

Ectopic Hamartomatous Thymoma

— A case report —

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INTRODUCTION

Ectopic hamartomatous thymoma is a distinctive benign lesion of lower neck which is firstly described by Rosai et al., in 1984¹⁾. Its microscopic findings are characterized by four components: cellular areas made up of spindle cells; epithelial islands composed of solid nests, trabeculae, and cysts; mature adipose tissue; and lymphocytes, sometimes arranged in a Hassall's corpuscle-like fashion. The spindle cell components are compatible with epithelial cells which are demonstrated by electron microscopy and immunohistochemistry. So, this lesion is suggested for thymic hamartoma which is ectopically arrested at cervical portion during the migration in embryonic period.

We recently experienced a case of anterior neck mass which showed the above histologic features of ectopic hamartomatous thymoma, microscopically. The spindle cells also revealed epithelial nature by electron microscopy and immunohistochemistry. This lesion is so rare and only five cases have been reported in English literatures, and it is the first case in our country.

CASE HISTORY

A 49-year old man was admitted to the Korea university hospital, department of surgery, for evalu-

ation of anterior neck mass which was slowly growing for five years. His past history was unremarkable except for known hypertension for several years. Physical examination revealed high blood pressure, measuring 180 mmHg in systolic phase and 120 mmHg in diastolic phase. A soft nontender mass was palpated at anterior neck just above the sternal notch with smooth surface and its size was about 4×5 cm in cross.

On laboratory examination, diabetic evidence such as high blood sugar (FBS 170 mg/dl, PP2hr. 234 mg/dl) and glucosuria. The CBC finding suggested polycythemia with high hemoglobin (18.0 g/dl) and hematocrit (54%) levels. The differential count and platelet count were within normal limits.



Fig. 1. Location of the lesion: just above the sternal notch, deep to the platysma. The mass is midline-crossing with well circumscribed bilobulated appearance, measuring 5×4×2.5 cm.

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The chest X-ray showed hypertensive heart change and the abdominal sonogram suggested diffuse fatty infiltration of the liver. The electrocardiogram showed left ventricular hypertrophy and first degree A-V block.

At operation, the tumor was located just above the sternal notch, deep to the platysma and in close relation with insertional area of sternocleidomastoid muscle (Fig. 1). It was relatively well circumscribed and showed little adhesion with other structures such as muscle, thyroid, trachea, or vessels. Total excision was carried out.

MATERIAL AND METHODS

Multiple paraffin-embedded tissue blocks were available from the resected mass. Hematoxylin and eosin sections were prepared using the conventional technique. Masson trichrome stain was performed to one of this section. The avidin-biotin immunoperoxidase method was applied to paraffin-embedded blocks for the demonstration of the followings: cytokeratin, CEA, vimentin, UCHL1, and L26. For electron microscopic examination, samples were

obtained from formalin-fixed tissue, and rinsed with saline followed by fixation using 2.5% paraformaldehyde and 1% osmium tetroxide. Semi-thin sections were made and ultra-thin sections were stained with uranium acetate and lead citrate. These were examined with a Hitachi H-600 electron microscope at an voltage of 75kv.

RESULTS

1. Gross finding

The specimen was a gray tan bilobulated mass, measuring 5×4×2.5 cm in dimension. It was not truly encapsulated but the external surface was smooth and well circumscribed. The cut surface displaced gray white, myxoid areas and islands of adipose tissue with multiple cysts ranging from 0.2 cm to 0.3 cm in diameter.

2. Light microscopic finding

Microscopically, the hematoxylin and eosin stain revealed four components (Fig. 2): 1) spindle cells, 2) epithelial cells, 3) adipose tissue, 4) lymphocytes. The spindle cells were dominant component forming



Fig. 2. Islands of adipose tissue admixed with large expanses of spindle cells and variable sized cysts (H&E, ×40).

