

Pulmonary Metastasis 12 Years After Resection of Thymoma with Microscopic Capsule Invasion

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We report on a 50-year-old female who developed pulmonary metastasis 12 years following the resection of a thymoma with microscopic capsular invasion. The patient was found to have a mediastinal mass at the age of 18 years; however, she refused to undergo surgery. At the age of 38 years, the patient underwent surgery for resection of the tumor; it was diagnosed as a macroscopically encapsulated thymoma with microscopic capsular invasion. Multiple pulmonary metastases occurred 12 years following the resection of the tumor; all the metastatic masses were resected. Although the patient suffered from myasthenia gravis 4 months following the resection of pulmonary metastases, she remains free of myasthenia gravis with no recurrence of tumor at 2 years post-surgery. Long-term follow-up is essential for the detection of recurrence after resection of a thymoma with microscopic capsular invasion, and surgery could be the best treatment for distant metastasis in case of resectable lesions.

Key words: thymoma – pulmonary metastasis – prognosis – post-thymectomy myasthenia gravis

INTRODUCTION

Thymoma is usually a slow-growing tumor; however, it displays unpredictable behavior on rare occasions (1,2). Although intrathoracic recurrence occurs sometimes in patients with invasive thymoma, few cases of distant metastasis following resection of a non-invasive thymoma have been reported. We report a patient who developed pulmonary metastasis 12 years following the resection of a macroscopically encapsulated thymoma with microscopic capsular invasion.

CASE REPORT

The patient was a 50-year-old female. At the age of 18 years, a mediastinal mass, approximately 3 cm in diameter, was noticed on a routine chest X-ray (Fig. 1). The mass gradually increased in size; however, the patient refused to undergo surgery. At the age of 38 years, the patient was admitted to our hospital for resection of the mediastinal tumor, which had increased to 10 × 6.5 cm in size (Figs 2 and 3). The serum level of anti-acetylcholine receptor (AChR) antibody (Ab) was found to be elevated to 5 nmol/l (normal range, <0.2 nmol/l); however, the patient did not experience any symptoms of myasthenia gravis (MG).

A thymoma was diagnosed following percutaneous needle aspiration biopsy. Therefore, a thymo-thymectomy was performed via a median sternotomy. During surgery, the tumor was found to be significantly compressing the adjacent organs; however, no invasion was observed. Although the tumor was macroscopically encapsulated (Fig. 4), microscopic examination revealed capsular invasion that was confined within the thymic tissue (Fig. 5). On histology, the thymoma was found to be of a mixed lymphocytic and epithelial type. The epithelial cells were mixed with polygonal and spindle cells. Following the resection of the primary tumor, the patient was followed-up by CT scanning annually, without adjuvant chemotherapy or radiation therapy. Twelve years following the resection (patient age, 50 years), a chest CT scan showed bilateral pulmonary nodules. One nodule (10 mm in diameter) was observed in the right lung, and two nodules (3 and 10 mm in diameter, respectively) were observed in the left lung (Fig. 6). These tumors were resected by bilateral thoracotomy. Microscopic examination of the resected tumors showed findings that were similar to those of the primary thymic tumor. Four months following the resection of the pulmonary metastases, the patient complained of diplopia and ptosis, and the serum level of anti-AChR Ab was found to be elevated to 14 nmol/l. The edrophonium chloride (antirex) test was found to be positive. Therefore, postoperative MG was diagnosed, and the patient was treated with an anti-cholinergic drug (pyridostigmine bromide) for 12 months. She is doing well 24 months following the resection of

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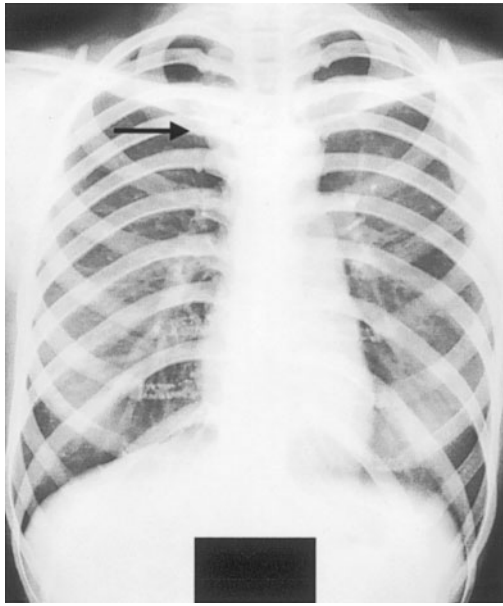


Figure 1. Chest X-ray at the age of 18 years shows the mass shadow in the right, upper mediastinum (indicated by an arrow).

