Radiology Case Reports 19 (2024) 4531–4534

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Brain metastases from a thymoma: Case report for a rare secondary localization ☆

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ARTICLE INFO

Article history:
Received 4 June 2024
Revised 4 July 2024
Accepted 5 July 2024

Keywords:
Metastases
Thymoma
Pneumology
Neurosurgery

ABSTRACT

Thymomas are benign epithelial neoplasms originating from the thymus gland and are among the most common primary mediastinal tumors. Malignancy is typically determined by evidence of pathological invasion beyond the capsule, with local invasion being the primary mode of spread to adjacent organs. Distant metastases are exceedingly rare. We present the case of a 63-year-old man who exhibited symptoms suggestive of increased intracranial pressure and motor deficit. Brain imaging revealed multiple intracranial lesions. Surgical intervention was performed to excise the largest lesion. Subsequent body CT scan and pathological examination confirmed that the brain metastases originated from a primary thymoma, classified as B3. The patient was recommended for adjuvant chemotherapy and radiotherapy, but unfortunately passed away at the initiation of therapy. The prognosis for patients with brain metastases from thymomas remains poor. Optimal management strategies typically involve prompt surgical intervention whenever feasible, followed by adjuvant therapy aimed at improving mean survival rates.

Introduction

Thymic epithelial tumors are among the most commonly encountered tumors of the anterior mediastinum in adults, though they remain rare with an annual incidence rate ranging from 1.3 to 3.2 cases per million [1]. Thymomas are cytologically benign but are considered to be malignant when there is evidence of pathologic invasion beyond the capsule [2]. Among thymomas, 7% to 36% are malignant. These typically

☆ Competing Interests: The authors do not have any conflicts of interest to declare concerning this article.

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https://doi.org/10.1016/j.radcr.2024.07.025

spread by local invasion to adjacent structures and metastasize to distant organs in less than 3% of cases [3]. Common sites of extrathoracic metastases include liver, bone, and lymph nodes [4], with renal and splanchnic metastases being quite rare but reported [1,4]. To date, only 68 cases of brain metastases from a thymoma have been documented [1]. Here, we report a new case of multiple brain metastases originating from a malignant thymoma.

Case report

We report the case of a 63 years old man with no notable medical history. He presented with progressively worsening headaches over the past 2 months. Fifteen days prior to admission, he developed numbness in the right upper and lower limbs, as well as a slurred speech. On physical examination, he was fully conscious patient but exhibited right hemiparesis and Broca's aphasia. Additionally, a painless mass was found on the anterior cervical region.

Brain MRI (Fig. 1) revealed 2 intracerebral lesions: the larger one in the left frontal lobe, and the smaller in the left occipital lobe. Both lesions were surrounded by significant perilesional edema. The decision was made to operate the patient to resect the frontal lesion, as it was considered to be causing the symptoms. Initially, the patient refused surgery and was lost to follow-up for 6 months. He was later readmitted to our department with status epilepticus and underwent emergency surgery. Peroperative, a total monobloc resection of a greyish, hemorrhagic, and friable lesion was performed. Postoperative follow up was uneventful, and the patient recovered full consciousness and experienced no further seizures or additional deficits. Control CT scan (Fig. 2). showed no complications but revealed a new occipital lesion compared to the preoperative imaging. Pathological examination (Fig. 3) confirmed the presence of a metastasis from an invasive thymoma. The patient was referred to oncology department. A body CT scan (Fig. 4) revealed an anterior mediastinal mass, associated to an osteolysis of the sternal manubrium, and a nodular hepatic lesion. A biopsy of the mediastinal mass confirmed the diagnosis of an invasive thymoma classified as B3. The patient began chemotherapy based on Etoposide and Carboplatine, but he suffered a myocardal infarction several days after his second chemotherapy cycle, which led to his death.

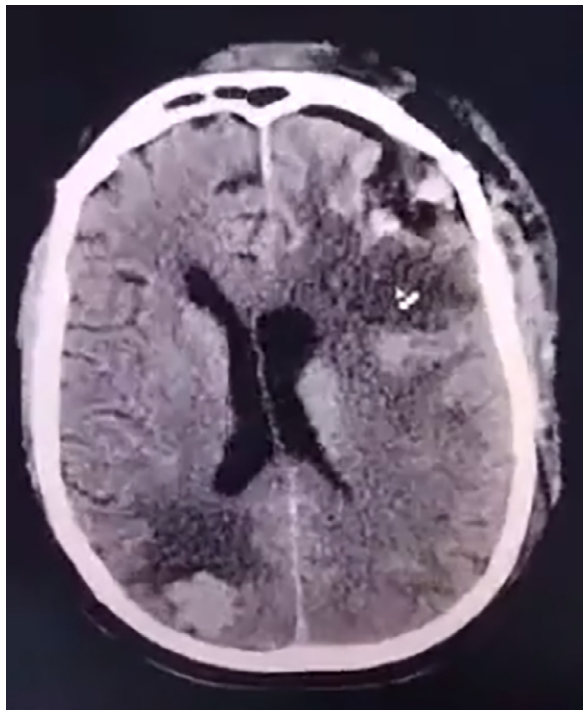

Fig. 2 – Axial section of a postoperative brain CT scan showing a total resection of the left frontal tumor, with the appearance of a "new" right occipital lesion.