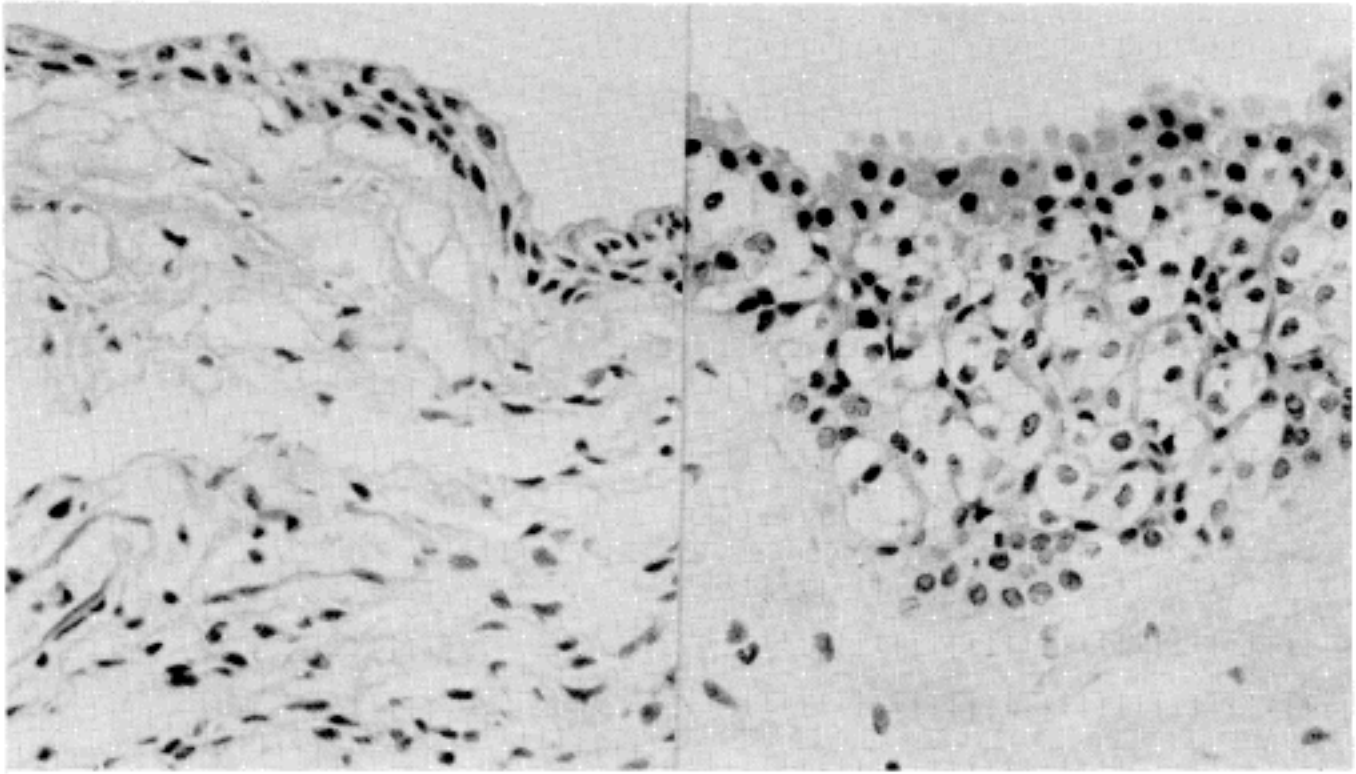


Fig. 3. Cystic spaces lined by stratified squamous epithelium (left) or cuboidal cells with apocrine metaplasia (right) (H&E, $\times 250$).

