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Case Report

Ectopic Cervical Thymoma: A Case Report with ^{18}F-fluorodeoxyglucose Positron Emission Tomography Findings

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Ectopic thymoma is considered to arise from ectopic thymus tissue deposited as a result of the abnormal mislocalization of thymus tissue during the embryonic stage. An 86-year-old man visited our hospital with chief complaints of hoarseness and a mass in his anterior neck. A preoperative needle biopsy of the mass did not yield a definitive diagnosis. A positron emission tomography (PET) study revealed heterogeneous accumulation of ^{18}F-fluorodeoxyglucose (FDG) in the tumor. The tumor, affecting the left sternocleidomastoid muscle, the recurrent laryngeal nerve, the internal carotid vein, and the brachiocephalic vein, was resected using a combination of a collar incision in the neck and a median incision in the sternum. Immunohistochemically, the tumor was diagnosed as an ectopic thymoma of the neck. To date, only a few cases of ectopic thymoma presenting with FDG accumulation have been reported. Our experience indicates that ectopic thymoma should be kept in mind during the differential diagnosis of neck tumors with FDG accumulation appearing on PET images.

Key words: ectopic thymoma, thyroid tumor, positron emission tomography (PET)

The thymus develops on the ventral side of the third and fourth branchial arch, and descends to the anterior mediastinum during intrauterine development. Mislocalization of thymus tissue during this process can lead to the development of ectopic thymus gland tissue at various sites [1]. Ectopic thymoma developing from such ectopic thymic tissue is a very rare disease. We recently encountered a case of ectopic type A thymoma developing from the thyroid gland; this lesion was difficult to distinguish from a thyroid tumor preoperatively. Similar to intrathoracic thymomas, the ectopic thymoma in the neck region in this case also showed enhanced accumulation of ^{18}F-fluorodeoxyglucose (FDG) on positron emission tomography (PET), making preoperative diagnosis difficult.

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Case Report

The patient was an 86-year-old man. He visited our hospital with chief complaints of hoarseness and an elastic-soft mass in the anterior neck that had increased in size rather rapidly. A hematological examination revealed evidence of renal dysfunction (creatinine level, 1.61 mg/dl) and an elevated thyroglobulin level (112 ng/ml), but no thyroid function

abnormality or abnormal elevation of the serum carcinoembryonic antigen (CEA) level. A detailed examination using a laryngoscope revealed left recurrent laryngeal nerve paralysis. A neck CT revealed a low-attenuation mass (75×64 mm) in the left lobe of the thyroid that was not associated with any cervical lymph node enlargement (Fig. 1). Magnetic resonance imaging (MRI) of the neck revealed a tumor that was iso-intense with muscle on T1-weighted images (Fig. 2A), while a fat-suppression (short TI inversion recovery) T2-weighted image revealed the fibrous septum as a low-intensity area in the tumor (Fig. 2B). Tumor infiltration of the left sternocleidomastoid muscle and the left internal carotid vein was suspected, whereas tumor infiltration of the left brachiocephalic vein, trachea or esophagus could not be ascertained during the MRI examination. Because of the patient's impaired renal function, contrast material was not used for the CT or MRI examinations. PET/CT examinations revealed heterogeneous FDG accumulation in the tumor, with a maximum standardized uptake value (SUV-max) of 7.77 (Fig. 3). No abnormal FDG accumulation was noted at any site other than in the tumor. In view of the clinical course (relatively rapid increase in size) and the findings obtained using diagnostic imaging, the patient was suspected of having a malignant tumor (*e.g.*, undifferentiated thyroid cancer). A core needle biopsy (CNB) of the tumor revealed a dense proliferation of cells with relatively

