〈Case Report〉

A case of an atypical variant of type A thymoma presenting with a gradually enlarging tumor over a 10-year period

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ABSTRACT **Background:** Type A thymomas are generally recognized as benign tumors with a good prognosis. However, in recent years, there have been some reports of type A thymomas exhibiting cytologic atypia and aggressive behaviors, such as recurrence and metastasis, this type of tumor was added newly as an atypical type A thymoma variant to the WHO thymoma classification in 2015. In this study, we present a case of in which an atypical type A thymoma variant grew slowly over a period of 10 years.

Case Description: An 86-year-old female patient was referred to our hospital for further examination of a gradually enlarging anterior mediastinal tumor that was detected during medical follow-ups between 2007 and 2016. While we suspected non-invasive thymoma based on the preoperative radiological examination, histopathological examination of the resected tumor revealed marked nuclear atypia, mitotic figures, and necrotic lesions. Immunohistochemical studies confirmed the diagnosis of atypical variant of type A thymoma. The patient developed lung metastases 48.4 months after the surgery. We elected not to treat the recurrence, and the patient remains alive 77.7 months after the surgery.

Conclusion: Careful follow-up is necessary in patients diagnosed as having an atypical variant of type A thymoma, considering the risk of postoperative recurrence and distant metastasis.

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Key words：Thymoma, Atypia, Mediastinal tumor

BACKGROUND

It has been reported that type A thymomas are mediastinal tumors with an excellent prognosis[1)]. However, there have also been several reports in recent years of cases with an atypical clinical course, with rapid progression and recurrence after surgery[2－5)]. Based on these reports, the atypical type A thymoma variant was newly added to the WHO classification of thymomas in 2015[6)]. We report a case of an 83-year-old female patient with

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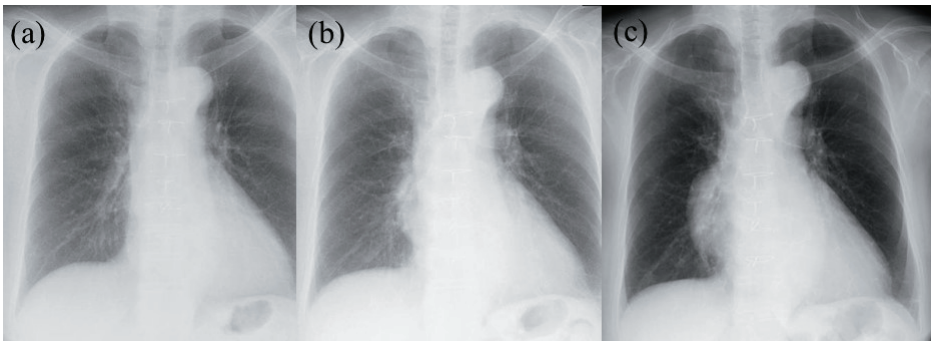

Fig. 1. Plain chest x-ray showing mediastinal tumor measuring 2.5 cm in diameter in 2007 (a); 4.5 cm in diameter in 2013 (b); 7.5 cm in diameter in 2016 (c).

an atypical variant of type A thymoma, in whom the tumor enlarged gradually over a period of 10 years.

CASE REPORT

An 83-year-old woman who had undergone aortic valve replacement was referred to our hospital for an abnormal opacity detected on the chest X-ray during follow-up examinations. The tumor had been observed for about 10 years and had increased in diameter by about 5.0 cm during this period (Fig. 1). Contrast-enhanced computed tomography of the chest showed an anterior mediastinal tumor measuring 7.0 cm in diameter. The tumor showed intratumoral calcification and heterogeneous contrast enhancement. There was no sign of invasion of the surrounding organs (Fig. 2). Serological testing for anti-acetylcholine receptor antibody was negative, and the patient was suspected as having eye muscle-type myasthenia gravis, based on her complaint of diplopia.

Based on the above findings, the tumor was preoperatively diagnosed as a non-invasive thymoma. Since the patient had already undergone aortic valve replacement via a median sternotomy, we performed tumor resection via a right thoracotomy. Intraoperatively, no evidence of invasion of the surrounding organs was noted, and the tumor could be completely resected.

