Recurrence and Malignant Transformation of Thymoma After 26 Years – A Rare Presentation

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Abstract

Thymoma is a mediastinal tumour with malignant potential, which has a recurrence rate after complete resection ranging from 5 to 50%. It is an epithelial neoplasm of the thymus, which commonly lies in the anterior mediastinum. Here we present an interesting case of a 58 year old female patient on treatment for Myasthenia Gravis for the past 26 years. She had undergone thymectomy with dissection of pericardium and adjacent pleura 26 years back. Now she had presented with worsening myasthenia symptoms, underwent treatment comprising of steroid pulse therapy and plasmapheresis along with regular medications. She was evaluated for left lung collapse, which revealed a thymoma involving left lung and a solitary deposit on the right side probably metastasis. Though the recurrence rate of thymoma is high, this case is unique as it recurred as malignant thymoma after 26 years.

Keywords: Thymoma, thymic carcinoma, myasthenis gravis, recurrence

Introduction

The thymus is a lymphoepithelial organ that is derived embryologically from the third and fourth pharyngeal pouches, which descend to the anterior mediastinum in the sixth week of human gestation. [1] Thymoma is the most common neoplasm of the anterior mediastinum, accounting for 20-25% of all mediastinal tumors and 50% of anterior mediastinal masses. Thymoma accounts for <1% of all adult malignancies. Thymic carcinoma is a rare carcinoma of the thymus representing less than 1% of thymic malignancies. Arising from the thymic epithelium, it exhibits an overt propensity for capsular invasion and metastasis. Patients with mediastinal thymomas are often clinically asymptomatic (50%-60%) or present with local symptoms (30%-40%) or with associated systemic parathymic disease syndromes (30%-40%). Myasthenia gravis (MG) is the most common systemic parathymic syndromes. About 30-40% of patients who have a thymoma experience symptoms suggestive of MG and 20% of patients suffering from MG is associated with thymoma. The prognosis is worse for patients with symptomatic thymomas because these patients are more likely to have malignant thymomas. The single most important factor predicting the outcome of patients with thymomas is evidence of invasion. All thymomas have to be resected due to their malignant potential. Malignant thymomas are often fatal with metastasis to regional lymph nodes, bone, liver and

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lung. [2] Patients presenting with advanced disease have a 5-year survival rate of 30-50%.

Case Report

A 58 year old female, a known case of myasthenia gravis since 26 years and diabetes mellitus since 10 years on regular medications with pyridostigmine and metformin, reported with complaints of gradually worsening breathlessness since three months and intermittent episodes of fever since 10 days. Her past history suggested that she had ocular myasthenia with thymic shadow on x-ray 26 years back. CT thorax showed an anterior mediastinal mass suggestive of thymic mass. Median sternotomy was done followed by dissection of thymus with removal of pericardium and its adjacent pleura as the tumour extended to the pericardium and mediastinal pleura. There was adherence to pericardium. Histopathology report of the dissected specimen was benign thymoma with residual persistent thymus and features of thymic hyperplasia. There was no evidence of malignancy.

On examination at presentation in the outpatient, she had tachycardia, tachypnea and an oxygen saturation of 88% on room air. There were features of oculo-pharyngeal myasthenia and respiratory system showed features of left lung collapse. Chest x-ray showed complete left lung collapse with ipsilateral tracheomediastinal shift (Figure 1). Arterial blood gas analysis showed hypoxemia with respiratory alkalosis. Contrast enhanced CT thorax revealed a left lung mass with intraluminal extension into left main bronchus and complete collapse of left lung (Figure 2). It also showed a well-defined lobular mass on right lower lobe (Figure 3). Fibreoptic bronchoscopy was performed which showed a lobulated mass with smooth margins obstructing left main bronchus (Figure 4). Bronchoscopic biopsy from mass showed undifferentiated carcinoma and immune-histochemical analysis (IHC) analysis revealed B3 Thymoma. Histopathology showed lobulated architecture with cellular lobules, intersecting fibrous bands, epithelial cells and lymphocytes (Figure 5). Focal cystic changes were also seen.