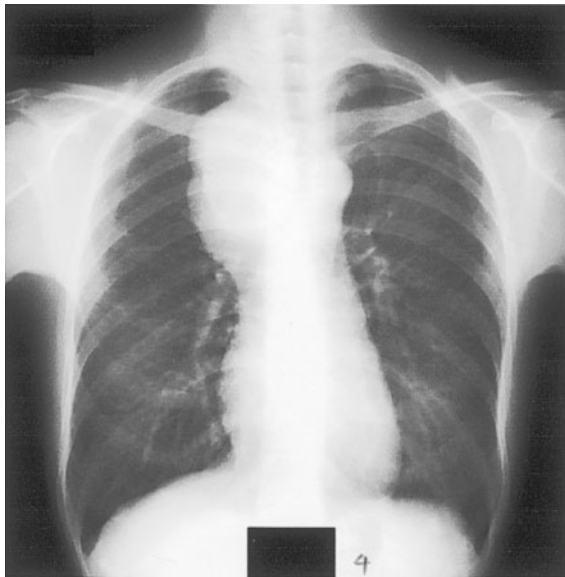


Figure 2. Chest X-ray at the age of 38 years shows that the mass has increased in size to 10 cm × 6.5 cm.

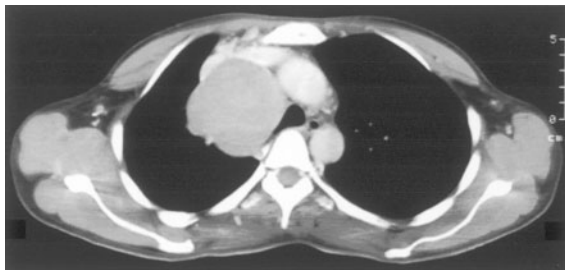


Figure 3. Chest CT scan shows the tumor in the middle compartment of the mediastinum compressing the lung, superior vena cava and trachea.

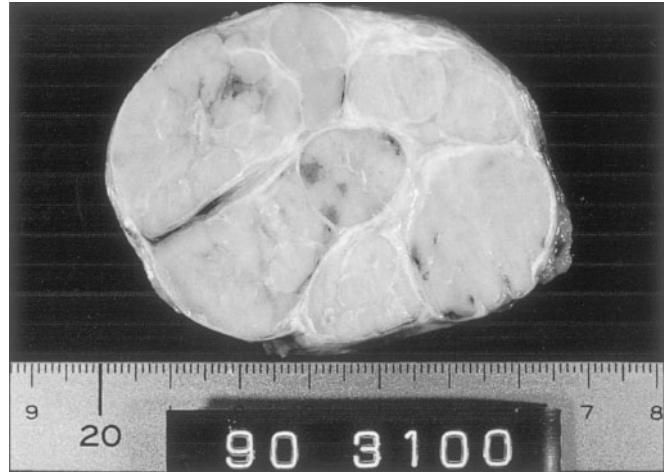


Figure 4. Macroscopic finding of the primary tumor. The cut surface shows a completely encapsulated mass.

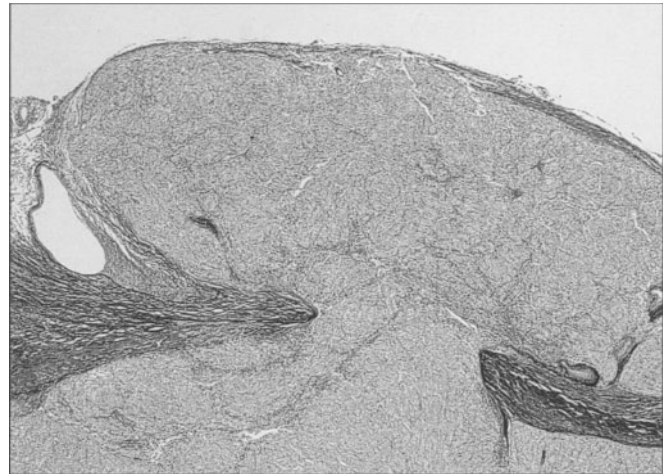


Figure 5. Microscopic picture shows that the tumor invades the capsule but remains confined within the thymic tissue.

