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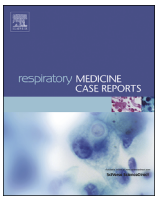

Case Report

Atypical type A thymoma component identified by pulmonary metastasectomy 11 years after surgery of type AB thymoma

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ABSTRACT

Atypical type A thymomas exhibit more aggressive features than conventional type A thymomas. Type AB thymomas rarely have atypical type A components. We report a rare case of type AB thymoma with an atypical type A component, that was identified after pulmonary metastasectomy 11 years after the primary surgery and long-term follow-up after recurrence.

A 61-year-old female underwent extended thymectomy for an anterior mediastinal tumor 11 years prior and was diagnosed with type AB thymoma (Masaoka stage II). Five years ago, follow-up computed tomography showed well-circumscribed pulmonary nodules up to 1.0 cm in both lungs. All the pulmonary nodules grew slowly; however, one of the nodules grew to 1.6 cm, and thoracoscopic wedge resection was performed for diagnosis. Pathologically, the pulmonary nodule was consisted of type A thymoma component. Conventional type AB thymomas are usually locally aggressive neoplasms; thus, we reviewed the tissue slides of primary thymomas. Histologically, cytological atypia, hypercellularity, and increased mitosis are observed in the type A component. Consequently, the diagnosis was revised to a type AB thymoma with an atypical type A component. The pulmonary nodule exhibited the same atypical type A features. Pulmonary metastasectomy was performed two more times as volume-reduction surgery. The residual metastasis was located only in the lung with slow growth, 4 years after the first pulmonary resection; therefore, we followed up as an outpatient without treatment.

1. Introduction

Type A thymomas are mediastinal tumors with a generally good prognosis [1]; however, they rarely develop distant metastasis as postoperative recurrence [2]. The World Health Organization (WHO) classification in 2015 defined high-grade thymoma as atypical type A thymoma and, classified it as a new subtype of thymomas in 2021 [3]. Type AB thymomas with atypical type A components have been rarely reported [4,5]. Herein, we report a rare case of type AB thymoma with an atypical type A component, which was identified by pulmonary metastasectomy 11 years after the primary site resection. We also describe the 4-year follow-up course after the initial metastasectomy with repeated pulmonary resection.

Abbreviations: CT, computed tomography; WHO, World Health Organization.

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2. Case presentation

A 61-year-old non-smoking female had undergone extended thymectomy for an anterior mediastinal tumor 11 years previously (Fig. 1A). Pathologically, the mediastinal tumor was diagnosed as a type AB thymoma, Masaoka stage II, and WHO classification stage I (Fig. 1B–D). No additional treatment was administered. One year later, stage I papillary thyroid carcinoma was incidentally detected and the patient underwent a left thyroid lobectomy. She had an unremarkable postoperative course for both neoplasms and followed up as an outpatient. Six years later, a follow-up chest computed tomography (CT) scan revealed five well-circumscribed solid pulmonary nodules up to 1.0 cm, one in the upper lobe of the right lung, one in the lower lobe of the right lung, and three in the lower lobe of the left lung (Fig. 2A–E). Retrospectively, we could detect a 0.3 cm pulmonary nodule in the right lower lobe and a 0.2 cm pulmonary nodule in the left lower lobe 2.7 years after initial thymoma resection. All the nodules grew slowly at 0.2 cm of year. Stage I type AB thymoma rarely metastasizes to distant organs; therefore, the pulmonary nodules were suspected to have metastasized from thyroid carcinoma. Owing to the small size and slow growth rate, additional treatment, such as isotope therapy, was not indicated, and the patient was followed up without treatment. However, 4 years later, the nodules had grown to 1.6 cm, and thoracoscopic wedge resection of the right lower lobe was performed for diagnosis. Pathologically, the proliferation of spindle to oval tumor cells with oval nuclei indicated metastasis of the type A thymoma component (Fig. 3A). We reviewed tissue slides of the primary type AB thymoma. Pathologically, cytological atypia, hypercellularity, and increased mitosis (5–6/10 HPF) were present in the type A thymoma component (Fig. 3B), indicating an atypical type A. Hence, the diagnosis of primary thymoma was modified to type AB thymoma with an atypical type A component. The Ki-67 labeling index was 5–10 %. The pulmonary nodule had pathological findings similar to those of the primary site and was finally diagnosed as a pulmonary metastasis of an atypical type A thymoma component. Six months later, two residual pulmonary nodules in the left lower lobe were resected by basal segmentectomy as a volume reduction surgery. As with the initial pulmonary metastasectomy, the atypical type A component metastasized. Two years later, a 0.6 cm and a 0.5cm nodules in the right upper and middle lobes, respectively, were resected by thoracoscopic wedge resection, and the same diagnosis was made. Four years have passed since the initial pulmonary metastasectomy, and four pulmonary nodules up to 0.5 cm were left in the bilateral lung, but no other metastases were detected. Pulmonary nodules were followed up without treatment.

