2C). The squamous epithelium was the dominant epithelial component. Some of the large cysts contained inspissated eosinophilic material or they were lined by a layer of glandular epithelium overlying several layers of squamous epithelium (Fig. 2D). Frequently noted were areas where the plump, spindle cells merged with the epithelial component. The proportion of fat cells was different from area to area. The lymphocyte population was sparse and admixed with epithelial cells. There was no significant cytologic atypia or mitotic figures in either the spindle or epithelial components.

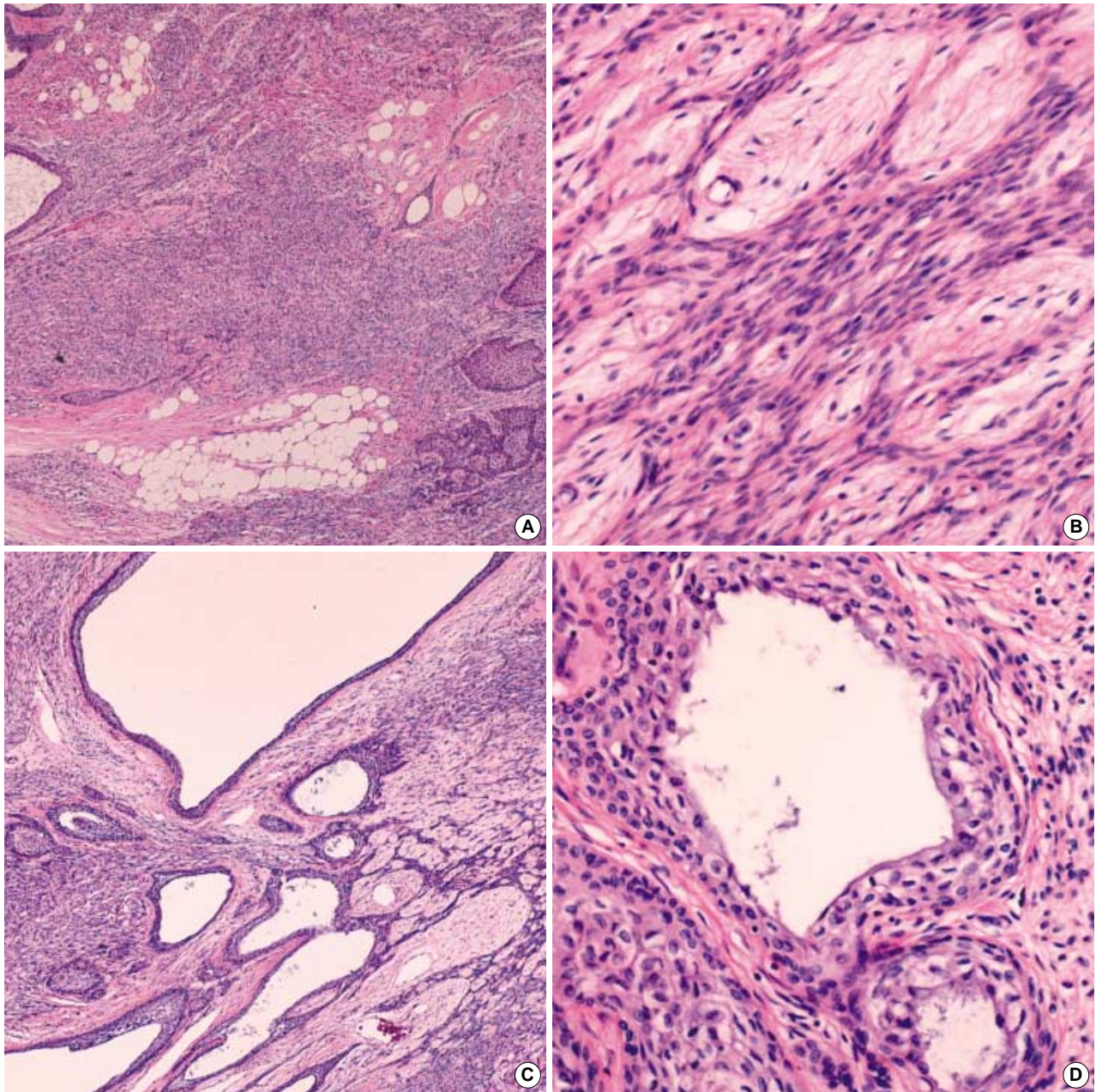
Immunohistochemical staining for cytokeratin (AE1/AE3, 1:50, DAKO, Glostrup, Denmark) was positive in both the epithelial and spindle cell components (Fig. 3A). The epithelial cells, but the not spindle cells, were also positive for epithelial membrane antigen (EMA) (E29, 1:60, DAKO, Glostrup, Denmark) (Fig. 3B). The plump, spindle cells were diffusely positive for smooth muscle actin (SMA) (1A4, 1:40, DAKO, Glostrup, Denmark) (Fig. 3C), calponin (CALP, 1:50, DAKO, Carpinteria, CA, USA), and p63 (4A4, 1:50, DAKO, Glostrup, Denmark) and the fibroblast-like spindle cells were positive for CD34 (QBEnd-10, 1:30, DAKO, Glostrup, Denmark) (Fig. 3D). The epithelial

and spindle cells were uniformly negative for desmin (ZC18, 1:60, Zymed, San Francisco, CA, USA) and S-100 protein (1:150, Zymed, San Francisco, CA, USA).

