Three Cases of Multiple Thymoma with a Review of the Literature

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Three cases of patients with synchronous multiple thymoma are reported. Two patients had two thymomas each and the remaining patient had three. The thymomas in each patient all displayed similar histological findings, of which the WHO histological classification were type B2, A and B1, respectively. With a modified Masaoka staging system, the thymomas were determined to be stages II-1 and I in patient 1, one of stage III and two of stage I in patient 2, and two of stage II-1 in patient 3. We reviewed nine reported cases of multiple thymoma in which histological findings were provided and discuss whether they developed from multicentric origin or from intra-thymic metastasis.

Key words: thymoma – multiple developments – multi-centric development – recurrence

INTRODUCTION

Although it is well known that multiple thymoma can develop in a single patient, its actual incidence is very low. Also it remains controversial whether the cases represent disease of multi-centric origin or intra-thymic metastasis. To address this issue, we present three cases of patients with multiple thymoma and also review the reported cases of which histological findings have been provided (1–8).

MATERIALS AND METHODS

From 1981 to 2005, 96 patients with thymoma were treated by thymo-thymomectomy in the Department of Thoracic Surgery of Kumamoto University Hospital. Of these, three patients (3.1%) had multiple thymomas. The histological type of each thymoma was classified according to the World Health Organization (WHO) classification system (9). The tumor stage was classified by a modified Masaoka classification (10).

CASE REPORT

PATIENT 1

A 69-year-old male with ocular type myasthenia gravis (MG) was admitted to our hospital for surgical treatment of an anterior mediastinal tumor. The serum level of anti-acetylcholine receptor antibody (AchR Ab) was elevated to 8 nmol/l (normal level < 0.2 nmol/l). Computed tomography (CT) showed a well-defined mass bounded on the ascending aorta (Fig. 1). Thymo-thymomectomy was performed via median sternotomy. While pathological examination diagnosed the tumor as type B2 thymoma 23 × 12 mm in size, pathological examination revealed another type B2 thymoma 2 × 2 mm in size located within the same lobe (Fig. 2). The patient is now alive without recurrence of thymoma and with complete remission of MG 5 years after surgery.

PATIENT 2

A 74-year-old male without MG was admitted to our hospital for surgical treatment of an anterior mediastinal tumor. The serum AchR Ab level was within normal limits. CT revealed a small, ill-defined mass bounding on the ascending aorta (Fig. 3). The intra-operative findings revealed invasion of the tumor into the right middle lobe of the lung and also two additional tumors within the right thymic lobe. A thymo-thymomectomy was performed with wedge resection of the right middle lobe. Pathological diagnosis was type A thymoma in all three of the tumors, the respective sizes were 58 × 35, 24 × 7 and 10 × 8 mm. The patient was treated with post-operative radiotherapy (50 Gy). He is now alive without recurrence of thymoma 10 months after surgery.

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PATIENT 3

A 46-year-old male with ocular type MG was admitted to our hospital for surgical treatment of an anterior mediastinal tumor. The serum level of AchR Ab was elevated to 9.5 nmol/l. Computed tomography revealed a well-defined mass on the left upper side of the anterior mediastinum. Thymothymectomy was performed via median sternotomy. During the operation, another tumor was found within the right lower thymus. The sizes of the two tumors were 22 × 15 and 15 × 8 mm, respectively. Pathological diagnosis was type B1 thymoma in both tumors. While intra-operative findings did not show any invasion by the tumors, pathological examination revealed microscopic invasion into the surrounding thymic tissue in both, i.e. both

![Figure 1. Case 1. Computed tomogram (CT) showing well-defined mass (arrow) bound on the ascending aorta.](image1)

![Figure 2. Case 1. A small thymoma existing in the thymic tissue.](image2)
were stage II-1. The patient is now alive without recurrence of thymoma and with complete remission of MG, 6 years after surgery.

DISCUSSION

Multiple thymoma is a well-known phenomenon, but its occurrence is very rare. Bernatz et al. reported just three out of 138 (2.2%) thymomas to be multiple (11). Jaretzky et al. reported one (1.1%) multiple thymoma out of 95 cases of thymoma (12). However, these reports did not describe any histological differences between the multiple thymomas documented. In 1990, Nomori et al. reported one case of multiple thymoma and suggested the possibility of intra-thymic metastasis rather than multi-centric development based on histological, morphometrical and immunohistochemical findings (1). Since their report, nine cases with multiple thymoma have been reported with their histological findings provided (1–8). We reviewed these reports and present their respective clinicopathological characteristics in Table 1. Histological subtypes of thymoma by WHO classification were judged from the histological findings included in each report (9). The characteristics are as follows: (i) mean age was 57 ± 11-year-old (range: 28–81); (ii) there were eight males and four females; (iii) the numbers of thymomas were two in 11 patients, and three in one; (iv) of the total of 25 thymomas, three (12%) could be histologically classified as type A, 13 (52%) as type B1, eight (32%) as type B2, and one (4%) as type B3; (v) histological findings of the multiple thymomas in each patient were similar in 10 patients (83%), while the remaining two (17%) displayed different subtypes; (vi) the difference in tumor size between the thymomas in each patient was such that the smaller ones were usually larger than 25% of the main ones, except for case numbers 1 and 10, which displayed a greater than 10 times size difference between the tumors. Of the 25 thymomas, 20 were stage I (80%), three stage II-1 (12%), and the remaining two were stage III (8%).