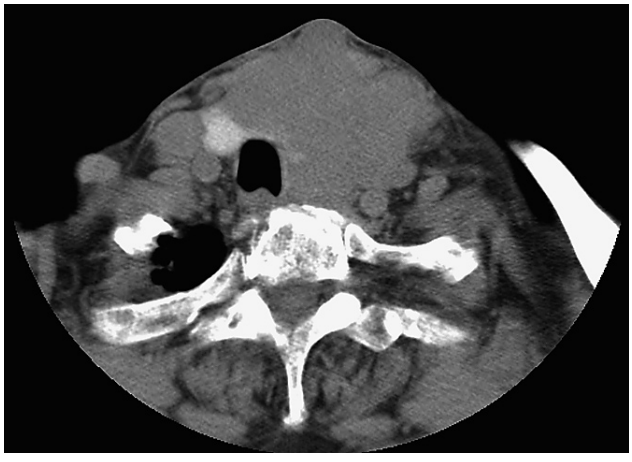

Fig. 1 CT image shows a low-attenuation mass (75×64 mm) in the left lobe of the thyroid.

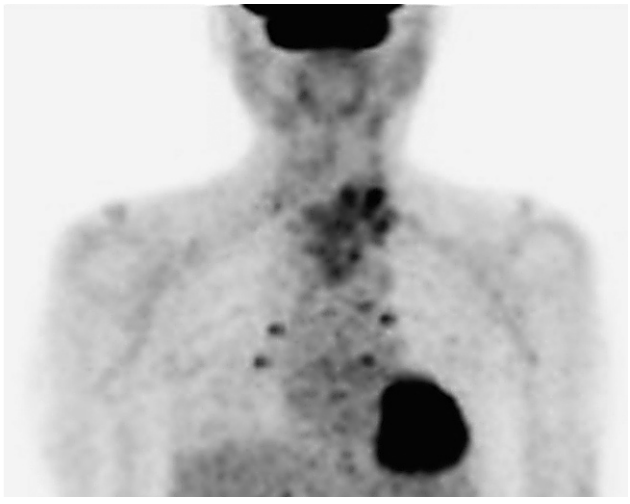

Fig. 3 PET/CT image shows the heterogeneous accumulation of FDG in the tumor (SUV-max: 7.77).

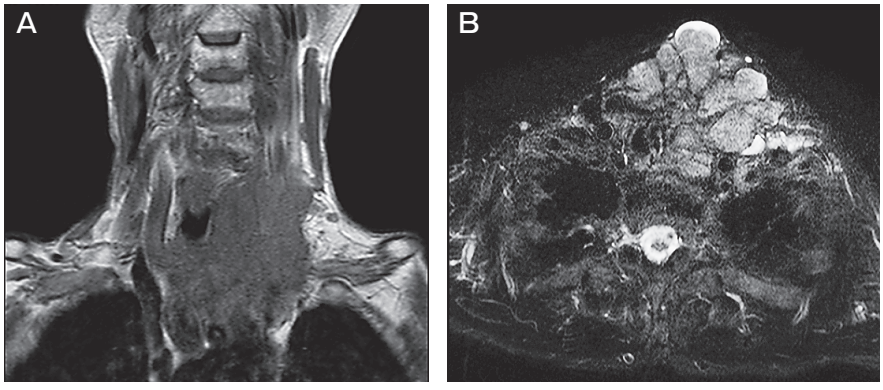

Fig. 2 (**A**) T1-weighted MRI image shows a tumor iso-intense with the muscle in the anterior neck; tumor infiltration of the left sternocleidomastoid muscle and left internal carotid vein was suspected. (**B**) A fat-suppression (short TI inversion recovery) T2-weighted image reveals the fibrous septum as a low-intensity area in the tumor.

uniform short spindle-shaped nuclei. Immunohistochemically, the tumor was positive for cytokeratin AE1 and AE3, and negative for thyroid transcription factor-1 (TTF-1). Thus, an epithelial tumor seemed likely, although a definitive diagnosis could not be established.

