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Malignant Glomus Tumor Originating in the Superior Mediastinum

— An Immunohistochemical and Ultrastructural Study —

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An extremely rare case of malignant glomus tumor originating in the superior mediastinum was evaluated immunohistochemically and ultrastructurally. A 78-year-old woman who had been suffering from dysphagia and dyspnea had poorly-defined soft tissue mass, 4.5× 2.5cm, in the superior mediastinum with direct invasion into the esophagus, trachea, and bilateral thyroid glands. This case is believed to be unique in several respects. There were neither recognizable findings of benign glomus tumor nor sarcomatous areas, in contrast to the previously reported cases. A definite direct invasion into the surrounding organs was identified. We therefore interpreted this case as primary malignant glomus tumor, not as glomangiosarcoma arising in a benign glomus tumor.

Key Words: *Malignant glomus tumor, Superior mediastinum, Glomangiosarcoma*

INTRODUCTION

Glomus tumor is an uncommon tumor usually located in the deep dermis or subcutis of an upper or lower extremity (Lumley and Stansfeld, 1972; Wood and Dimmick, 1977). It is now recognized that the tumor may also arise in sites where the normal glomus body may be sparse or even absent. Although the most common site is the subungal area of the finger (Tsuneyoshi and Enjoji, 1982), unusual locations have included the patella, chest wall, bone, stomach, eyelid, nose (Enzinger, 1988), and possibly the medi astinum (Brindly, 1949). Reviewing previously reported cases, malignant forms of glomus tumor have been divided into glomangiosarcoma or malignant glomus tumor. Glomangiosarcoma reported were 4 cases of Enzinger and Weiss (1988), one of Aiba et al. (1988) and one of Anagnostou et al. (1973). Malignant glomus tumors were reported, but only as exceptions. Hajdu (1986) showed only the photographs of malignant glomus tumors. Lumley's case (Lumley and Stansfeld, 1972), although regarded as round-cell sarcoma rather than malignant glomus tumor by Enzinger and Weiss (1988), showed a local invasion into many areas, but mitoses were very infrequent. Recently, we experienced a case of malignant glomus tumor directly invading the surrounding organs showing a distinct histopathologic pattern of glomus tumor but frequent mitoses without sarcomatous areas.

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CASE SUMMARY

A 78-year-old woman admitted to Kangnam St. Mary's Hospital, Seoul, on February 20,

1990, with complaints of dysphagia and intermittent dyspnea. She had been suffering from dysphagia and hoarseness for 2 years and was diagnosed as unilateral vocal cord paralysis at a local clinic. On March 2, 1990, dyspnea was suddenly developed and a tracheostomy was performed. Physical examination showed unremarkable findings except for a left vocal cord paralysis on paramedian position. A computed tomography of the neck (Fig. 1 and 2) showed a poorly-defined isodense mass, 4.5×2.5cm, in the superior mediastinum, about C5-7 level, with direct invasion into the trachea, esophagus, and bilateral thyroid glands. Esophagography sho-wed a focal luminal narrowing in the upper portion of the esophagus with preserved mucosal folds. Fiberscopy of the trachea showed an irregularly-shaped intraluminal protruding soft tissue mass, about 2× 3cm, at the distal end of the canula in the posterior wall. On thyroid scan, there was a poorly-defined small cold nodule in the right and left lobe. An excisional biopsy was performed through the tracheostomy site. After that, radiation therapy was started, with a total sum of 720 rad, to relieve the dyspnea and dysphagia. On March 16, sudden dyspnea developed, so a tracheal fiberoptic examination was performed. The tracheal lumen was ne-arly totally obliterated by a polypoid mass that showed an easily bleeding tendency at the distal end of the canula. The next morning, the patient became markedly dyspneic and cyanotic in the face and extremities, and then she expired.