It is controversial whether cases of multiple thymomas represent multi-centric origin or intra-thymic metastasis. From the characteristics of the 12 cases in Table 1, multi-centric development is suggested by the following characteristics: (i) the number of thymomas were usually less than three, which would be surprising if the source were in intra-thymic dissemination; (ii) there is little size difference between the thymomas in each case, except for case numbers 1 and 10; and (iii) most of the thymomas were stage I, which are essentially unable to spread into the thymic tissue.

However, the possibility of intra-thymic metastasis might be suggested by the finding that each of 10 patients (83%) were found to have similar histological characteristics in their thymomas. While it cannot be concluded at this point whether multiple thymomas are derived from multi-centric development or intra-thymic metastasis, we favor the former hypothesis because of the analysis presented above. While we cannot rule out the theory of intra-thymic metastasis, we believe that most multiple thymomas develop from identical tumor genesis events in each patient, thus resulting in the similar histological findings.
Conflict of interest statement
None declared.

References

Table 1. Reported cases with multiple thymoma of which histological findings are described

<table>
<thead>
<tr>
<th>References/cases</th>
<th>Age/sex</th>
<th>Thymomas</th>
<th>Maximum diameter (mm)</th>
<th>Stage (Modified Masaoka)</th>
<th>Myasthenia gravis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Nomori et al. 1990 (1)</td>
<td>28/F</td>
<td>2</td>
<td>B2 and B2</td>
<td>70 and 1.5</td>
<td>I and I +</td>
</tr>
<tr>
<td>2 Takeuchi et al. 1997 (2)</td>
<td>74/F</td>
<td>2</td>
<td>B1 and B1</td>
<td>90 and 83</td>
<td>I and I –</td>
</tr>
<tr>
<td>3 Okada et al. 1998 (3)</td>
<td>37/F</td>
<td>2</td>
<td>B1 and B1</td>
<td>55 and 35</td>
<td>I and I –</td>
</tr>
<tr>
<td>4 Okada et al. 1998 (3)</td>
<td>70/M</td>
<td>2</td>
<td>B2 and B2</td>
<td>50 and 24</td>
<td>I and I –</td>
</tr>
<tr>
<td>5 Gotoh and Yokoi 2000 (4)</td>
<td>57/F</td>
<td>2</td>
<td>B1 and B1</td>
<td>39 and 32</td>
<td>I and I –</td>
</tr>
<tr>
<td>6 Hirai et al. 2001 (5)</td>
<td>42/M</td>
<td>2</td>
<td>B1 and B2</td>
<td>40 and 30</td>
<td>I and I –</td>
</tr>
<tr>
<td>7 Ishibashi et al. 2003 (6)</td>
<td>47/M</td>
<td>2</td>
<td>B1 and B1</td>
<td>60 and 25</td>
<td>I and I +</td>
</tr>
<tr>
<td>8 Nonami and Moriki 2004 (7)</td>
<td>81/F</td>
<td>2</td>
<td>B1 and B1</td>
<td>80 and 25</td>
<td>I and I –</td>
</tr>
<tr>
<td>9 Yoneda et al. 2004 (8)</td>
<td>44/M</td>
<td>2</td>
<td>B2 and B3</td>
<td>64 and 60</td>
<td>I and III –</td>
</tr>
<tr>
<td>10 The present cases</td>
<td>69/M</td>
<td>2</td>
<td>B2 and B2</td>
<td>70 and 15</td>
<td>II-1 and I +</td>
</tr>
<tr>
<td>11 The present cases</td>
<td>74/M</td>
<td>3</td>
<td>A, A and A</td>
<td>40, 24 and 10</td>
<td>III, I and I –</td>
</tr>
<tr>
<td>12 The present cases</td>
<td>46/M</td>
<td>2</td>
<td>B1 and B1</td>
<td>22 and 15</td>
<td>II-1 and II-1 +</td>
</tr>
</tbody>
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M, male; F, female.
*WHO classification judged from the histological findings written in each report.