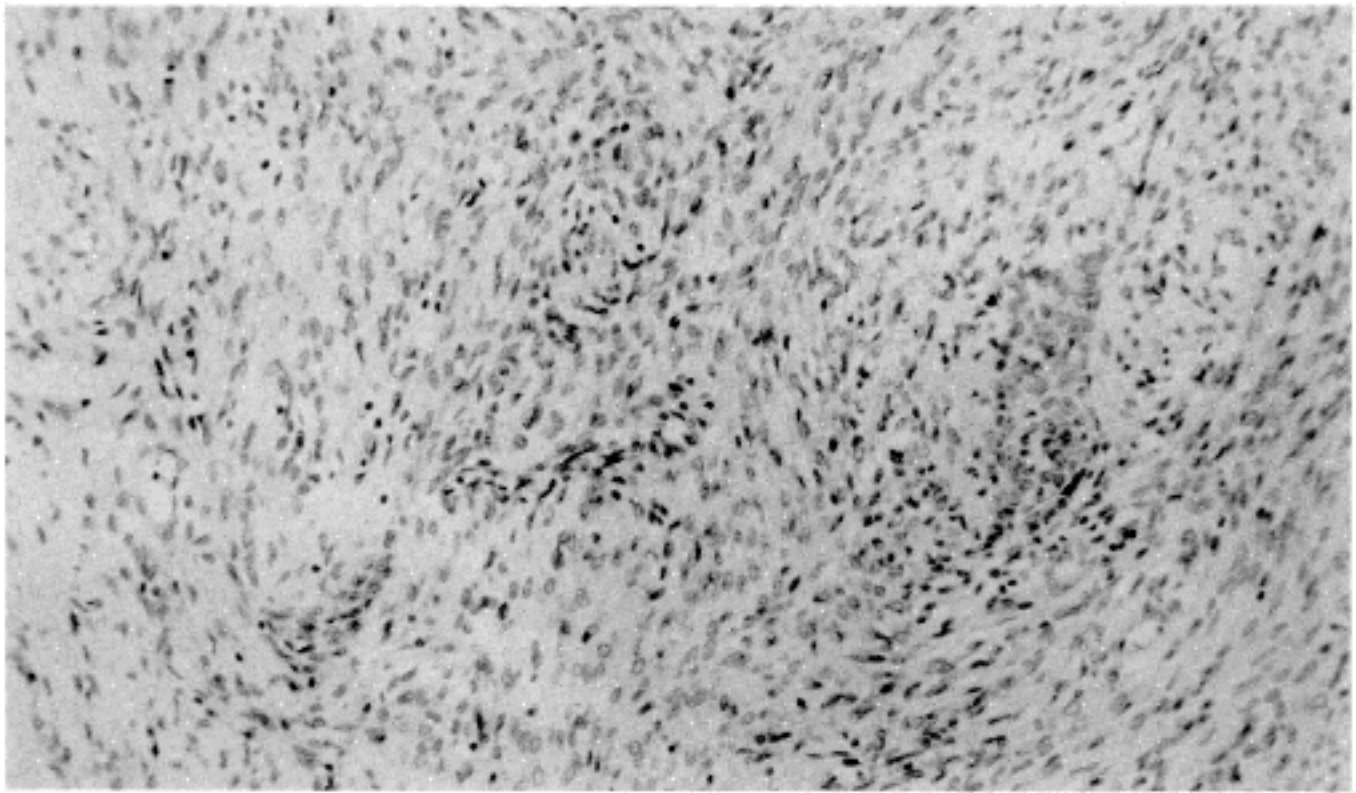


Fig. 4. Cellular spindle cell area with transition of epithelial cells to spindle cells (H&E, $\times 40$).

large expanses of haphazardly arranged sheets, vague fascicles, or suspicious storiform pattern. These spindle cells were mimicking fibroblasts or smooth muscle cells showing long cytoplasmic process with indistinct margin, fine chromatin pattern, and small inapparent nucleoli. Cytologic atypism was minimal and mitoses were not found. On Masson

trichrome stain, the cytoplasm of spindle cell was stained as red color with fine intercellular bluish collagen staining.

The second component, epithelial cell, was arranged as nests, glands and cyst-linings. The epithelial cells making tubules or cystic spaces were mainly cuboidal, but columnar or flattened cells were also