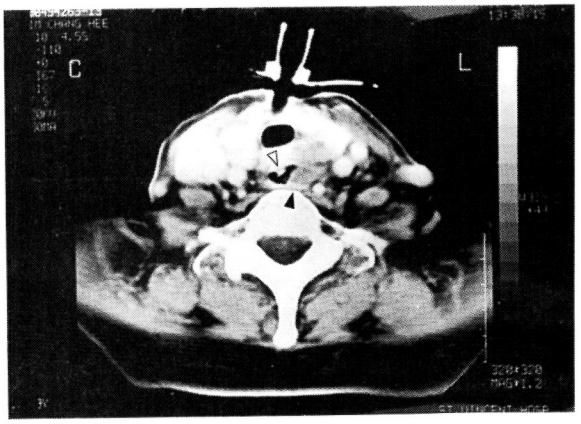

Fig. 1. Neck CT. shows poorly defined isodense mass(dark arrow head) in the superior mediastinum, C5 level, with a mural nodule within the esophagus(clear arrow head).

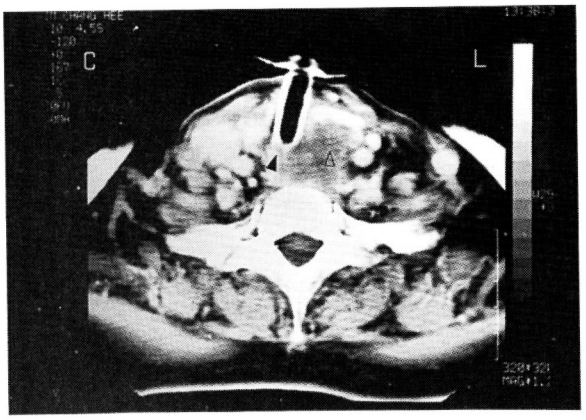

Fig. 2. Neck CT. shows direct invasion into the trachea(dark arrow head), esophagus with total luminal obliteration and thyroid gland (clear arrow head) by tumor mass, C6 level.

MATERIALS AND METHODS

For light microscopy, the biopsied specimen was fixed with 10% formalin and then sta-ined with hematoxylin and eosin (H&E). Special stains used were periodic acid-schiff stain with or without diastase treatment, Masson's trichrome, silver impregnation for reticulin, May-Grunwald-Giemsa, toluidine bl-ue, and alcian blue stain. Deparaffinized sections were stained immunohistochemically with avidin-biotin-peroxidase complex (ABC) method against vimentin, desmin, actin, myosin, S-100 protein, Factor Ⅷ-related antigen and cytokeratin after 0.1% trypsin pretreatment for 30 minutes at room temperature. Mayer's hematoxylin stain was used as a nuclear counter-stain.
For electron microscopy, fresh tissues were fixed in 2.5% glutaraldehyde solution (buffered pH 7.2) and postfixed in 1% phosphate buffered osmium tetroxide. Following dehydration, the tissue blocks were embedded in Epon 812 and cut on a LKB ultratome Ⅲ.
Ultrathin sections were stained with uranyl acetate and lead citrate and examined under a JEM 100B electron microscope.

RESULT

The biopsied specimen grossly was several whitish-gray to tan-brown irregularly-shaped rubbery tissue fragments up to 0.7×0.5cm.
Upon light microscopic examination, they showed tracheal mucosa, which were lined by stratified squamous epithelium and submucosa replaced by tumor mass. Characteristically, the tumor had abundant capillary-sized vessels which had small round to dilated endothelium-lined lumina surrounded by uniform sheet-like epithelioid tumor cells (Fig. 3). The stroma was frequently edematous and loose textured with infiltration of some neutrophills and a few eosinophils. In other areas with more cellular composition, the tumor cells were arranged diffusely in solid sheets around the less conspicuous vessels (Fig. 4). The centrally-located nuclei were large, round, or polygonal and vesicular. One or several prominent eosinophilic nucleoli were found. More than 10 mitotic figures/10HPF(high power field) were present, alt-hough there was only mild nuclear pleomorphism. The cytoplasm was abundant, pale, and eosinophilic and showed focal vacuolar degeneration. In PAS stained preparation, with or without diastase pretreatment, showed a scanty amount of intracytoplasmic glycogen but accentuated cytoplasmic outlines (Fig. 5). The toluidine blue and giesa stained preparations showed no mast cells.
In immunohistochemical stains, there was a

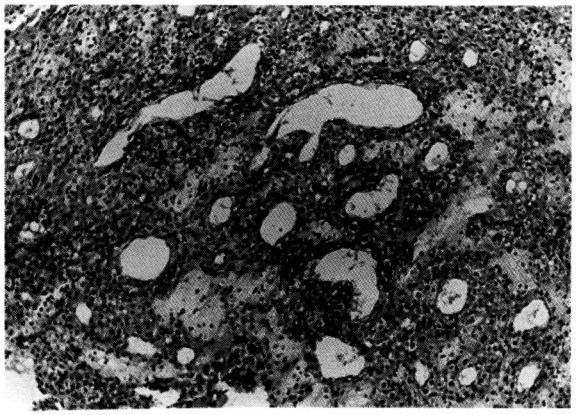

Fig. 3. There are abundant endothelium-lined capillary sized vessels surrounded by sheet-like epithelioid cells (H&E, ×100).