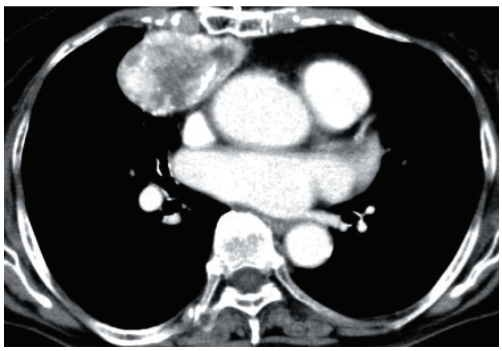

Fig. 2. Contrast-enhanced CT image of the chest showing a large oval mass not invading the surrounding organs in the anterior mediastinum.

Histopathological examination of the resected tumor revealed that it was surrounded by a fibrous capsule and composed of spindle-shaped and polygonal cells. In a part of the tumor, however, the tumor cells showed marked nuclear atypia, with numerous mitotic figures (2-4/field of view) and necrotic changes (Fig. 3). Immunohistochemical analysis showed strongly positive staining of the tumor cells for Glut-1 and a Ki-67 index of about 20% (Fig. 4). Based on these findings, the patient was diagnosed as having typical type A thymoma admixed with an atypical type A thymoma variant. The atypical type A thymoma component accounted for about 10% of the tumor area. In view of the absence of invasion beyond the capsule, the tumor was diagnosed as a Masaoka stage II tumor.

Mutations in the GTF2I gene were not examined.

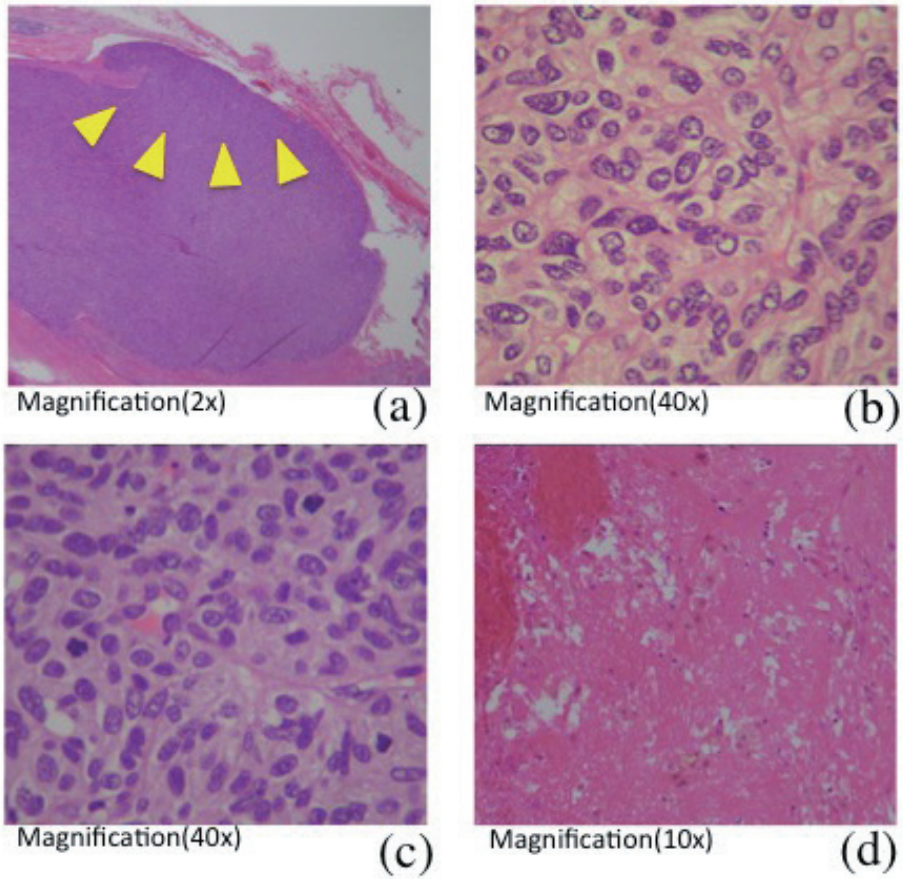

Fig. 3 Light-microscopic findings in hematoxylin & eosin-stained sections: evidence of invasion outside the capsule (a); spindle-shaped and polygonal cells with marked nuclear atypia (b); high mitotic activity (c); necrotic changes (d).