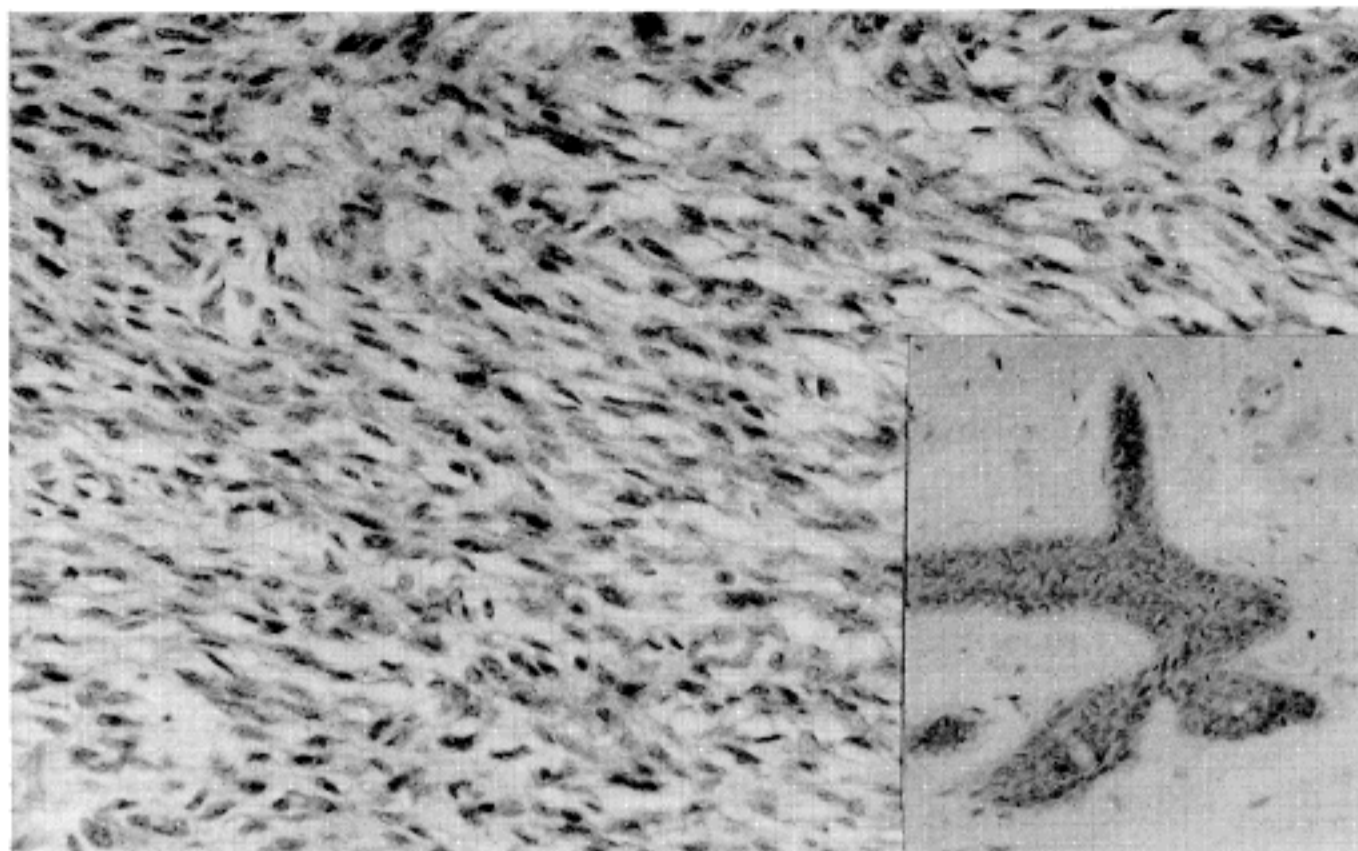


Fig. 5. Immunohistochemical staining for cytokeratin showing positive reaction both in spindle cells and epithelial cells (inset) ($\times 250$).