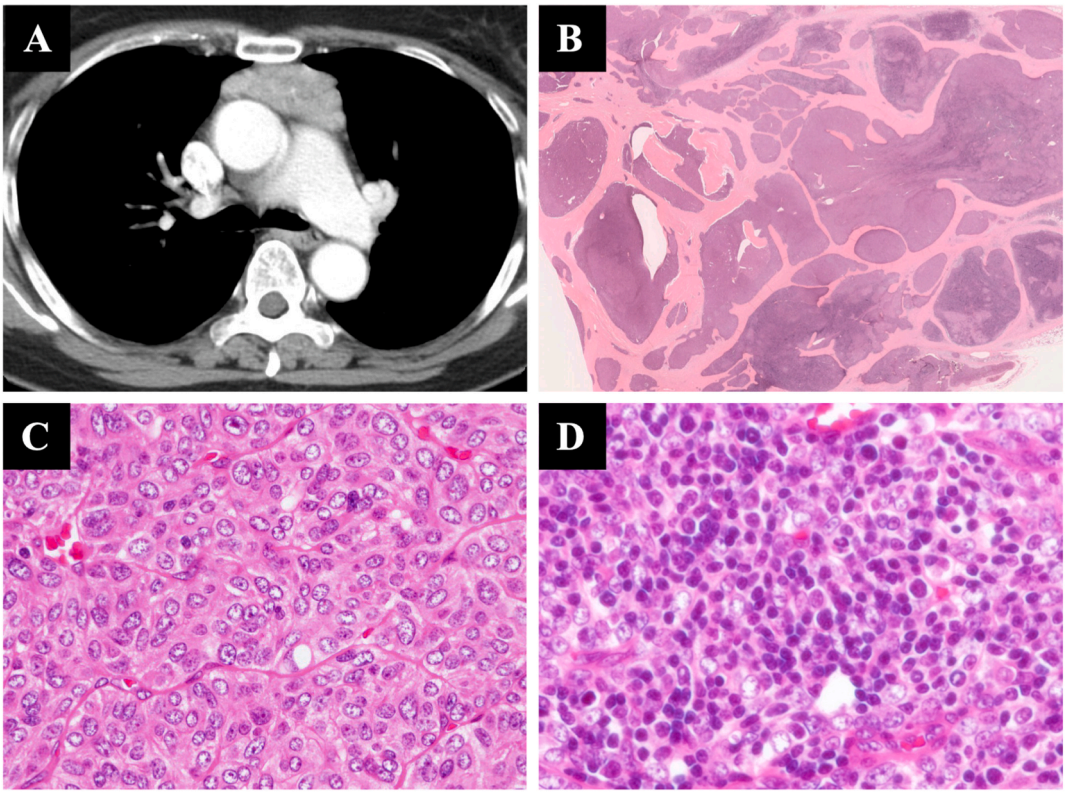

Fig. 1. Radiological and pathological findings of initial anterior mediastinal tumor. (A) Computed tomography findings of primary surgery. A 5.8 cm mass was present in the anterior mediastinum. (B) Low-power view. The lobulated growth pattern was comprised of epithelial cells divided by fibrous bands. High-power view of a type AB thymoma. The type A component is composed of atypical spindle cells (C), whereas the type B component is primarily composed of polygonal tumor cells rich in lymphocytes (D).