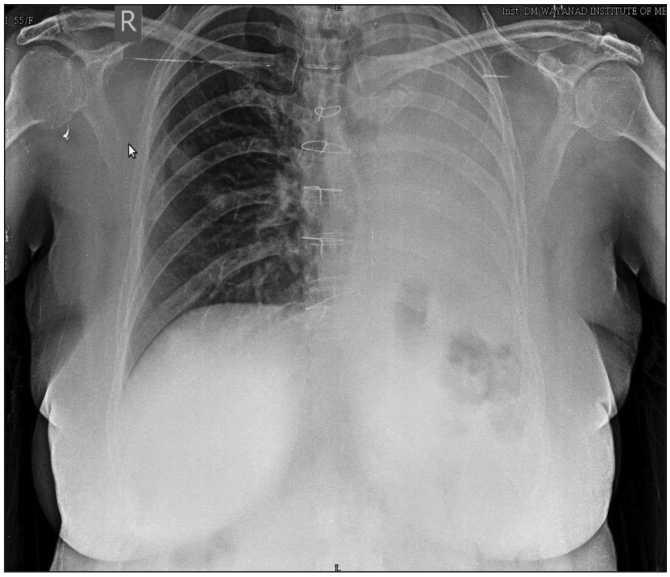

Figure 1: X-ray chest PA (incomplete film) showing left lung collapse. There is a small ill-defined opacity in the right midzone. Sternal wires due to previous thoracotomy are visible.

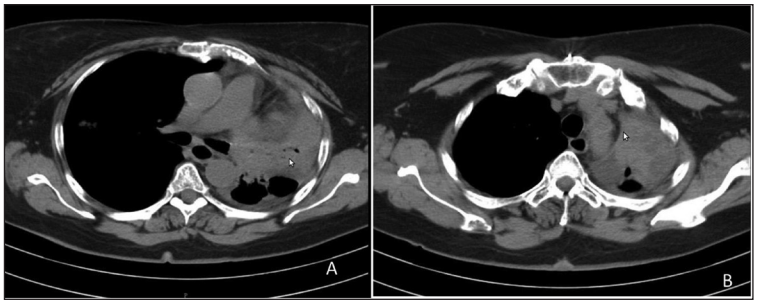

Figure 2A: shows a mass with necrosis and intraluminal extension to left main bronchus; 2B: shows complete collapse of left lung with ipsilateral mediastinal shift.

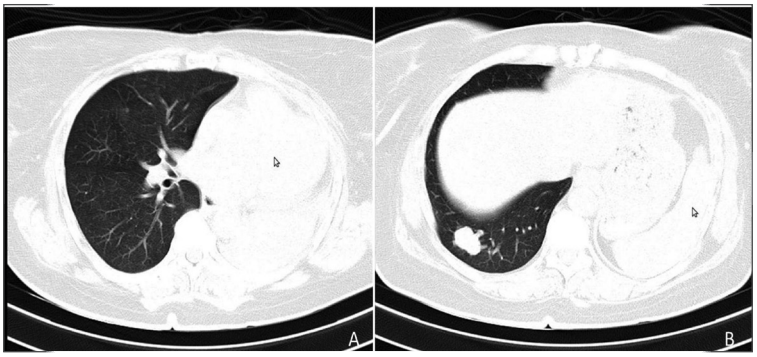

Figure 3A: shows collapse of left lung; 3B shows an irregular lobulated nodular density in the right lower lobe.

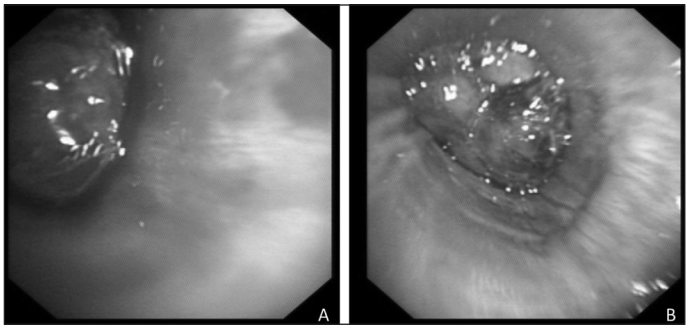

Figure 4A & B: showing highly vascular intraluminal lesion occluding the left main bronchus

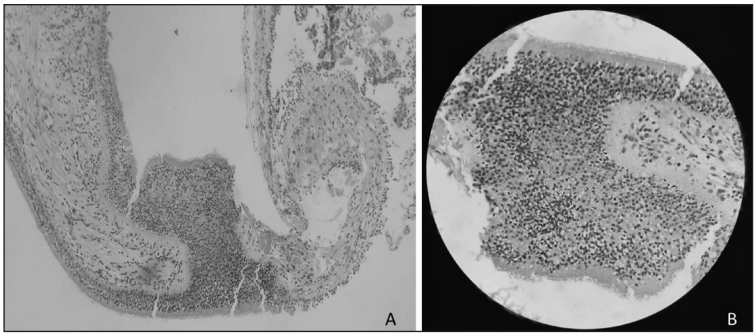

Figure 5: Low magnification (A) showing lobulated architecture with cellular lobules and intersecting fibrous bands, High magnification (B) showing neoplastic epithelial cells, various lymphocytes associated with focal cystic changes