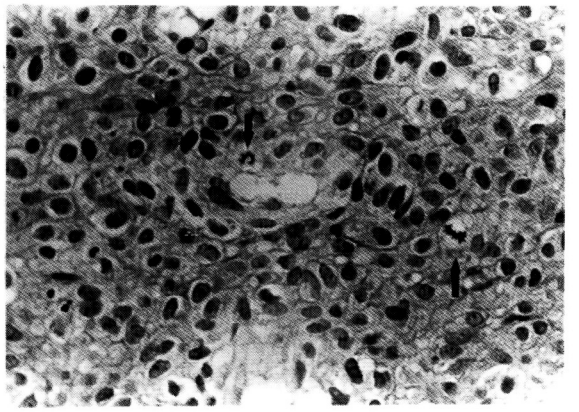

Fig. 5. More accentuated cytoplasmic outlines. Note ample mitosis(dark arrow) (PAS, ×400).

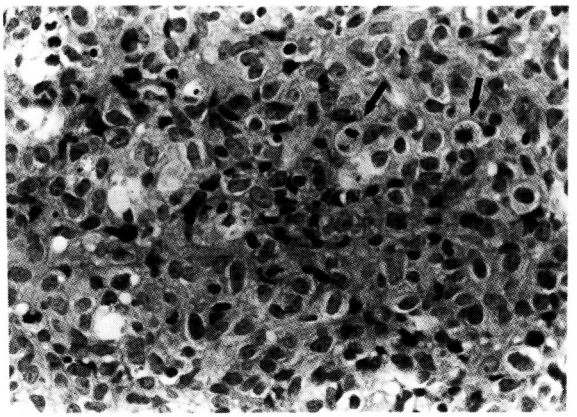

Fig. 4. Diffusely arranged solid sheets of tumor cells with ample mitosis(dark arrow) in the more cellular areas (H&E×400).

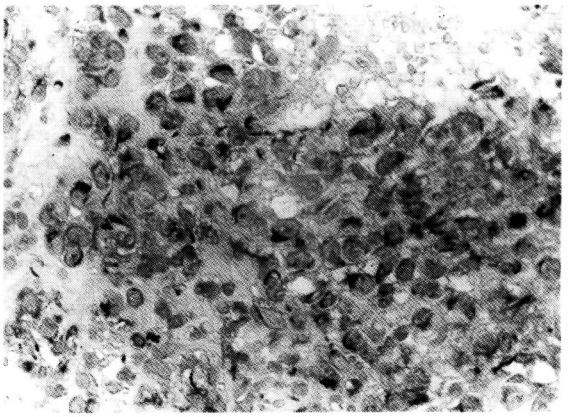

Fig. 6. Immunohistochemical stain for vimentin is strongly positive (ABC method, x 400).

