

Brain Metastasis from Invasive Thymoma Mimicking Intracerebral Hemorrhage: Case Report

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Abstract

A 55-year-old man with an 8-year history of invasive thymoma presented with sudden onset of left hemiparesis. Computed tomography (CT) and magnetic resonance (MR) imaging showed a right frontal lobe intracerebral hemorrhage and the possibility of brain metastasis could not be rejected. The patient underwent removal of the hematoma. Histological examination showed brain metastasis from invasive thymoma. To the best of our knowledge, this is the first reported case of hemorrhagic brain metastasis from invasive thymoma (non-cancerous) mimicking intracerebral hemorrhage.

Key words: brain metastasis, tumor hemorrhage, hemorrhagic metastasis, invasive thymoma, thymic carcinoma

Introduction

Neoplasms arising from thymic epithelial cells are classified as thymomas and thymic carcinomas by the World Health Organization (WHO) classification.¹⁾ Approximately 30% of thymomas are invasive; however, they rarely (3–5%) metastasize beyond the thorax.²⁾ In this report, we present a case of hemorrhagic brain metastasis from invasive thymoma presenting with sudden onset of hemiparesis.

Case Report

A 55-year-old man had an 8-year history of invasive thymoma. He had undergone resection of a mediastinal tumor via thoracoscopy and irradiation of 40 Gy total to the mediastinal region 8 years before. Thereafter, pleural disseminations and multiple bone metastases, including to the spine, rib, and pelvis, had developed 4 years and 6 months before, respectively. The patient had received multiple debulking surgeries with chemo-radiotherapy. The pathological diagnosis was type B3 invasive thymoma (non-cancerous).

Six months after bone metastases was detected, he presented with sudden onset of left hemiparesis. His Glasgow Coma Scale score was 15 and neurological

examination revealed severe left hemiparesis. Computed tomography (CT) showed right frontal lobe intracerebral hemorrhage (Fig. 1). Contrast-enhanced magnetic resonance (MR) imaging showed an unremarkable enhanced intraaxial mass with slight perifocal edema appearing to be acute hematoma, but the possibility of hemorrhagic metastasis could not be rejected (Fig. 2). Digital subtraction angiography showed no tumor stain. The patient underwent removal of the hematoma. Small corticotomy was performed at the premotor area and hematoma located in the motor cortex was observed. Histological examination showed brain metastasis from invasive thymoma. Pathological findings revealed a small quantity of epithelioid cells inside the hematoma (Fig. 3A). There were no tumor cells in the perifocal damaged brain. Immunohistochemical studies showed that these cells were positive for keratin (Fig. 3B) and negative for CD5 and CD117 (not shown), which were useful for differential diagnosis of thymoma or thymic carcinoma. These features were compatible with metastases from type B3 thymoma.

The patient's postoperative course was uneventful. Postoperative MR imaging showed no residual tumor and no other metastases. His hemiparesis improved and he was able to walk aided by a walker. His systemic metastases progressed slowly and became resistant to therapy. He underwent palliative care and was transferred to a rehabilitation hospital.

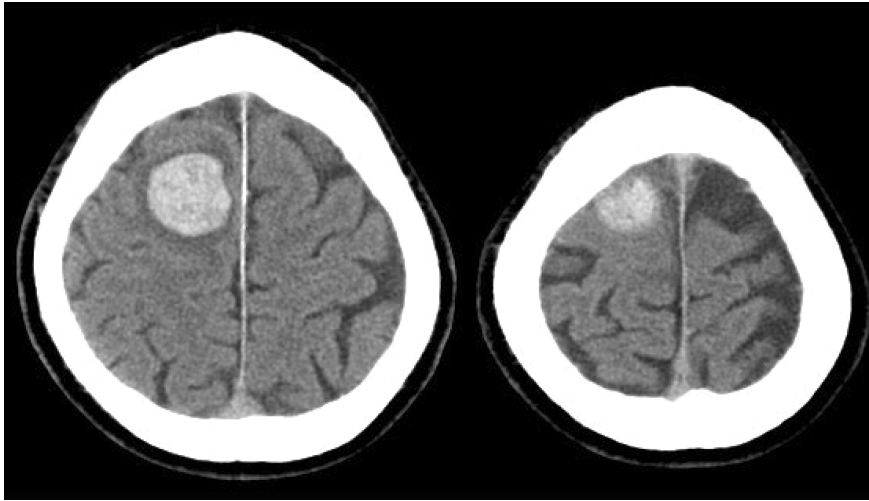


Fig. 1 Computed tomography at the first consultation showing right frontal lobe intracerebral hemorrhage.