## DISCUSSION

EHT is a rare neoplasm with a peak incidence in the fourth and fifth decades and it has a striking male predominance. It is usually seen as a very slow growing and well-circumscribed mass in the lower neck, but it does not affect the thyroid gland, the larger vessels of the neck or the mediastinum.<sup>1-7</sup>

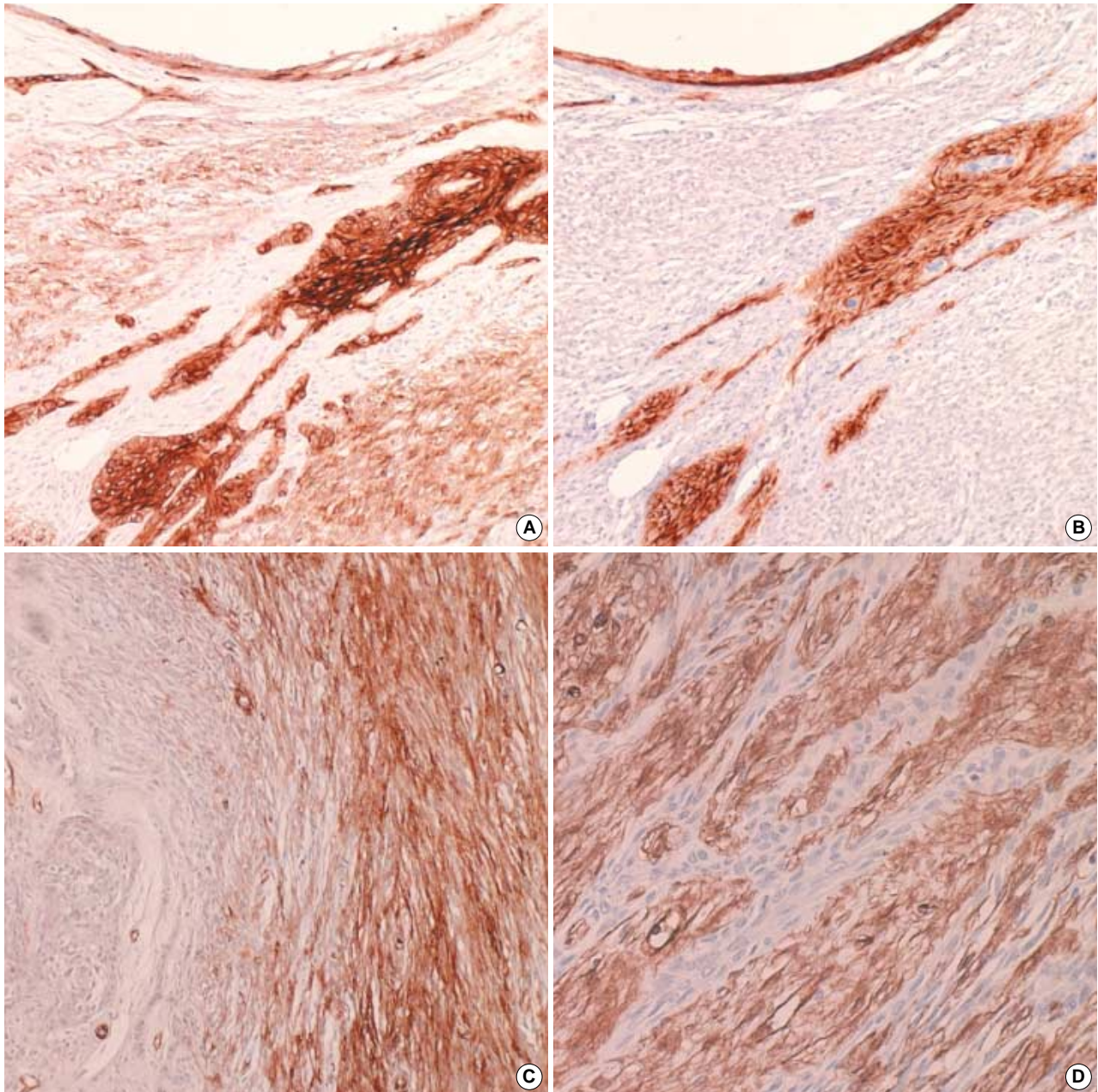
Rosai *et al.*<sup>1</sup> introduced the currently used appellation "ectopic hamartomatous thymoma" to reflect their belief that the tumor arises from the third branchial (pharyngeal) arch derivatives that are sequestered in the soft tissue of the neck, and it is composed of abnormal thymic tissue, which is derived from the third branchial arch. Lee *et al.*<sup>5</sup> demonstrated the presence of CD99+ lymphocytes in EHT and they supported the opinion of Rosai *et al.* because CD99 had been considered as a useful marker of immature thymocytes. However Fetsch *et al.*<sup>6</sup> insisted that EHT is an inaccurate designation for this distinctive tumor because of the following observations. First, definite thymic tissue has never been identified in the periphery of the reported tumors. Second, the plump, spindle cells in EHT showed morphologic, ultrastructural and immunohistochemical findings that are consistent with myoepithelial cells and myoepithelial cells are not a com-



