Thymic Squamous Cell Carcinoma with Multiple Brain Metastases

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Abstract—Thymic carcinomas are rare epithelial malignancies with marked invasive tendency which can metastasize to distant organs, most commonly to the lung, bone, liver, kidney and extra-thoracic lymph nodes. Central nervous system metastasis is extremely rare and only 45 such cases have been reported in the English literature. We reported a 42-year-old male with thymic squamous cell carcinoma and lung and bones metastases. He underwent thymomectomy and pulmonary lobectomy with concurrent chemo-radiotherapy. Based on the clinical symptoms of severe headache and vomiting and the results of brain computed tomography and magnetic resonance imaging scans, 2 metastatic tumors with a cystic component were diagnosed. We resected the metastatic tumors and the signs of increased intracranial pressure subsided immediately after the operation. The patient underwent continuous chemotherapy systemically and whole brain irradiation for disease control. This presentation suggests that surgical resection with concurrent chemo-radiotherapy is the treatment of choice for thymic carcinomas with brain metastases.

Key Words: Thymic squamous cell carcinoma, Brain metastasis, Immunohistochemistry

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INTRODUCTION

Thymic carcinomas are rare neoplasms⁹. Patients with thymic carcinomas often present with chest pain, cough, shortness of breath, fatigue, weight loss and anorexia. They have a poor prognosis with a 5-year survival rate of 14.5%-23%⁹. In 1.5% to 15.5% of cases, thymic carcinomas metastasize to distant organs, including the lung, bone, liver, kidney and extra-thoracic lymph nodes⁹. There were only 45 such cases of the brain metastasis reported in the literature⁹. It is possible that the tumor presents with solid or cystic changes, causing hemorrhage or extradural extension, thus mimicking meningioma. We report one patient with brain metastases from thymic carcinomas and discuss the treatment of this patient.
CASE REPORT

A 42-year-old man had thymic squamous cell carcinoma with lung metastasis in September 2002. He underwent thymectomy and pulmonary lobectomy with concurrent chemo-radiotherapy. Thereafter, multiple bone metastases developed. He underwent palliative radiotherapy and chemotherapy with combinations of different regimens between September 2003 and October 2007. In the beginning of November 2007, he had progressive headache with vomiting. No obvious neurological deficits or seizures were reported. The brain computed tomography (CT) and magnetic resonance imaging (MRI) scans showed a well-defined cystic lesion in the right fronto-parieto-occipital region measuring approximately 6.0 × 4.8 cm, with enhancement of the solid compartment (Fig. 1). The differential diagnosis of the lesion includes metastatic tumor, cystic astrocytoma, hemangioblastoma and inflammatory cysts such as those observed in cysticercosis.

The patient underwent a right fronto-parieto-occipital craniotomy performed via a U-shaped scalp incision. A small corticotomy was performed and a clear yellowish fluid was drained out. Two separate solid tumors at the base of the cystic lesion were noted (Fig. 2) and grossly total resection of both solid tumors was achieved.

Microscopic examination of the surgical specimens revealed sheets of bizarre cancer cells with marked tumor necrosis and focal squamous differentiation (Fig. 3). The tumor cells were detected by the immunohistochemical stain for cytokeratin (AE1/AE3), CK5/6, CD5 and CD117 (Fig. 4), but were negative for TTF-1. These features were compatible with those of metastatic poorly...
differentiated squamous cell carcinoma from the thymus.

The patient’s preoperative symptoms were immediately relieved after surgery and he remained neurologically intact. In addition, radiation therapy consisting of a total 3000 cGy in 10 fractions to the whole brain was resumed, and systemic chemotherapy was scheduled.

DISCUSSION

Thymic carcinomas, classified as type C thymomas according to the WHO classification, are rare neoplasms in the anterior mediastinum, representing 0.06% of thymic neoplasms \(^{(1)}\). They are a heterogeneous group of aggressive, invasive epithelial malignancy \(^{(6)}\). The mean age of diagnosis of thymic carcinomas is 50 years with slight male dominance. Most patients present with symptoms of chest pain, cough, shortness of breath, fatigue, weight loss, and anorexia and have a poor prognosis with 14.5%-23% of 5-year survival rate \(^{(2)}\). Surgery is the treatment of choice and total tumor resection results in improved prognosis \(^{(7,8)}\). Radiotherapy combined with chemotherapy helps reduce local recurrence and prolong survival time \(^{(9-11)}\).

In 1.5% to 15.5% of cases, thymic carcinomas metastasize to distant organs \(^{(3)}\). The most common sites of distant metastases are the lung, bone, liver, kidney and extra-thoracic lymph nodes \(^{(6)}\). Brain metastasis from thymic carcinomas is rare and only 45 cases had been reported in the literature \(^{(5)}\). The most common symptom is headache \(^{(3)}\). The appearance of metastatic brain lesions varies. Al-Barbarawi et al. reported the first known Australian case. There were 2 lesions in this case, one within the left frontal lobe with cystic necrosis and hemorrhage and the other in the parietal lobe with hemorrhage \(^{(12)}\). Kong et al. reported 49 patients with thymic carcinomas; 6 of them developed brain metastases \(^{(5)}\). Four patients had a single lesion, and 2 patients had multiple lesions. Cystic changes were found in 2 cases. In the literature, the present case is the 46th case of brain metastases from thymic carcinoma, and it is the 10th case with multiple metastases \(^{(13)}\). The cystic change or hemorrhage in the metastatic lesions does not appear to be uncommon.

Approximately 10% of central nervous system tumors have peritumoral cysts \(^{(14)}\), which are due to increased tumor vascular permeability leads to the formation of plasma ultrafiltrate. The increases of interstitial pressure within the tumor drives the shift of extracellular plasma ultrafiltrate from the interstitial space of the tumor to the interstitial space of the surrounding brain tissue. When the absorption of interstitial fluid by the surrounding brain tissue exceeds the extravasation of the plasma ultrafiltrate, peritumoral cysts form \(^{(15,16)}\). In our case, the 2 metastatic tumors were close to each other; therefore their peritumoral cysts fused. Based on the mechanism of peritumoral cyst formation, tumor excision can resolve cyst formation. Cyst wall removal or wide fenestration is not necessary.

Because brain metastases from thymic carcinomas are extremely rare and no definite treatment has been established. A review of the literature suggests that prompt surgical resection of the tumor with adjuvant

Figure 4. The tumor cells were strongly immunoreactive for AE1/AE3 (A) and CD 117 (C), and were focally immunoreactive for CD5 (B). (Avidin-biotin complex, ×100)
radiotherapy and chemotherapy is required to decrease intracranial pressure (ICP) and improve long term outcome of this disease. Tamura et al. reported 1 case in which no recurrence of the metastatic tumor was observed on MR images 6 months after surgical resection and adjuvant chemotherapy. Further, gamma knife radiosurgery appears to be an effective treatment if the tumor size is small. Nicolato et al. reported 1 case with 2 metastatic lesions and the patient underwent gamma knife radiosurgery for the 2 lesions. The patient was free of neurological signs and radiological recurrence for 13 months. Our case had a good Karnofsky performance status score (KPSS) of more than 70. Therefore, we resected the metastatic tumor for definite diagnosis, decrease of ICP, and increasing the survival time.

In conclusion, thymic carcinoma is a rare malignancy that rarely metastasizes to the brain. The intracranial metastatic lesions have variable appearance. The extensive surgical resection of the tumor combined with radiotherapy and cisplatin-based chemotherapy is indicated for improving the quality of life and increasing the survival time of patients, especially of those with a good KPSS.

REFERENCES