Discussion

Thymic epithelial tumors (TETs) are derived from the epithelial parts of the thymus. They are the most common primary anterior mediastinal neoplasms. The highest prevalence is between 50 and 60 years of age, and both sexes are affected equally.³⁾ They are detected incidentally on a chest X-ray in about half of all cases.⁴⁾ Otherwise, thymomas is presented with coughing, dyspnea, chest pain, signs of upper airway congestion, and neoplasm syndromes such as myasthenia gravis.⁴⁾

In 1999, a WHO committee led by Dr. Rosai proposed a histologic classification system for TETs that stratified thymomas into five distinct entities (type A, AB, B1, B2, and B3) and differentiated them from thymic carcinomas (type C), based on the absence or presence, respectively, of overt cytological features of malignancy.^{1,5)} Thymic carcinomas account for 18–22% of primary TETs.^{6,7)} In addition, thymomas are classified as either non-invasive (previously called “benign”) or invasive (previously called “malignant”). Noninvasive thymomas are those in which the tumor is encapsulated. Invasive thymomas have spread to nearby structures over the capsule. The WHO classification has been shown to be an important prognostic indicator among patients with TETs, with 5- and 10-year survival rates of 100% and 95–100%; 93–100% and 90–100%; 89–93% and 81–85%; 82–83% and 70–71%; and 43–71% and 33–40%, for type A, AB, B1, B2, and B3, respectively. The 5-year survival rate for type C is 23–34%.^{7–11)}

In general, TETs are known to recur locally and to disseminate as an intrathorax lesion with a few reported cases of metastasis to the liver and bone.^{12,13)} Brain metastases from TETs are extremely rare and no definite treatment has been established. It has been reported that the mean survival period of TETs with a single brain metastasis is about 256 days, whereas for multiple brain

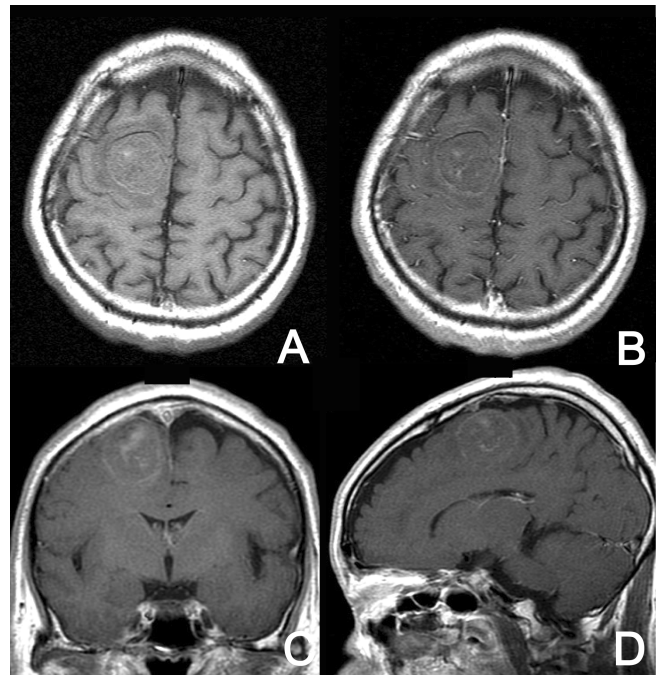


Fig. 2 A: Axial T₁-weighted magnetic resonance (MR) imaging showing an acute hematoma in the right frontal lobe. B–D: Gadolinium-enhanced T₁-weighted MR imaging showing no markedly enhanced lesion.

metastases it is only 64.4 days.¹⁴⁾ Treatment necessitates a multimodality approach, including surgical resection, postoperative radiotherapy, and/or chemotherapy.