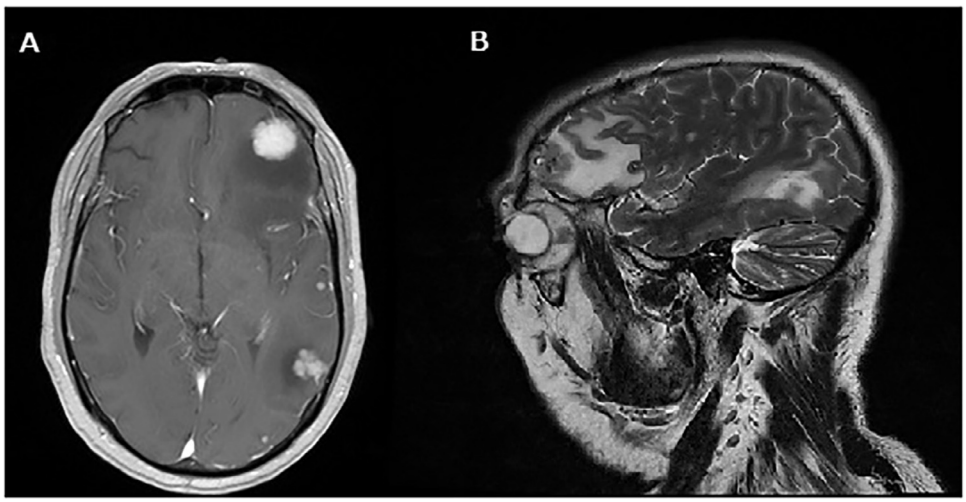

Fig. 1 – Axial (A) and sagittal (B) sections of a brain MRI on T1-WI with contrast injection (A) and T2-WI (B) showing 2 intracerebral lesions located on the left frontal and the left occipital lobes.

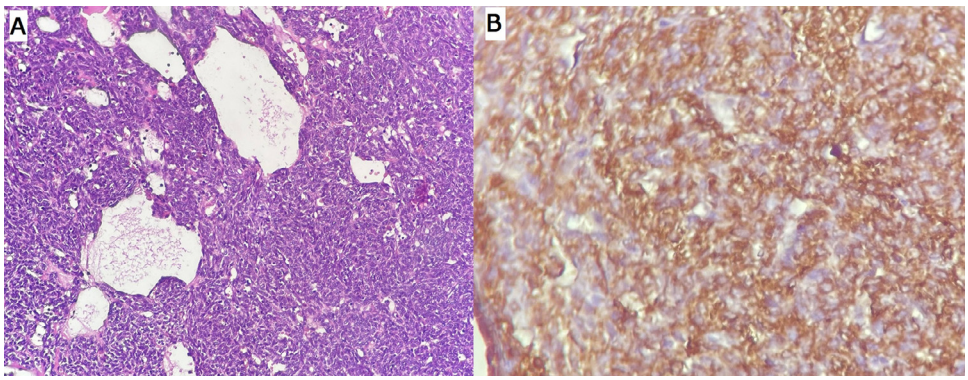

Fig. 3 – (A) Pathologic examination (He x 200) showing a highly dense cellular proliferation with lobular architecture containing globular cells with an oval nucleus and eosinophilic cytoplasm. Presence of scattered lymphocytes. (B) Coloration with cytokeratine showed a diffuse an intensive positivity.