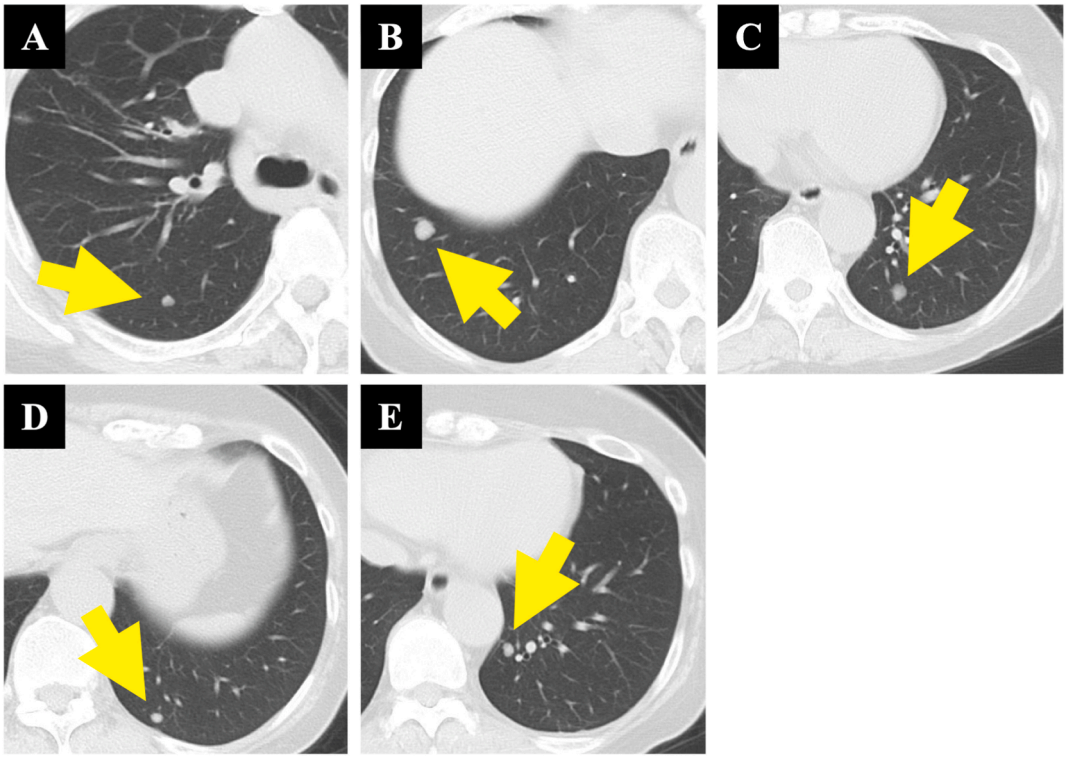

Fig. 2. Preoperative computed tomography findings. (A–E) Five well-circumscribed pulmonary nodules up to 1.0 cm was detected in the bilateral lung.

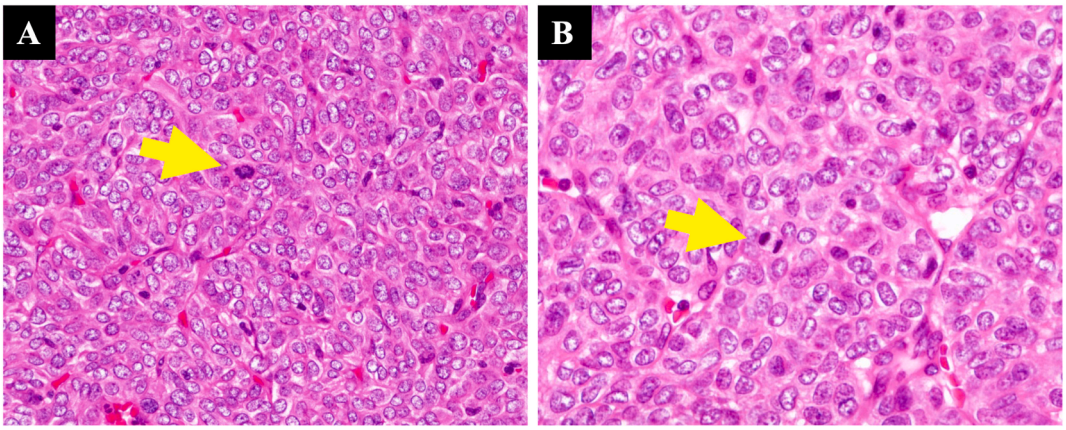

Fig. 3. Pathological findings of the atypical type A component of pulmonary nodule and primary thymoma. (A) Spindle to oval tumor cells with oval nuclei are proliferated, consistent with pulmonary metastasis of type A thymoma component. Moreover, hypercellularity and increased mitotic counts (arrow) were present, indicating atypical type A thymoma. (B) Reviewing the primary thymoma, similar findings indicating an atypical type A thymoma were detected.