To our knowledge, there are around 40 cases of brain metastases from TETs (including carcinomas) in the literature.^{15,16)} These lesions were reported to have typical findings of metastasis such as a hypervascular nature, intra-axial location, cystic change, and necrosis.^{2,15,16)} Among them, 2 cases presented with tumor hemorrhage radiographically. One showed a tumor with hemorrhagic

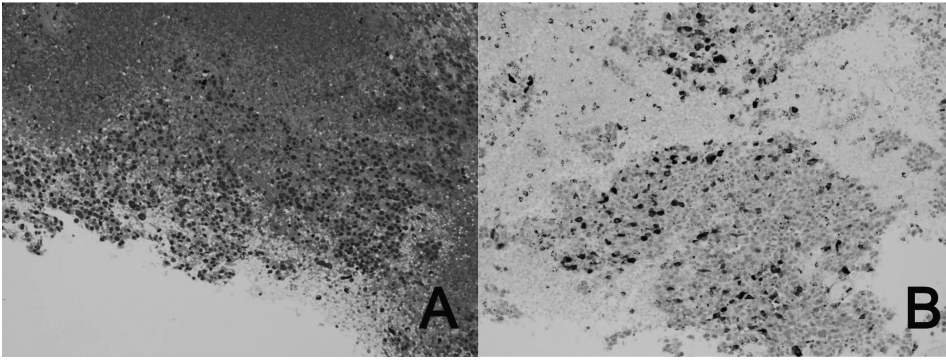


Fig. 3 Photomicrographs of the resected specimen of the hematoma showing epithelioid cells surrounded red blood cells (A: hematoxylin and eosin stain $\times 200$). Epithelioid cells positive for AE1/AE3 (B: cytokeratin AE1/AE3 antibody stain $\times 200$) and negative for CD5 and CD117 (not shown).

Table 1 Summary of brain metastases from thymoma (non-cancerous)

Case No.	Author (year)	Age (yrs)/ Sex	WHO class	Disease duration*	Symptom	Location	CT/MRI finding	Treatment	Prognosis
1	Kanayama et al. (2005) ¹⁷⁾	80/M	B2	5 y	Visual impairment	Pituitary	CE (+; massive), Cyst (-)	S	6 m
2	Kong et al. (2005) ²⁾	33/F	B3	12 y 8 m	Headache, hemiparesis	Rt. frontal	CE (+; ring), Cyst (+)	S + R	8 m
3	Gamboa et al. (2008) ³⁾	77/F	A	1 y 2 m	Seizure	Multiple	CE (+; massive), Cyst (-)	S + R	17 m
4	Ohata et al. (2011) ¹⁸⁾	48/F	AB	2 y 5 m	Headache, vomiting	Rt. temporal	CE (+; massive), Cyst (+)	S	NA
5	Present case	55/M	B3	8 y 8 m	Hemiparesis	Rt. frontal	Hemorrhagic, CE (-), Cyst (-)	S	Alive

*Disease duration; duration from first diagnosis of thymoma to diagnosis of brain metastasis. CE: contrast enhancement, CT: computed tomography, F: female, M: male, m: month, MRI: magnetic resonance imaging, NA: not available, R: radiation, Rt: right, S: surgery, y: year.

necrosis,¹⁹⁾ and the other showed a tumor with peripheral hemorrhage.²⁰⁾

By contrast, a review of the English literature, published since the present WHO classification system was established, revealed only four cases of thymoma (excluding carcinomas) with brain metastasis (Table 1).^{2,5,17,18)}

The histological types were type A, AB, B2, and B3, respectively. The current patient is considered to be the fifth case. In our review of brain metastases from invasive thymoma, it is possible that the tumors present with contrast effects and cystic changes (Table 1).

Furthermore, to the best of our knowledge, this is the first reported case of brain metastasis from invasive thymoma presenting with tumor hemorrhage causing the sudden onset of hemiparesis. Computed tomography and magnetic resonance imaging showed acute lobe intracerebral hemorrhage. Finally, brain metastases and tumor hemorrhage could not be rejected. Hematoma removal was performed, and brain metastasis from invasive thymoma was detected by histopathological examination.

In conclusion, brain metastases from TETs are extremely rare and may cause tumor hemorrhage with sudden onset symptoms, just like intracerebral hemorrhage. If patients with TETs present intracerebral hemorrhage, biopsy or

surgical resection is required for accurate pathological diagnosis and intensive multimodal therapies should be considered immediately under correct diagnosis.

Conflicts of Interest Disclosure

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