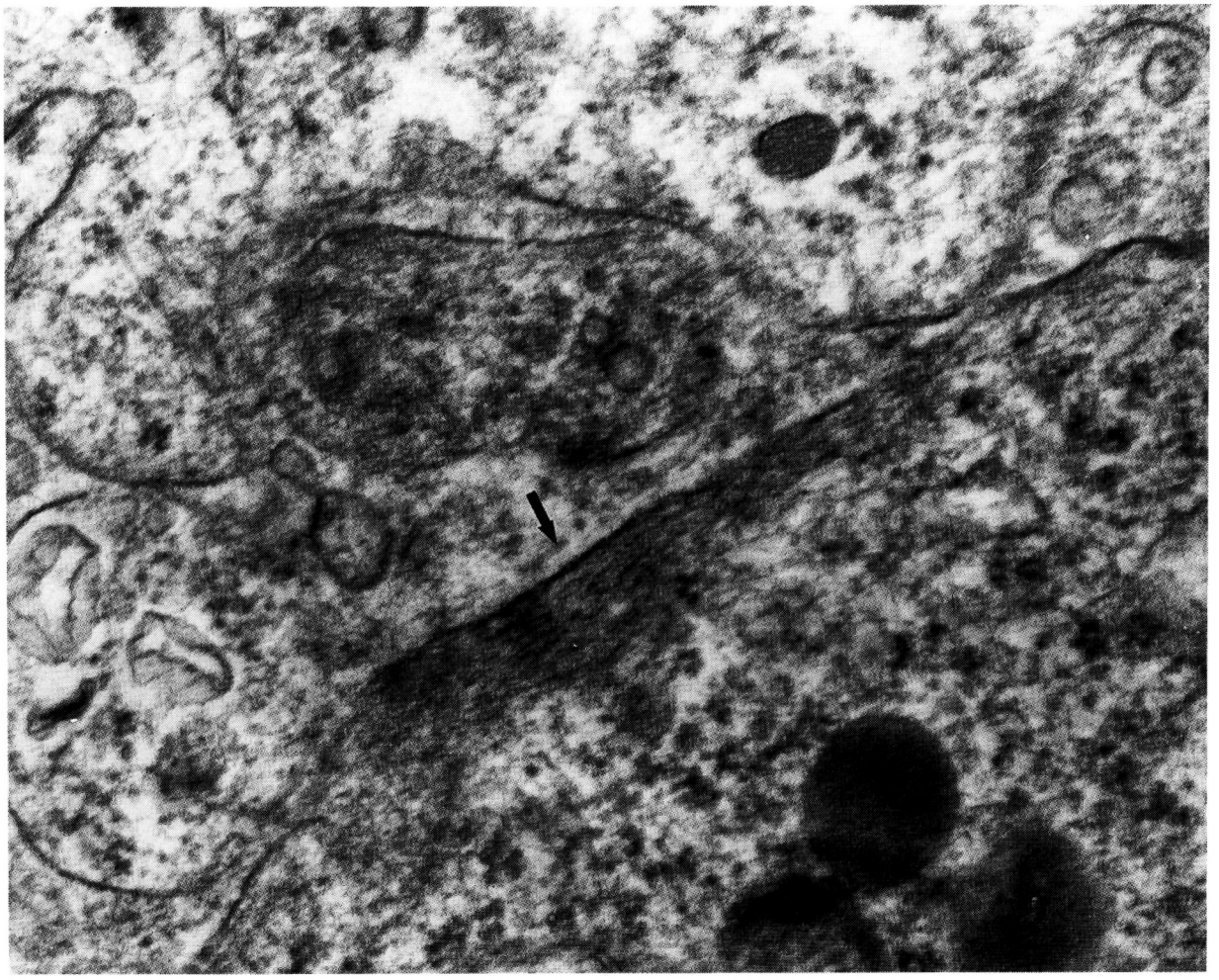

Fig. 7. Electron microscopy shows subplasmalemmal dense plaques(dark arrow), but not numer ous(× 50,000).

strongly positive reaction in staining for vimentin (Fig. 6) but a weakly positive reaction in stains for actin and myosin. The tumor did not express desmin, cytokeratin, S-100 protein, or factor Ⅷ-related antigen.

Upon electron microscopic examination, the tumor cells were somewhat degenerated in spite of being a fresh specimen, probably due to the biopsy done during the tracheostomy state, so that we could find only the tumor cells surrounded, not by definite external lamina, but by partial external lamina material. Thin filaments with dense bodies were distinctly present but in small numbers (Fig. 7), and pinocytic vesicles were present but not numerous (Fig. 8). Intermediate-sized filaments were also present. Nonspecifically, cytoplasmic organells such as mitochondria, rough endoplasmic reticulum, and free ribosomes had considerably increased.