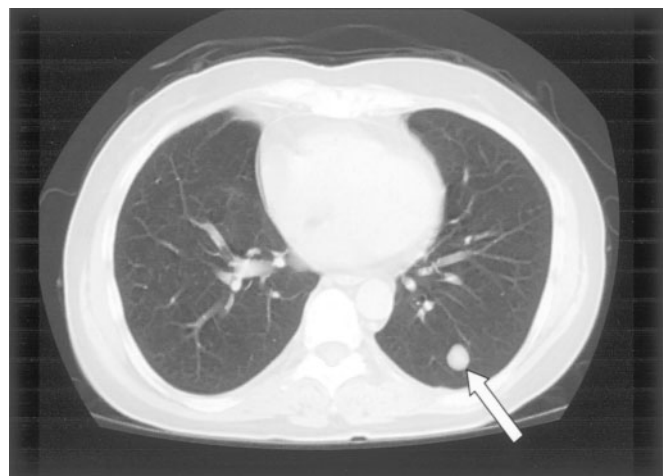


Figure 6. Chest CT scan showing one of the metastatic lesions in the left lung (indicated by an arrow).

Table 1. The patients with distant metastasis from encapsulated thymoma: a review of literatures

Patient No.	Reference No.	Age yrs.	Sex	Metastasis		Treatment	Follow-up	
				Time yrs.	Site		Time yrs.	Outcome
1	5	49	F	8	Sternum	Total excision	21	Alive without disease
				19	Thyroid	Total excision		
2	5	49	F	2	Liver	Total excision	3	Dead from disease
3	5	20	F	8	Pleura, lung	Total excision	11	Alive with disease
				10	Pleura, lung	Total excision		
4	6	51	F	14	Lung	Total excision	18	Alive without disease
5	7	43	M	4	Pectoralis muscle	Total excision	Not described	
6	8	49	F	–	Lung, spleen, cerebellum, liver, kidney, ovary	Autopsy case	–	–

the pulmonary metastasis with no evidence of recurrence of thymoma or MG symptoms; however, the serum level of anti-AchR Ab remains elevated (12 nmol/l).

DISCUSSION

The postoperative recurrence rate for invasive and non-invasive thymoma has been reported to be 11–36% and 0–7%, respectively (3,4). The majority of recurrences are local, and distant metastasis is rare, particularly following the resection of non-invasive or microscopically invasive thymoma. To our knowledge, only six cases of distant metastasis following the resection of a non-invasive thymoma have been reported (Table 1) (5–8). The clinical characteristics of the six patients were as follows: (i) ages between 20 and 51 years (mean 44 ± 12 years); (ii) five females and one male; (iii) the interval between primary tumor resection and recurrence ranged from 4 to 14 years (mean 7 ± 5 years); (iv) one patient suffered from MG; and (v) the sites of metastasis were the lungs in three patients, liver in two patients and pleura, pectoralis muscle, brain, bone, thyroid and spleen in one patient each. Five of the six patients underwent a total excision of the metastases; three patients survived for 1–4 years following the excision. Microscopic capsular invasion was detected in the thymoma of the present patient; however, it was confined within the tissue of the thymus gland (Masaoka's stage II) (3). Furthermore, it showed slow progression, i.e. the interval between initial detection and primary tumor resection was 20 years and that between the primary tumor resection and treatment of the lung metastases was 12 years (a total of 32 years). Although the present tumor displayed very slow growth, it had invaded the capsule and was potentially malignant; this resulted in distant metastasis. Therefore, a long-term follow-up is essential in order to detect recurrence even after the resection of a macroscopically non-invasive but microscopically invasive thymoma.

The treatment of recurrent thymoma remains controversial due to the unpredictable natural history of this tumor. Ruffini

et al. reported the outcome in 30 patients with recurrent thymoma and drew the following conclusions: (i) total resection of a locally recurrent thymoma resulted in a better prognosis than that observed with radiation therapy; and (ii) the 5-year survival rate was 100% following resection of local recurrence; this was significantly better as compared to the 30% 5-year survival rate following resection of distant metastasis (9). Although these data did not suggest that the resection of distant metastasis from a thymoma resulted in prognostic benefit, Table 1 shows the possibility of long-term survival following the resection of distant metastases from an encapsulated thymoma. We believe that surgical treatment may result in a good prognosis for patients with distant metastases from an encapsulated or microinvasive thymoma due to its slow-growing characteristic.

The present patient suffered from MG, 4 months following the resection of pulmonary metastases. The occurrence of post-thymectomy MG has been reported in 4.6% of patients without symptoms of MG prior to surgery (10,11). Early as well as late onset of post-thymectomy MG has been reported; the former could be caused by subclinical MG that existed prior to surgery, and some cases of the latter could be caused by the recurrence of tumors (10). To our knowledge, the present patient is the first case who suffered from MG following the resection of metastatic thymoma. The patient had elevated serum level of anti-AchR Ab prior to the resection of primary tumor and did not have any clearly demonstrable remnant thymus or recurrent thymoma at the time of the occurrence of MG. Therefore, it is considered that a surgical stress caused by the excision of the lung metastases could have manifested the subclinical MG.

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