Metastatic Skull Base Tumor From Thymic Carcinoma Mimicking Tolosa-Hunt Syndrome

—Case Report—

Satoshi TSUTSUMI, Yusuke ABE, Yukimasa YASUMOTO,
Saori SHIONO*, and Masanori ITO

*Departments of Neurological Surgery and *Pathology,
Juntendo University Urayasu Hospital, Urayasu, Chiba*

Abstract

A 39-year-old male without contributory medical history had sustained progressive double vision, ptosis, and trigeminal pain for 2 weeks. Physical examination revealed total ophthalmoplegia and visual field defect with normal blood examination and chest radiography. Cranial computed tomography revealed a hyperdense mass in the left frontotemporal fossae with bony erosion. Magnetic resonance imaging confirmed a broad-based, intensely enhanced extraaxial tumor of $4 \times 4 \times 4$ cm diameter with dural tail sign. Cerebral angiography demonstrated insignificant blood supply both from the internal carotid and middle meningeal arteries. Nearly total tumor resection was achieved via orbitofrontotemporal craniotomy. Intraoperative findings revealed the extraaxial tumor with broad attachment to the dura mater and invasion to the optic and oculomotor nerves. Histological examination revealed hypercellular tumor with significant cell atypism, mitotic activity, and focal necrosis. Immunohistochemical staining was positive for AE1/3 and c-kit, but negative for glial fibrillary acidic protein. Systemic examination performed postoperatively revealed a thymic tumor without additional remote lesions. The final diagnosis was metastatic brain tumor from thymic carcinoma. Rapid progression of neurological impairment inconsistent with a benign extraaxial tumor needs prompt surgical intervention.

Key words: metastatic brain tumor, skull base, thymic carcinoma, surgery

Introduction

Thymic carcinoma originates from the thymic epithelial cells, and accounts for only 0.2–1.5% of all malignancies.⁶⁾ Most thymic carcinomas occur in adults, with a mean age of 50 years and slight male dominance.¹³⁾ Thymic carcinoma manifests as chest pain, shortness of breath, cough, and superior vena cava syndrome in 68.3% of cases.¹³⁾ In contrast, up to 23.7% of cases are asymptomatic and found incidentally on chest imaging.⁸⁾ Thymic carcinoma has a poor prognosis because of the high degree of malignancy, early metastasis, and delayed diagnosis. The overall 5-year survival rate is estimated to be 14.5%.^{13,16)} The incidence of distant metastasis varies from 1.5% to 15%.^{2–4,11–13)} Thymic carcinoma most frequently metastasizes to the liver, followed by the kidney and extrathoracic lymph nodes.¹¹⁾ Brain metastases are rare and usually metachronous, and the intracranial metastatic foci are rarely identified before verification of the primary lesion.^{2,3,15)}

Here we describe a case of metastatic skull base tumor from thymic carcinoma manifesting as rapidly progressing ophthalmopathy and trigeminal pain, referred as Tolosa-Hunt syndrome.

Case Report

A healthy 39-year-old male was aware of left ptosis and double vision that deteriorated rapidly for 2 weeks. Retroorbital dysesthesia on the affected side appeared 1 week before first presentation. His past medical history was unremarkable. The patient was a non-smoker and had not experienced recent weight loss, chest pain, shortness of breath, cough, or general fatigue.

Neurological examination revealed complete ptosis and total ophthalmoplegia on the left, and visual field defect in the upper lateral quadrant. Blood examination and chest radiography showed no abnormalities. Computed tomography (CT) of the head revealed a hyperdense mass in the left frontotemporal fossae with bony erosion in the medial part of the lesser wing of the sphenoid bone (Fig. 1). Magnetic resonance imaging confirmed an intensely enhanced extraaxial tumor of $4 \times 4 \times 4$ cm diameter, appearing as isointense on both T₁- and T₂-weighted images, with localized meningeal enhancement and broad attachment to the planum sphenoidale, superior and lateral walls of the cavernous sinus, and medial half of the lesser wing of the sphenoid bone (Fig. 2). Neither additional intracranial mass lesions nor abnormal meningeal enhancement was found. Cerebral angiography demonstrated

tumor staining via the inferolateral trunk of the internal carotid artery and middle meningeal artery. The supraclinoid portion of the left internal carotid artery showed segmental narrowing (Fig. 3).

Tumor resection was performed via orbitofrontotemporal craniotomy. Intraoperatively, the tumor was found to be entirely located extraaxially, with broad attachment to the cranial base dura mater, and encasing the supraclinoid portion of the internal carotid artery and proximal part of the anterior choroidal artery with erosion of the arachnoid membrane, which were easily dissected from the tumor without exerting excessive traction. A part of the tumor was found to invade into the cavernous sinus which was left unresected. No parenchymal invasion was identified in the surrounding brain, whereas part of the tumor was found to blend with the optic and oculomotor nerves, suggesting invasion. Nearly total removal was achieved following piecemeal resection.