DISCUSSION

The malignant form of glomus tumor is extremely rare. It has been described that th-ere are two malignant counterparts of glomus tumor (Aiba et al, 1988). One is glomangiosarcoma, 4 cases of which have been reported by Enzinger and Weiss(1988), 1 by Aiba et al. (1988), and 1 by Anagnostou et al. (1973). Glomangiosarcoma is usually characterized by sarcomatous areas and occupies a portion of the benign glomus tumor(Aiba et al., 1988 ; Enzinger, 1988). Histologically, it con-

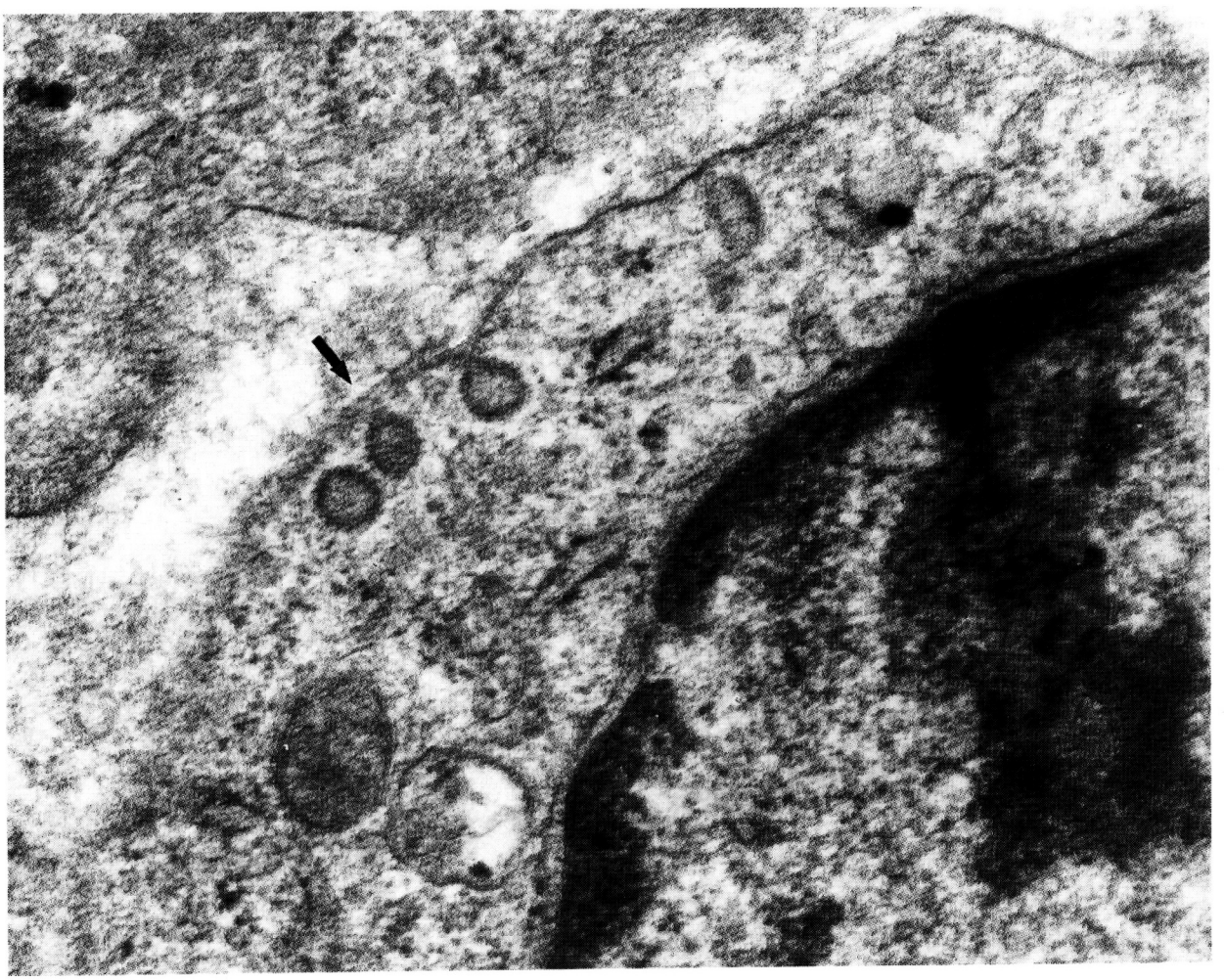

Fig. 8. Electron microscopy shows pinocytotic vesicles (dark arrow), but not numerous(×50,000).

sists of disoriented short stubby spindle cells reminiscent of an intermediate form between fibrosarcoma and leiomy-osarcoma. It shows only a moderate degree of pleomorphism but usually frequent mitotic activity. It has been considered that the most important diagnostic criteria for the malignant form of glomus tumor is believed to be mitotic activity(Aiba et al.,1988) rather than metastasis, because there is no evidence of metastasis in the previously reproted cases of glomangiosarcoma (Aiba et al.,1988; Anagnostou et al., 1973; Enz-inger and Weiss, 1988).