3. Discussion

Conventional type A and AB thymomas are common locally advanced neoplasms that demonstrate good prognosis, with 10-year disease-free survival rates of 95 % and 90 %, respectively [1]. By contrast, 3.8 % of type A thymomas have aggressive features and present with postoperative distant metastases [2]. To distinguish such unusual entities, atypical type A thymoma was newly classified as a subtype of thymomas in 2021. Atypical type A thymomas are defined as those with one or more of the following pathological features: (a) hypercellularity, (b) increased mitotic count, and (c) focal necrosis. There are no quantitative criteria for increased mitotic counts, but conventional type A thymomas are defined as 4 cells/2 mm^2; hence, larger mitotic counts are needed for atypical type A thymomas [3].

In atypical type A thymomas, there is no difference in sex, and the age is apporoximetely 50–70 years old [4,6–10], which is similar to that of conventional type A thymomas [2]. Consistent with the present case, a type AB thymoma with an atypical type A component has also been reported [4,5]. The present case showed hypercellularity and increased mitotic counts (5–6 cells/2 mm^2) in the

type A component, but no necrotic areas were observed. The median Ki-67 labeling index was reported to be 1.2 % for type A and 4.5 % for type AB thymomas [11], whereas that of atypical type A thymoma was higher of 19.5 (8.9–30) % [4,6,8,10,12,13]. In this case, the primary thymoma had a relatively high Ki-67 labeling index of 5–10 %, consistent with previous reports. Moreover, a previous report demonstrated the feasibility of the level of standardized uptake value of positron emission tomography-CT for predicting thymoma aggressiveness according to the WHO histologic type [14]. However, despite the high aggressiveness of atypical type A thymomas, the fluorodeoxyglucose uptake was as similar as conventional type A thymomas; hence, radiological differentiation is difficult [6].

In the present case, the initial thymoma subtype was type AB, and atypical type A components could not be demonstrated. Moreover, we could not consider metastasis of the thymoma because distant metastasis of completely resected stage I type AB thymoma is rare (1.6 %) [15] and the patient had a medical history of thyroid carcinoma with a recurrence pattern, often presenting as multiple lung metastases. In addition, primary surgery was performed before 2015, when the concept of atypical type A thymoma was proposed, which might also lead to overlooking atypical type A thymoma components. When distant metastasis is suspected after type A or AB thymoma resection before 2015, recurrence of the atypical type A component should be considered, and a pathological review of the primary thymomas is needed.

As atypical type A thymoma is a new classification, the number of cases is small, and there are no comprehensive reports on its prognosis. The mean recurrence-free survival of atypical type A thymoma was 39.7 (7–107) months [2]. Therefore, 10-year follow-up period is reasonable, as in the case of conventional thymomas. Furthermore, tumor necrosis nests has been reported to be a poor prognostic factor [2]; hence, careful follow-up in the early postoperative period is recommended in such case. Forty-three percent of atypical type A thymomas experience tumor recurrence. The lungs and liver account for 70 % of the metastatic organs [2]. This recurrence rate is much higher than that of conventional type A (4 %) and type AB thymomas (2 %) [16]. Furthermore, no established treatment for the recurrence of atypical type A thymoma was advocated. In this case, due to the slow growth rate of the lung metastasis and the absence of other metastasis, we performed lung metastasectomies three times as a volume reduction surgery, without any chemotherapy [17,18]. The patient is still alive with residual small pulmonary nodules 11 years after the initial recurrence and 15 years after the primary surgery. Long-term follow-up after the recurrence of type AB thymomas with atypical type A component were extremely rare [4], and further case studies are needed.

4. Conclusion

- We encountered a rare case of type AB thymoma with an atypical type A component that was identified by pulmonary metastasectomy 11 years after the primary surgery.
- An atypical type A component could present with distant metastasis, even in type A or AB thymomas; therefore, careful pathological evaluation and follow-up are needed.

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Author statement

Makoto Hirai: Conceptualization, Data curation, Visualization, Writing - original draft. Mikito Suzuki: Conceptualization, Project administration, Visualization, Writing - original draft, Writing - review & editing. Tomohiro Imoto: Data curation. Reiko Shimizu: Data curation, Writing - review & editing. Masahiko Harada: Writing - review & editing. Tsunekazu Hishima: Data curation, Writing - review & editing. Hirotoshi Horio: Supervision, Writing - review & editing.

Declaration of competing interest

The authors have no conflicts of interest.

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