Histological examination showed the tumor was hypercellular and consisted of significantly atypical cells with

high nucleus/cytoplasm ratio and mitotic activity, arranged in a medullary pattern, and including focal necrosis (Fig. 4A, B). Immunohistochemical staining was positive for AE1/3 and c-kit (Fig. 4C, D), but negative for glial fibrillary acidic protein. Cytokeratin, chromogranin A, and CD56 were positive in very small areas of the tumor. The MIB-1 labeling index was 40% (Fig. 4E). Those findings were highly indicative of metastatic carcinoma.

Postoperatively, the patient underwent a systemic survey using positron emission tomography which revealed a thymic tumor located in the anterior mediastinum. Extracranial metastatic foci were not found. Blood examinations for screening neoplasms and endocrine function showed normal findings. Therefore, we considered that the metastatic brain tumor from thymic carcinoma was highly likely. Postoperative course was uneventful, although the patient's ophthalmoplegia and visual impairment did not improve. Intensive chemotherapy with carboplatinum administered postoperatively showed transient partial response, but the tumor progressed and the patient died of systemic metastasis at 16 months after the onset.

Fig. 1 Computed tomography scan of the head showing a large hyperdense mass in the left frontotemporal fossae with erosive change in the lesser wing of the sphenoid bone (arrowhead).

Fig. 3 Left internal (A) and external (B) carotid angiograms, lateral projections, revealing tumor staining via the inferolateral trunk of the internal carotid artery and the middle meningeal artery (arrowhead) with segmental narrowing in the supraclinoid internal carotid artery (arrow).

Fig. 2 T₁-weighted magnetic resonance images with gadolinium-diethylenetriaminepenta-acetic acid confirming a well-circumscribed, broad-based, extraaxial tumor of 4 × 4 × 4 cm diameter, with homogeneously intense enhancement and focal meningeal enhancement (arrowheads).

Fig. 4 Photomicrographs showing the hypercellular tumor consisted of atypical round cells with high nucleus/cytoplasm ratio and mitotic activity, arranged in a medullary pattern, and including necrotic foci (A, B: hematoxylin and eosin stain, A: $\times 40$, B: $\times 200$). Immunohistochemical staining was positive for AE1/3 (C: $\times 400$) and c-kit (D: $\times 200$). The MIB-1 labeling index was 40% (E: $\times 200$).

Discussion

Thymic carcinoma has only recently been recognized as a distinctive entity in accordance with the establishment of the methods of immunohistochemical staining.^{1,13,16} Clinically, thymic carcinoma differs from thymoma in the absence of paraneoplastic syndromes, such as myasthenia gravis or pure red cell aplasia. Histologically the tumor often infiltrates extensively into surrounding tissue.

Thymic carcinoma cells are highly atypical, arranged in diffuse sheets, and partially show the pseudoalveolar pattern. Mitotic figures are frequent and diffusely positive for cytokeratin. Tumor cells are partially positive for neuron-specific enolase and protein gene product 9.5, but negative for chromogranin A and synaptophysin. Dispersed tumor cells expressing neuroendocrine markers are found in 60% of thymic carcinomas and have been assumed to represent a separate category of neuroendocrine tumors arising from the thymus.^{1,12}

Extracranial neoplasms occasionally metastasize to the intracranial dura mater with infrequent formation of a dural-based mass lesion, mimicking meningioma.^{5,9,10,14,16,17} To date, four such cases from thymic carcinoma have been documented.^{1,7,15,16} Three of them

presented as an extraaxial tumor located on the temporal convexity, frontal convexity, and parasagittal dura mater, and developed during the clinical course after the diagnosis of thymic carcinoma or were found incidentally during systemic survey of thymic carcinoma. Therefore, metastatic foci could be assumed on the initial neuroimaging study. Only one case was a cranial metastasis from asymptomatic thymic carcinoma, in which thymic carcinoma was identified on postsurgical chest CT after histological verification of the metastatic focus.¹⁵ The present patient was a non-smoker and not aware of chest pain, shortness of breath, cough, general fatigue, or recent weight loss. In addition, preoperative blood examination and chest radiography showed normal findings. In contrast, the present case mimicked Tolosa-Hunt syndrome with rapid progression for 2 weeks. Moreover, intraoperatively tumor invasion to the cranial nerves was identified. Such clinical and intraoperative findings were inconsistent with the appearance on neuroimaging study which was highly suggestive of benign pathology such as meningioma.

Optimum treatment strategy for thymic carcinoma remains undefined. Currently, a multimodality approach combining radical surgical resection, platinum-based combination chemotherapy, and radiotherapy is the preferred therapy for thymic carcinoma, although the overall 5-year survival rate is still estimated as low as 14.5%.^{7,13,16}

Involvement of the central nervous system carries a poor prognosis. Treatment of brain metastasis from thymic carcinoma includes microsurgical resection, whole brain irradiation, stereotaxic radiosurgery, and combinations, which are similar to the options for other brain metastases.^{1,3,7,13,15,16}

Rapid progression of neurological impairments inconsistent with neuroimaging findings of a benign extraaxial tumor may suggest metastatic tumor from an asymptomatic primary malignancy and needs prompt surgical intervention for histological verification.

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Address reprint requests to: Satoshi Tsutsumi, M.D., Department of Neurological Surgery, Juntendo University Urayasu Hospital, 2-1-1 Tomioka, Urayasu, Chiba 279-0021, Japan. e-mail: shotaro@juntendo-urayasu.jp