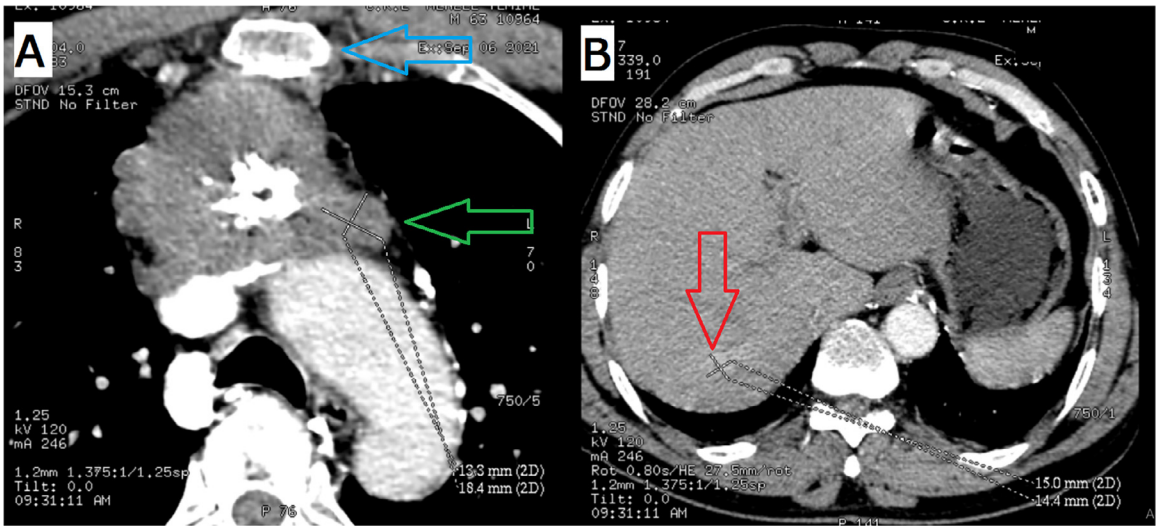

Fig. 4 – (A) Axial section of a thoracic CT scan showing an anterior mediastinal mass (Red arrow), associated to an osteolysis of the sternal manubrium (blue arrow). (B) Axial section of an abdominal CT scan showing a nodular hepatic lesion (Green arrow).

Discussion

Thymomas are rare tumors with an annual incidence of 1–5/million people [4]. They originate from the epithelial cells of the thymus and are the most common primary neoplasm of the anterior mediastinum [5]. The highest prevalence occurs between the fifth and the sixth decade of life, affecting both sexes equally [6]. The main symptoms related to thymomas include dyspnea, coughing, chest pain, signs of upper airway congestion, and paraneoplastic syndromes such as myasthenia gravis [7]. Thymomas are often incidentally detected on chest X-rays [6]. The World Health Organization classifies thymomas into 5 types (A, AB, B1, B2, and B3) and distinguishes them from thymic carcinomas (type C) based on the presence or absence of overt cytological features of malignancy [8,9]. Thymomas are further classified into invasive (previously called malignant) and noninvasive (previously called benign) [10]. Differentiating between high grade thymomas and thymic carcinomas can be challenging, as they may share similar histologic features: immature T cells around the tumor cells, squamous metaplasia, infiltration, atypia, and active mitosis. Immunohistochemistry: is often helpful, with markers like GLUT-1, MUC-1, CK5/6, CD117, P63, CD5, and CEA being positive for carcinomas, while CK19, TdT, and CD1a are highly suggestive for type B3 thymomas [11].

Noninvasive thymomas are encapsulated tumors [5,12]. Invasive thymomas spread beyond the capsule to infiltrate surrounding structures. Metastasis from malignant thymomas and thymic carcinomas primarily occurs in the lungs, bones, liver, and kidneys [2,4]. Intracranial metastases are much rarer. According to a comprehensive review by Belda-Sanchis [1] in

2021, only 68 cases of intracranial metastases from a thymic origin have been reported.

Brain metastases from invasive thymomas most commonly present metachronously [13]. few patients have cerebral lesions diagnosed before the primary tumor site is identified [14,15]. This was the case with our patient, who was initially diagnosed with a brain mass, and the mediastinal mass was only found during postoperative staging. Most patients are diagnosed with brain metastases after metastases have developed at extrathoracic sites, primarily the bones, lungs, and liver [12,16]. Radiological findings typically show features related to a hypervascular nature, intra-axial location, necrosis and hemorrhage. They may also contain calcified or cystic components [16].

Patients with invasive thymoma have a 5-year survival rate ranging between 15% and 23% after surgery, compared to an excellent survival for noninvasive thymomas [15]. Survival drops to an average of 12 to 18 months after the appearance of extrathoracic metastasis [2]. Among these, metastases involving the central nervous system are associated with the worst prognosis: the average survival time is reduced to 256 days for single brain metastasis and only 64,4 days for multiple brain metastases [2,17].

Aggressive management is necessary to improve long-term outcomes, which remain poor in these patients [7,8]. Thymic aggressive thymomas and thymic carcinomas are reported to be responsive to cisplatin-based chemotherapy [2,15]. However, the impact of these treatments on patients with multiple cerebral metastases has not significantly improved overall survival. Recent reports [1,12] suggest a multimodal approach combining surgical resection of the brain metastasis for diagnosis and to reduce intracranial pressure, followed by radiotherapy and chemotherapy as soon as the diagnosis is made. The role of radiotherapy remains uncertain for both the primary tumor and metastasis [18]. In case of multiple brain metastases, the decision for surgical intervention is made on a case-by-case basis.

Conclusions

Although thymomas are mainly benign, some subtypes can metastasize and spread to the brain. Cerebral involvement of aggressive thymomas is associated with a poor prognosis. Close monitoring and research into novel treatment strategies are essential to improve survival in these patients.

Patient consent

A written consent has been obtained from the patient's deceased patient's legally represented relatives (his daughter) regarding this manuscript.

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