Unusual clinical behaviour of thymoma with recurrent myasthenia gravis

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Abstract

A 58-year old man with thymoma and myasthenia gravis (MG) had undergone thymectomy 8 years ago with histopathologically confirmed non-invasive WHO-type AB thymoma. After 5 years of complete remission, symptoms of MG resurfaced, and a recurrent anterior mediastinal mass was detected for which he received radiotherapy. He presented to us 3 years later with productive cough and exertional dyspnoea; the positron emission tomography–computed tomography scan revealed a metabolically active pulmonary nodule in the right lung as the only site of disease for which a right lower lobectomy was done. Microscopy established an intrapulmonary WHO-type B2 thymoma and the patient is currently asymptomatic on steroids, anticholinesterase and immunosuppressant therapy. We discuss the variable and unpredictable course of thymomas; the possibility of transformation into more aggressive types with each recurrence, association with recurrent MG post-thymectomy and presentation several years later with metastatic disease.

Keywords: Thymoma • Myasthenia gravis • Intrapulmonary thymoma • Pulmonary metastasis

INTRODUCTION

Thymomas are an uncommon group of anterior mediastinal tumours with highly variable behaviour. Whether benign or malignant, they have been shown to invade locally, recur and metastasize. We present a patient with an unpredictable series of events–diagnosed myasthenia gravis (MG) with resected WHO-type AB thymoma with recurrent MG and local recurrence 5 years after thymectomy and distant intrapulmonary recurrence 3 years later.

CASE REPORT

A 58-year old man presented with a 4-month history of productive cough and dyspnoea on exertion. There was no history of haemoptysis, chest pain, fever or weight loss.

Eight years ago, he had been diagnosed with a thymoma and MG for which a conventional thymectomy (not extended) was done. Histopathology confirmed a mixed epithelial and lymphocytic thymoma, WHO-type AB with intact capsule with no capsular invasion (Masoaka stage I). He was in complete remission for a year after surgery following which the anticholinesterase inhibitors were discontinued. He remained asymptomatic on immunosuppressants (Azathioprine) only for the next 3 years after which he developed myasthenia crisis with respiratory distress, requiring hospitalization and ventilatory support. Computed tomography (CT) scan showed an anterior mediastinal mass suggestive of recurrent thymoma. He was treated with radiotherapy in another institute, 44 Gy/22 fractions and boost of 12.9 Gy/6 fractions; reasons for not considering surgery were not documented. He was diagnosed with follicular bronchiolitis presumably exacerbated by immunosuppressant therapy. He received pyridostigmine, azathioprine and methyprednisolone with which he was asymptomatic.

He presented to us 3 years later with productive cough and exertional dyspnoea. The CT scan of the thorax revealed a 2 × 2.5 cm right lower lobe lung mass with extensive reticulonodular opacities involving both lower lobe lung fields (Fig. 1). PET/contrast enhanced computed tomography thorax showed a heterogeneously enhancing metabolically active mass 2 × 2.5 cm in the anterobasal segment of the right lower lobe (standardized uptake value_{max} 2.4) and no mediastinal mass. Pulmonary function tests were suggestive of severe chronic obstructive pulmonary disease. A well-circumscribed firm nodule measuring 3 × 2.5 cm was identified in the right lung lower lobe and a right lower lobectomy (frozen section of the nodule was reported as either neuroendocrine or salivary gland tumour) was done, following which the patient had an uneventful postoperative recovery. Histopathology revealed an intrapulmonary WHO-type B2 thymoma with an invasive edge, with the lung showing follicular bronchiolitis and organizing pneumonia (Fig. 2a). All margins of resection were free of tumour. The tumour expressed CK5/6, p63 and CK19 (Fig. 2b and c) and was negative for CD56, synaptophysin and chromogranin, CD20 and Mic2. All lymph nodes were free of tumour. We did not consider adjuvant treatment as complete resection was done and there is no strong evidence favouring the role of chemotherapy in this setting. He was symptom free on steroids, anticholinesterase and immunosuppressant therapy on last follow-up.
DISCUSSION

Thymomas are an uncommon heterogeneous group of anterior mediastinal tumours that are generally considered indolent. However, several series have reported the ability of these tumours to invade locally, recur, as well as metastasize even after resection, including early stage (Masoaka I) thymomas. WHO types A–C show a clear and graded deterioration of prognosis: medullary (A) and mixed (AB) tumours are considered relatively ‘benign’, are usually not locally aggressive and have little chance to recur [1]. A retrospective study of 207 patients with thymic malignancies by Evoli et al. [2] report no patients with type A or AB thymomas, irrespective of the stage experienced tumour relapses. Our case is one of the uncommon indolent-type AB thymomas to recur several years after complete remission. There has been a recent report, however, of a high recurrence rate even with capsulated, type A and AB thymomas [3].

Thymomas are associated with MG in 30–50% of the cases, but only 15% of patients with MG have thymomas [4]. The present case was initially diagnosed with MG which led to the diagnosis of a thymoma. Similarly, the recurrent symptoms 5 years later prompted the diagnosis of a recurrent thymoma. In a retrospective evaluation of 255 patients, Ruffini et al. [5] report that MG is strongly correlated with early-stage thymomas and WHO-type B thymomas. In their study, out of 105 patients with MG, 26% had type AB thymoma and 34% had type B2 thymomas.

Complete remission rates after thymectomy is highly variable ranging from 7 to 63% [4]. In patients without preoperative MG, 1–3% may develop MG postoperatively [6]. Thymectomy does not preclude the recurrence of MG and can manifest several years after surgery, suggesting an extra-thymic mechanism of production of acetylcholine receptor antibodies [7]. Ectopic sites of thymoma should be sought for in cases presenting with recurrent symptoms, other possibilities being an extra-mediastinal thymoma or distant metastasis. Recurrences after thymectomy may be treated with re-operation provided complete resection is achieved [8]. Though most patients with recurrence would recur even after surgery, they have reasonably good outcomes with 5- and 10-year survivals of 82 and 58%, respectively, compared with 38 and 26% in patients treated non-surgically [8]. Our patient received radiotherapy for the first recurrence at an outside institution for undocumented reasons.

The difference in WHO type of the initial thymoma and the intrapulmonary metastatic thymoma is notable in our patient although WHO histology is not an established prognostic marker with the exception of thymic carcinoma. The initial mediastinal thymoma was WHO-type AB whereas the intrapulmonary thymoma was of a higher, more malignant type B2 with an invasive border, suggesting the possibility of transformation into a more malignant type of stage with each recurrence. Venuta et al. [1] have described a similar observation of tumour progression in thymomas, whereby tumour recurrences have shown a transformation from a low-grade histological type to that of a higher
grade, as well as transition among well, moderately and poorly differentiated areas within the same neoplasm.

Conflict of interest: none declared.

REFERENCES