With immunohistochemical study, some monoclonal antibodies were helpful to defferentiate between the glomangiosarcoma and the glomus tumor. Although, previously reported cases(Aiba et al., 1988; Enzinger and Weiss, 1988; Harvey and Walker, 1987) revealed positive reaction for vimentin, actin, and myosin both in the gloman-iosarcoma and the glomus tumor, it was worthy of noting the differences of their intensity. Vim-entin was stained more strongly in the glomangiosarcoma than in the glomus tu-mor, whereas actin and myosin were stained more strongly in the glomus tumor than in the glomangiosarcoma(Aiba et al., 1988). Desmin was negative both in the glomus tumor and the glomangiosarcoma (Enzinger and Weiss, 1988). In this case, there were strong positivity for vimentin, weak positivity for actin and myosin. The lack of immunoreactivity for S-100 protein in this case supported the possibillity of malignancy, as the case reported by Aiba et al.(1988).

Ultrastructurally, glomus tumor cells (Aiba et

al., 1988; Enzinger and Weiss, 1988; Tsuneyoshi and Enjoji, 1982) were characterized by the presence of basal lamina, numerous pinocytotic vesicles, abundant thin filaments with scattered dense bodies in the cytoplasm and at the plasma membrane. These findings strongly supported the smooth muscle origin of the glomus tumor. Glomangiosarcoma cells (Aiba et al., 1988; Enzinger and Weiss, 1988) were also surrounded by the basal lamina, but pinocytotic vesicles and thin filaments with dense bodies were present only in a small numbers. And nonspecific organells, such as mitochondria, rough endoplasmic reticulum, and free ribosomes were considerably increased.

Although glomangiosarcoma shared some common ultrastructural, conventional, and immunohistochemical properties with glomus tumor, some less specific features, such as positive reaction for vimentin, elongation of cytoplasm, increased amount of nonspecific cytoplasmic organells, and increased mitotic activity, were more predominant than glomus tumor. Also some characteristic features of glomus tumor, such as epithelioid arrangement, mast cell infiltration, the presence of schwann cells, and a positive reaction for substance P fibers, were absent in glomangiosarcoma (Aiba et al., 1988).

The other is the malignant glomus tumor thought to be derived directly from the glomus body, that is still reported only rarely (Hajdu, 1986). Hajdu (1986) only displayed photographs of malignant glomus tumors and atypical glomus tumors without explanations, both of which showed a similar morphology to benign glomus tumor. Lumley's case (Lumley and Stansfeld, 1972) had a malignant tumor showing local invasiveness and recurrence, but the tumor cells bore a histologic resemblance to benign glomus tumor that showed an absence of pleomorphism and very infrequent mitoses. There were no areas of benign glomus tumor. It was then regarded as round cell -sarcoma by Enzinger and Weiss (1988).

The present case is unique in several respects. Upon microscopic examination, it showed histopathologic features of glomus tumor with relatively mild pleomorphism but ample mitotic activity, so it was difficult to accept as a malignant tumor, except for the ample mitotic antivity. In contrast to glomangiosarcoma, neither sarcomatous spindled areas nor preexisting benign glomus tumor were found, but it shared common features with glomangiosarcoma in that no mast cell infiltration was found and nonspecific cytoplasmic organells had considerably increased. Clinically, although direct invasion into the surrounding organs, such as the trachea, esophagus, and bilateral thyroid glands, was identified, we regrettably could not evaluate the presence of metastasis to the other organs as we did not perform the autopsy. Consequently, we concluded that it was better to regard it as a malignant glomus tumor rather than a glomangiosarcoma. We hope to establish the more reliable diagnostic criteria for malignant glomus tumor by accumulating the data, as yet there have been numerically insufficient reported cases to evaluate definitely.

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