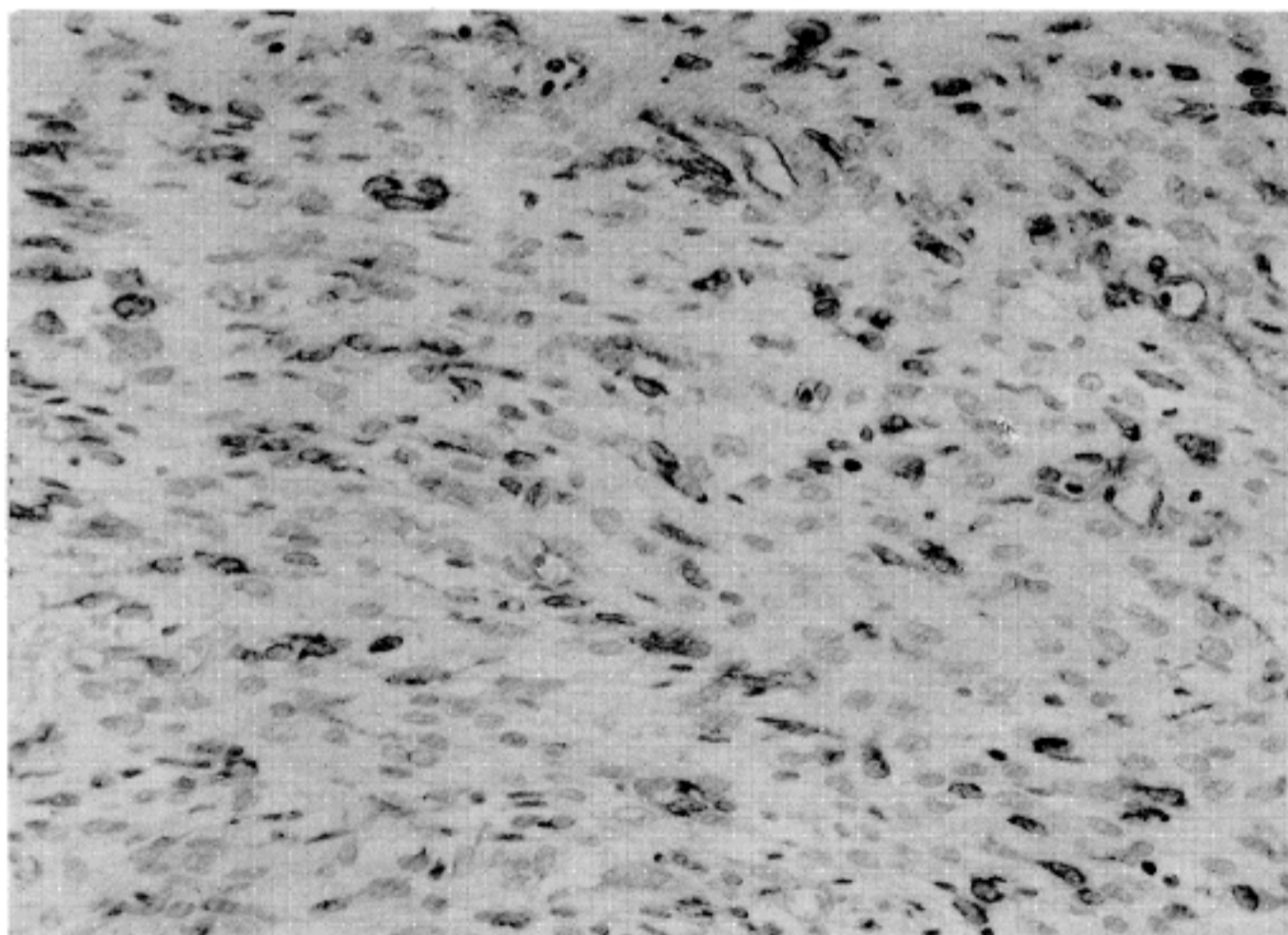


Fig. 6. Immunohistochemical staining for vimentin showing positive reaction in spindle cells ($\times 250$).

present. Occasionally, apocrine metaplasia and foamy cytoplasmic change were seen (Fig. 3). Some

small cyst-lining cuboidal cells showed two or more layers of stratification. The cells contained round or