**Fig. 2.** (A) The tumor shows haphazard admixture of spindle cells, epithelial nests, and mature adipose tissue. (B) The bland-looking spindle cells are arranged in fascicles and have fine chromatin with inconspicuous nucleoli. The delicate, fibroblast-like spindle cells are present between bundles of plump, spindle cells. (C) The epithelial component forms variable-sized cysts, solid nests and anastomosing cords. (D) Some cysts possess a layer of glandular epithelium overlying several layers of squamous epithelium.

ponent of the thymus. Third, the lymphocytes, that were initially considered as an integral component of this tumor are rather sparse and there is no intimate relationship between the lymphocytes and epithelial cells. They thought that EHT is derived from remnants of the cervical sinus of His based on the clinicopathologic and immunohistochemical analysis of 21 cases; Fetsch *et al.*<sup>6</sup> recommended the designation “branchial anlage mixed

tumor” as a substitute for EHT. The cervical sinus of His is a small pocket of ectoderm that is derived from the second, third and fourth branchial clefts, and it normally disappears by the end of the seventh week of development in the majority of individuals.<sup>8</sup> If it persists, it can grow as a mass composed of primitive ectoderm that shows a mixed tumor-like morphology.<sup>6</sup> Our immunohistochemical results showed diffuse positive staining



**Fig. 3.** Immunohistochemical stains for (A) cytokeratin, (B) EMA, (C) SMA, and (D) CD34. The epithelial component shows positive staining for cytokeratin and EMA, and the plump, spindle cells are positive for cytokeratin and SMA. The delicate, fibroblast-like spindle cells are positive for CD34.

for cytokeratin and EMA in the epithelial component and positive staining for the myoepithelial markers-SMA, calponin and p63- in the plump, spindle cell component. These results coincide quite well with the epithelial and myoepithelial differentiation of the tumor. EHT differs from conventional thymoma according to the lack of distinctive lobulation and the presence of discrete solid and cystic epithelial nests and islands of mature adipose tissue. There was no obvious thymic differentiation nor

normal thymic tissue observed in our case. We think that EHT is not an appropriate nomenclature to designate the origin and histologic findings of this distinctive tumor. We support Fetsch *et al.*<sup>6</sup> for the reclassification of this tumor as a branchial anlage mixed tumor.

Pathologists and clinicians should be aware of the existence of EHT in the lower neck region so as to differentiate it from a high-grade sarcoma or other tumors. Blending of spindle cells

and fat at the periphery of the tumor simulates the pattern of a sarcoma infiltrating fat, and the focal vague nuclear palisading of the spindle cells described in other reports is reminiscent of peripheral nerve sheath tumor.<sup>2,3</sup> The differential diagnoses should include mixed tumor of a salivary or sweat gland origin, peripheral nerve sheath tumor, spindle cell carcinoma and biphasic synovial sarcoma.<sup>6,7</sup> We could exclude mixed tumor of a salivary or sweat gland origin by the lack of hyalinized or chondromyxoid stroma in our case. EHT lacks the S-100 protein expression encountered in peripheral nerve sheath tumor of the soft tissue and it does not have the extent and degree of atypia or the level of mitotic activity typically seen in spindle cell carcinoma. Biphasic synovial sarcoma usually occurs in deep soft tissue of the extremities and it shows higher cellularity, greater nuclear hyperchromasia, mitotic figures and only focal or patchy cytokeratin positivity in the spindle cell component. All the reported cases of EHT have shown a benign clinical course, but this tumor may recur after incomplete local excision.<sup>6</sup>

In summary, EHT is a combination of developmental abnormality and neoplasm, and it can be readily distinguished by its characteristic anatomic location, distinctive histopathology and immunohistochemical characteristics. However its histogenesis and nomenclature are coming under challenge.

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