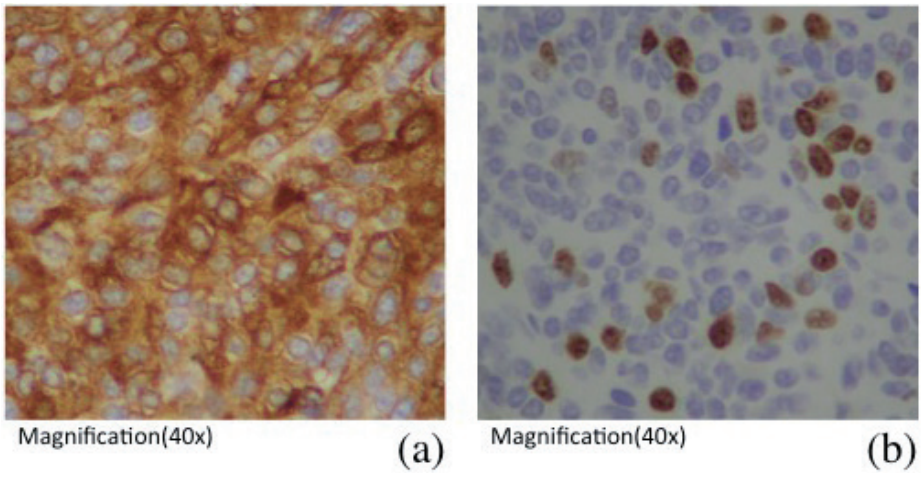

Fig. 4 Immunohistochemistry showing: positive staining for aberrant Glut-1 expression (a); the Ki-67 index was about 20% (b).

The postoperative course was uneventful, and the patient was followed up in our hospital without recurrence until 10 months after the surgery. The patient was then referred to a local physician for follow-up. At 48.4 months after the surgery, the patient was detected as having bilateral lung metastases. However, we opted not to treat the recurrent diseased, and the patient remains alive at 77.7 months after the surgery without treatment for recurrence.

DISCUSSION

Atypical type A thymoma variant was added to the type A family of thymomas in the WHO classification in 2015, based on several reports of cases of type A thymoma with recurrence and invasive disease. The diagnostic criteria for this type of tumor are: (1) comed-type tumor necrosis, (2) increased mitotic count (> 4/2 mm^2), and (3) nuclear crowding[6].

Vladislav *et al.* analyzed the data of 23 cases (3.8%) showing atypical features among 600 cases of type A thymoma[3]. Metastatic recurrence was observed in 9 out of the 23 patients (39%); this recurrence rate was significantly higher than that reported in cases of typical type A thymoma. The mean interval to metastatic recurrence from diagnosis was 36 months (7 to 107 months). The most frequently reported sites of metastasis are as follows: lung, 3 cases; liver, 3 cases; pleural dissemination, 2 cases; cervical lymph node, 1 case; thus, the frequency of distant metastases was higher than that reported for patients with typical type A thymoma. Presence of tumor necrosis, but not the tumor stage, tumor size or number of mitotic figures, has been reported as a predictor of recurrence. In our patient reported herein, during the approximately 10-year period after detection of the tumor, the tumor showed relatively rapid growth during the three years prior to surgery. Since histopathology revealed an admixture of typical type A thymoma and atypical type A thymoma variant, it is thought that the atypical part was the part that contributed to the rapid growth during the latter period. The Ki-67 index is used as a histological index to detect proliferating cells in tumor tissue[7]. The Ki-67 index has been used to distinguish among different types of thymic epithelial neoplasms. It has been reported that the Ki-67 index is usually less than 2% in typical type A thymoma, but more than 13.5% in thymic carcinoma. In the present patient, the Ki-67 index was 20%, consistent with the values seen in thymic carcinoma, reflecting the rapid growth of the tumor. In this case, the patient developed lung metastases 48.4months postoperatively.

Generally, surgery and chemotherapy are considered for recurrent thymoma. However, because of her advanced age, no treatment was given for the recurrent disease, and the patient remains alive 77.7 months after the surgery.

CONCLUSION

Atypical type A thymoma is known to undergo relatively rapid enlargement, with a relatively high rate of tumor recurrence and metastasis. In the present case encountered by us, an atypical type A thymoma that grew slowly over a 10-year period, but the rate of growth increased rapidly during the latter course of the disease. Patients with atypical type A thymoma require careful postoperative follow-up, considering the possibility of recurrence and distant metastasis.

CONFLICTS OF INTEREST

The authors state that they have no conflicts of interest.

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