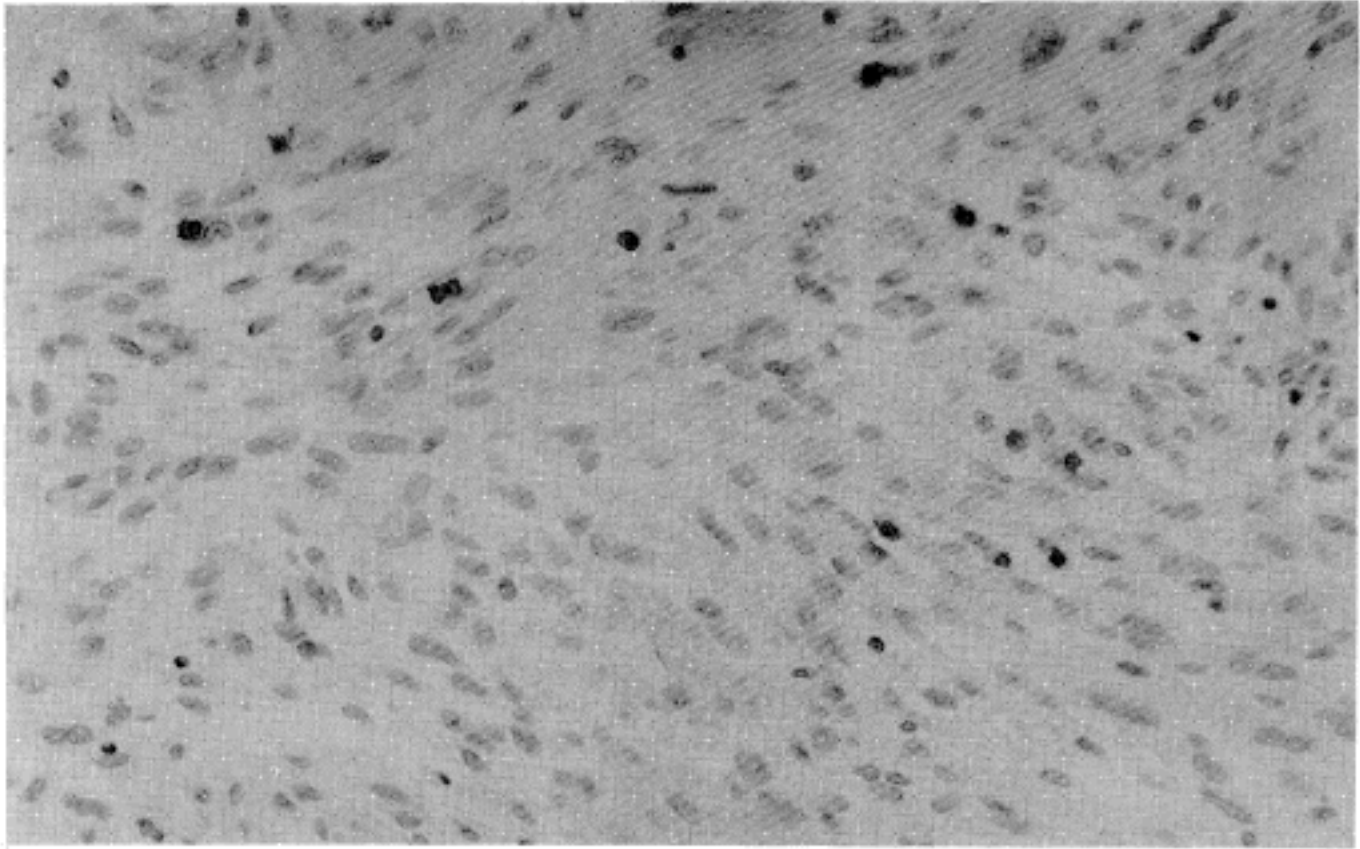


Fig. 7. Immunohistochemical staining for UCHL1 showing positive reaction in lymphocytes ($\times 400$).

oval nuclei with fine chromatin and small nucleoli. Neither cellular atypism nor mitosis was seen. The nest forming epithelial cells were squamoid without definitive keratinization. There were transitional areas from these epithelial cell nests to spindle cells (Fig. 4).

The adipose tissue component was mature island-forming element, occupying large proportion of the mass. Occasionally, several adipocyte aggregates were scattered in spindle cells.

Lymphocytes were scanty in number. They were mature with small round nuclei with little amount of cytoplasm and scattered between the spindle cells. They were hardly appeared as nodular aggregates and never form follicles with germinal centers.

3. Immunohistochemical staining

The stain for cytokeratin showed strong positivity in epithelial cells forming nests, tubules, and cysts. It was also positive in spindle cells but its degree was weaker than in epithelial cells (Fig. 5). The CEA staining revealed positivity both in epithelial cells and spindle cells, but the former portion showed

Table 1. Results of immunohistochemical staining

	Spindle cell	Epithelial cell
Cytokeratin	+	+++
CEA	+	+++
Vimentin	+	-

much stronger reaction than the latter. The vimentin staining was positive in spindle cells but totally negative in epithelial cells (Fig. 6). The results of immunohistochemical staining for cytokeratin, CEA, and vimentin are summarized in table 1.

The UCHL 1 staining for T cell showed positive staining in lymphocyte component (Fig. 7). But L26 staining for B cell was negative.

4. Electron microscopic finding

Sections were obtained from spindle cell component, which showed numerous intracytoplasmic tonofilaments and occasional desmosomes (Fig. 8). The nucleus was ovoid with slightly indented nucleolemma. Plentiful collagen fibers were seen in the intercellular space.