Tumor resection was undertaken via a combination of a cervical sleeve incision and a median sternal incision. The tumor lesions, which involved the left lobe of the thyroid, the left sternocleidomastoid muscle, the upper part of the thymus, the left recurrent laryngeal nerve and the left internal carotid vein, were resected together. In the caudal region, the left brachiocephalic vein was also affected by the tumor, suggesting the need for combined resection of the brachiocephalic vein and a prosthetic angioplasty. However, since the patient was of advanced age and had renal dysfunction, the combined resection of the brachiocephalic vein was not performed and the tumor in this area was left unresected. The resected specimen showed an internal lobulated architecture separated by fibrous septae (Fig. 4A). Histopathological examination of the resected specimen revealed that the tumor was mainly composed of poorly atypical quasi-circular/short spindle-shaped epithelial cells (Fig. 4B). Immunohistochemically, the tumor cells were weakly positive for p63, positive for 34betaE12, and negative for CD5 and CEA. Based on these findings, the tumor was diagnosed as an ectopic thymoma, World Health Organization (WHO) tumor type A and Masaoka stage III. Postoperatively, external radiotherapy (60 Gray) was administered for the residual tumor. At present, 12 months after the surgery, the residual tumor shows no sign of apparent re-growth.

Discussion

A thymoma is a tumor that develops from the epithelial cells of the thymus. Such lesions develop mostly in the anterior or superior mediastinum. Ectopic thymoma, developing in the neck, middle mediastinum, or posterior mediastinum, reportedly accounts for about 4% of all thymoma cases [2]. Thymoma of the neck region is considered to develop from ectopic thymus tissue in the neck deposited as a result of abnormalities during the course of the descent of the thymus tissue towards the anterior mediastinum after its intrauterine developments on the ventral side of the third and fourth branchial arch [1]. Although some investigators have reported that ectopic thymus tissue is seen in the neck in 1.8% of all patients with Basedow's disease [3], ectopic thymoma developing from ectopic thymus tissue in the neck is considered to be much rarer. Chan *et al.* analyzed 16 cases of ectopic thymoma of the neck, reporting that thymoma of the neck was more frequent among women than among men (women: men ratio = 7 : 1) and that the mean age of the patients was 42.7 (range: 11–71) years [4]. The present case was an elderly man (86 years) and seems to represent a non-typical case of thymoma of the neck.

In the present case, the preoperative diagnostic imaging findings suggested a malignant tumor, such as an undifferentiated thyroid cancer. CT and MRI

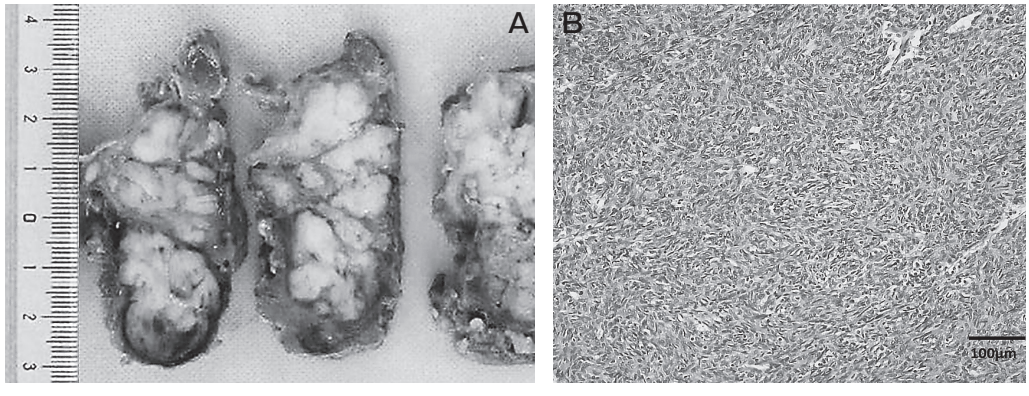

Fig. 4 (A) Resected, formalin-fixed specimen shows an internal lobulated architecture separated by fibrous septae. (B) Histopathological findings show that the tumor was mainly composed of poorly atypical short spindle-shaped cells, leading to a diagnosis of ectopic type A thymoma.