Discussion

This case report refers to a rare presentation of benign thymoma associated myasthenia gravis recurring after 26 years with malignant transformation. The thymus is a lympho-epithelial organ that is derived embryologically from the third and fourth pharyngeal pouches, which descend to the anterior mediastinum in the sixth week of human gestation.[1] Thymomas are an uncommon heterogeneous group of anterior mediastinal tumors that are generally considered benign. But it is a potentially malignant tumour. Usually complete resection is advised to prevent malignant transformation. When presenting with myasthenia gravis, thymus is resected even if there is no thymic enlargement. Thymic carcinoma on the other hand is a rare carcinoma of the thymus representing less than 1% of thymic malignancies. Arising from the thymic epithelium, it exhibits an overt propensity for capsular invasion and metastasis. The presence of cytological features of overt malignancy differentiates it from thymoma.[3]

Thymomas occur in all ages, but there is a broad peak between 40 to 60 years of age. The gender distribution of thymoma is approximately equal, although it is slightly more common in women in older age groups.[4]

Patients with mediastinal thymomas are often clinically asymptomatic (50-60%) or present with local symptoms (30-40%) or associated systemic parathymic disease syndromes (30-40%). Vague chest pain, dyspnea, and cough are the common symptoms of thymomas. Myasthenia gravis is the most common systemic parathymic disease syndrome. Other paraneoplastic/autoimmune syndromes include neuromuscular syndromes such as Lambert-Eaton myasthenic syndrome and myotonic dystrophy, autoimmune diseases such as systemic lupus erythematosus, polymyositis, Sjögren syndrome and ulcerative colitis, endocrine disorders like Addison disease and hyperthyroidism, hematologic diseases such as hypogamaglobulinemia, red cell aplasia, pancytopenia and aplastic anemia. Malignant thymomas are often fatal with metastasis to regional lymph nodes, bone, liver and lung.[2]

According to the latest classification of histologic criteria for thymic epithelial tumors by the World Health Organization (WHO) Consensus Committee, published in 2004, thymic epithelial tumors are classified into two major categories: thymoma (types A, AB, B1, B2, and B3) and thymic carcinomas.[5] Reported lymphogenous and hematogenous metastases are uncommon.

Earlier literatures reported very few cases of retroperitoneal invasive thymomas.[6] Treatment of thymoma is thymectomy with or without resection of adjacent structures depending on extent of tumor, whenever possible. Neoadjuvant chemotherapy or radiation or postoperative chemotherapy or radiation depending on stage and involvement of margins may be required. Relapse after primary therapy for a thymoma may occur after 10-20 years. Therefore, long-term follow-up probably should continue to be performed throughout the patient's life.

The International Thymic Malignancy Interest Group (ITMIG) has recently defined a standard set of definitions for recurrence.[7] The term 'recurrence' is appropriate if all disease has been potentially eradicated (R0 resection); recurrences are classified as local (anterior mediastinum), regional (intrathoracic not contiguous with the thymus), and distant (intrapulmonary and extrathoracic).

The recurrence rate of thymoma ranges according to different reports. In the study by Japanese Association for Research on Thymus (JART), among all the 2835 thymoma patients operated during 1991–2010, 420 (14.8%) experienced recurrence.[8] The average disease-free time till recurrence was 5 years, and recurrence after 32 years of initial surgery was also reported.[9] The time to relapse was 10 years for patient of clinical stage I, and 3 years for patient of stage II, III and IV. Most recurrence are local and regional.[10,11] About 46–80% of recurrent cases are found in the thoracic cavity,[12,13] and then in the mediastinum and lungs,[14] distant metastases occur in less than 5% of the cases.[15] In the report of Detterbeck *et al*, among patients with recurrences, the pleural space or the lung was involved in 58%

(most often as a nodule under the parietal pleura), the pericardium or mediastinum in 41%, bone in 10%, and liver in 8%. According to the study of The Japanese Association for Chest Surgery,[16] of 862 patients whose information is available, 67 (7.8 %) developed recurrence. The recurrence rates in stages I, II, III, and IV were 0.9, 4.1, 28.4, and 34.3%, respectively. Recurrence rate in thymic carcinoma is reported as 51%.

Conclusion

Thymoma with local extension to pericardium or pleura is often considered malignant. Even if the histopathology report is benign thymoma, it should be treated with radical surgery followed by radiotherapy. In such patients recurrence rate is high. These patients require lifelong monitoring. The case reported here had a histopathologically proven benign thymoma which was resected 26 years back. Peroperative findings suggested extension to pericardium and mediatinal pleura. Now the patient presented with intratoracic mass with lung collapse and histopathology showing evidence of B3 thymoma. Even though late recurrence is reported in thymoma, recurrence after 26 years with malignant transformation is rare.

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