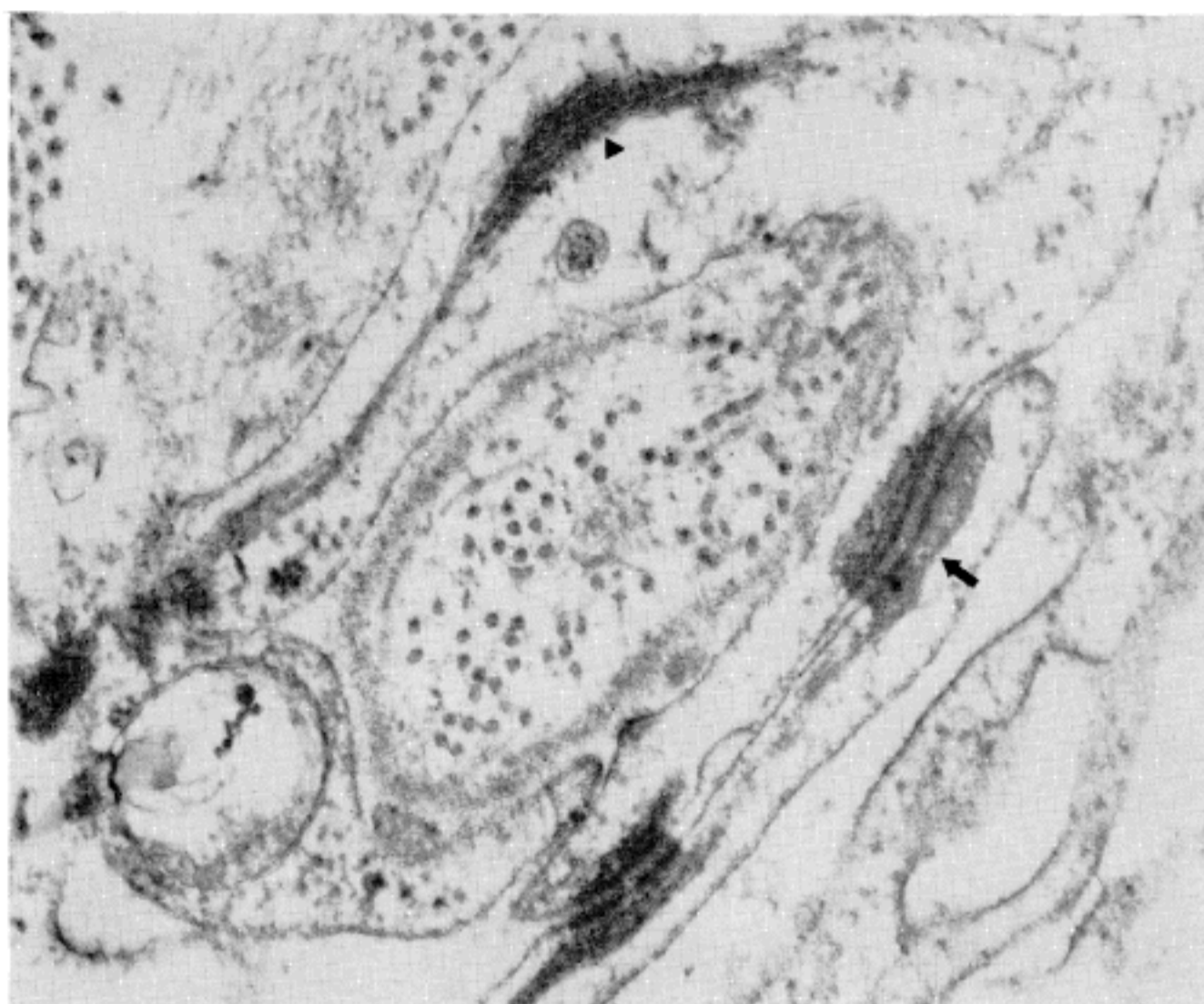


Fig. 8. Electron microscopic finding of spindle cell area showing intercellular desmosomes (arrow) and intracytoplasmic tonofilaments (arrow head) ($\times 40,000$).

Table 2. Summary of clinical features, therapy, and evolution

Case	Age & Sex	Location	Site	Therapy	Follow-Up
1	35 M	Left supraclavicular area	4x3x2cm	Local resection	A&W, 8yrs.
2	26 M	Left supraclavicular area	6x3x3cm	Local resection	A&W, 5yrs.
3	40 M	Suprasternal area	2cm	Local resection	A&W, 4yrs.
4	55 F	Left supraclavicular area	8x5x4cm	Local resection	A&W, 3yrs.
5	43 F	Right supraclavicular area	5x4x3cm	Local resection	A&W, 2yrs.

Abbreviation : A & W ; alive and well

DISCUSSION

This specific entity was firstly reported as ectopic hamartomatous thymoma by Rosai et al., at 1984¹⁾. They reported five cases of lower neck mass which showed specific cellular composition and location (supraclavicular or suprasternal) in close proximity

to the insertion of the sternocleidomastoid muscle and deep to the platysma, strongly suggested an origin from third branchial arch derivatives (Table 2). Also, histologically the mass was composed of epithelial cells which were consistent with thymic epithelia.

The thymus is developed from thymic primordia, which appear on the anterior aspect of the pharyn-

geal pouch, one on each side, during the latter part of the fifth prenatal week. Between the sixth and eighth weeks, the developing thymus is initially recognized as two hollow endodermal elongations that descend into the thorax and then fuse in front of the developing great vessels. The fusion medially of the two thymic diverticula involves only the mesenchymal connective tissue into which the thymic tissue has grown, and there is no fusion of the parenchyma of the two developing lobes. The pharyngeal opening of each diverticulum, the thymopharyngeal duct, is soon obliterated, but this stalk may persist for a period of time as a cellular cord²⁾. If the superior end of the thymic anlage fails to regress (eighth embryonic week), sequestered solid or cystic nodules of tissue may be left along the migration course and have been found incidentally. Thymic tissue may, therefore, occur in the neck, either as separate nodules of mature and well-differentiated tissue or in association with ciliated or columnar epithelial remnants of the pharyngeal outpouching³⁾. Lewis⁴⁾ in a review of the literatures in 1962, recorded 32 reports of which thymic tissue was present in the neck. In his paper, they were presented as cysts, isolated masses, persistent cords, or some combination of these. Benign or malignant neoplasia of the ectopic thymic tissue has not been reported in cervical thymic cysts³⁾, but both forms of neoplastic change have been reported in solid ectopic cervical thymuses⁵⁾. A visible connection with a normal mediastinal thymus has been reported in about one third of cases and suspected in others. At this point of view, our case was compatible with ectopic thymic location, although its connection with mediastinal thymic tissue was not confirmed. In addition, the bilobulated morphologic features were more encourageable to the suggestion of thymic origin of this mass.