examinations suggested tumor infiltration of the surrounding tissues, including the sternocleidomastoid muscle and the internal carotid vein. However, an adequate evaluation using diagnostic imaging was not possible because contrast material could not be used on account of the patient's impaired renal function. Regarding the diagnostic imaging features of thymoma of the neck, a septal structure visible within the tumor on T2-weighted MRI scans is important [5]. This feature was also seen in the present case and seems to be useful for the diagnosis of this disease. PET/CT examinations revealed heterogeneous FDG accumulation with a high SUV-max value. Even low-risk thymomas are known to be present with enhanced FDG accumulation [6–10]. The SUV-max values of low-risk thymoma (types A, AB, and B1) and high-risk thymoma (types B2 and B3) are significantly lower than that of thymic carcinoma, but no difference is observed between low- and high-risk thymomas [6–8]. FDG accumulation is also usually homogeneous in thymic carcinoma, whereas it is often heterogeneous in thymoma [6]. Although the high levels and homogenous accumulation of FDG in thymic carcinoma can be explained by the high tumor growth rate or cell density, the reason for heterogeneous FDG accumulation in the thymoma is still unclear [6]. In the present case, a correlation between the heterogeneous FDG accumulation and the fibrous septal structure in the tumor was suspected.

Cases of ectopic thymoma of the middle mediastinum presenting with enhanced accumulation of FDG and 11C-acetate have been reported [11]; however, thymoma of the neck with enhanced FDG accumulation has not been previously reported, and the present case may be the first such report. Meanwhile, regarding the accumulation of FDG in thyroid tumors, such accumulations have been reported not only in thyroid cancer, but also in some cases of benign thyroid tumors, such as Hashimoto's disease, subacute thyroiditis and multinodular goiter [12]. Therefore, thymoma of the neck may be difficult to recognize in cases with neck tumors presenting with enhanced FDG accumulation.

In the present case, CNB was performed preoperatively, but a definitive diagnosis was not obtained. We used 18-gauge needles for the tumor biopsy and examined the materials histochemically using immunohistochemical staining. Tumors developing in the thyroid gland usually originate from follicular epithelial cells, C cells and lymphocytes, but some thyroid tumors originate from thymus or parathyroid tissue. Thyroid tumors associated with the thymus include ectopic thymomas, ectopic hamartomatous thymomas, carcinomas showing thymus-like differentiation (CASTLE), and spindle cell tumors with thymus-like differentiation (SETTLE). All of these tumors are very rare [13], and ectopic thymoma represents a diagnostic pitfall especially when using fine-needle-aspiration cytology or frozen sections as specimens, where a lymphomatous process or undifferentiated carcinoma may be suggested [14]. Some investigators have attempted to diagnose cervical thymoma preoperatively using flow cytometry and fine-needle-aspiration biopsy (FNAB) specimens, and this method seems to be useful for the diagnosis of this tumor [15].

In the present case, the tumor was resected via a combination of a collar incision in the neck and a median incision in the sternum. Intraoperatively, the tumor was found to have widely invaded the surrounding organs, affecting the left brachiocephalic vein in the caudal region. Because the patient was elderly and had renal dysfunction, we avoided a combined resection and reconstruction of the left brachiocephalic vein. As a result, the tumor in this region was left unresected, and the operation constituted an incomplete resection. Reportedly, the 5-year survival rate for patients with Masaoka stage III thymoma is significantly lower after incomplete resection (35%) than after complete resection (94%) [16]. The prognosis of ectopic thymoma is unclear because of the small number of reports. Chan *et al.* reported that if an analogy with mediastinal thymomas can be drawn, the circumscribed/encapsulated ectopic thymomas could be curable by surgical resection in almost all cases, whereas the invasive ones may potentially be complicated by recurrence or metastasis [4]. Recently, preoperative induction chemotherapy and chemoradiotherapy for cases of locally advanced thymoma have been reported [17, 18], and further clinical studies evaluating the efficacy of these therapies are needed. Although there may be some room for argument over the validity of adopting such induction therapies for elderly patients with impaired renal function, such as in the present case, these treatments are likely to be essential for younger patients to achieve a complete resection of this tumor using multimodality therapy,

i.e., surgical resection combined with induction therapy or vascular reconstruction.

In conclusion, we encountered a rare case of ectopic cervical thymoma presenting with enhanced FDG accumulation on PET/CT images. Our experience suggests that ectopic thymoma should be kept in mind during the differential diagnosis of neck tumors with FDG accumulation on PET/CT images and a septal structure visible on MRI findings.

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