Microscopically, the component of the mass was consistent with thymus. It is well known that thymic epithelium can acquire a spindle, pseudomesenchymal configuration which is exhibited by the

neoplastic epithelial cells of so-called spindle cell thymoma^{6,7)}. In this case, transitional areas of squamoid epithelial cells to spindle cells suggest common cell origin in conjunction with immunohistochemical results. The immunohistochemical staining of spindle cells were positive for vimentin with weak positivity to cytokeratin and CEA. The cytokeratin was strongly positive in epithelial cell nests and cyst-lining epithelial cells but more weakly positive in spindle cells. However, the electron microscopic examination of spindle cells showed intracytoplasmic tonofilament and intercellular desmosomes which gave the confirmatory evidence of epithelial nature of these cells. Wright⁸⁾ reported immunohistochemical studies of 22 cases of thymoma, which results revealed strong positive reaction for cytokeratin in predominantly epithelial thymoma but trace positivity in spindle cell thymoma. Previously published report made description about epithelial nature of spindle cell in thymoma⁶⁾ and this ultrastructural characteristics were stated as particularly valuable criteria in situations where this was not obvious by light microscopy⁹⁾.

Rosai¹⁾ explained the adipose tissue component as the results of entrapment of normal cervical fat by the growing mass or as an involutionary phenomenon similar to that seen in the atrophic thymus. This explanation seems to be reasonable in our case and the latter is more favored by us because the gross morphology and operative finding suggested that the mass was not a remnant of thymus but a total ectopia of it.

The lymphocytic infiltration was not prominent but it was a important component. In normal thymic development, lymphocytes appear at the eighth prenatal week²⁾. Until now, it has been assumed that the lymphocytes in thymomas are of T lineage. According to the study by Wright, the UCHL1 staining is strong positive in normal thymus and myasthenic thymus⁸⁾. The results of our study showed positive

reaction for UCHL1 and negative to L26 in lymphocytic component. This finding is compatible with thymic origin of the lymphocyte, but not conclusive.

The question whether this entity is neoplasm or hamartomatous growth was discussing point in the paper of Rosai et al¹⁾. They concluded that it is neoplastic because of large size, enlarging tendency during adult life, focally prominent cellularity, and the fact that bulk of the lesion is made up of morphologically abnormal (spindle) cells.

The differential diagnosis of our case is teratoma. The cervical teratoma in adult is very rare and usually malignant¹⁰⁻¹²⁾. True teratomas contain tissues derived from more than two germ layers and usually exhibit a prominent neuroectodermal component. In this case, the cell components look entirely benign without neuroectodermal component. Although more than two germ layers are impart in this lesion, it is more reasonable to considering it as a hamartomatous lesion than teratoma, clinically and microscopically.

This patient showed polycythemia on laboratory finding, but this was not an associated finding to the anterior neck mass but was a secondary phenomenon of heavy smoking. Conservative excision is the treatment of choice¹⁾.

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국문요약

이소성 유과오종성 흉선종

— 1 증례 보고 —

고려대학교 부속 혜화병원 해부병리과

김준미 · 원남희 · 백승룡

이소성 유과오종성 흉선종은 1984년 Rosai등에 의해 기술된 양성종양으로서 특징적인 네가지 구성요소를 가지고 있는데 첫째, 풍부한 방추세포, 둘째, 성숙된 지방세포, 셋째, 집단, 육주 및 낭포를 둘러싸는 상피세포, 넷째, 림프구등이다.

본 증례는 49세 남자 환자의 흉쇄유돌근 부착부 근방 흉골직상부에서 발생한 5×4×2.5 cm 크기의 종괴로서 육안적으로 경계가 뚜렷하면서 절단면상 연회색이며 점액성부위와 지방조직 및 0.2 cm 내지 0.3 cm의 직경을 갖는 많은 낭포가 관찰되었다.

현미경적으로 이소성 유과오종성 흉선종의 네가지 특징적 구성요소가 관찰되었으며 이중 방추세포는 면역조직화학 염색상 cytokeratin, CEA 및 vimentin에 모두 양성반응을 보였고 전자 현미경 검사상 세포질내 tonofilament와 세포간 desmosome이 잘 관찰되었다. 이 종양은 경부에 생기는 비성숙 기형종과 감별이 필요하며 양성이므로 보존적 절제술이 요구된다.