Received: 1 July 2024 | Accepted: 7 August 2024

DOI: 10.1002/rcr2.70006

CASE REPORT

Respirology Case Reports OPEN ACCESS APSR WILEY

Successful treatment of type B2 thymoma with steroid and radiotherapy

Miho Fujiwara | **Hiromi Watanabe** | **Yuki Takigawa** | **Mayu Goda** | **Keisuke Shiraha** | **Tomoyoshi Inoue** | **Suzuka Matsuoka** | **Kenichiro Kudo** | **Akiko Sato** | **Ken Sato** | **Keiichi Fujiwara** | **Takuo Shibayama**

Department of Respiratory Medicine, NHO Okayama Medical Center, Okayama, Japan

Correspondence
Miho Fujiwara, Department of Respiratory Medicine, National Hospital Organization Okayama Medical Center, 1711-1 Tamasu, Okayama city, Okayama 701-1192, Japan.
Email: mqhsoc10@gmail.com

Associate Editor: Semra Bilaceroglu

Abstract

An 86-year-old woman with leg edema and dyspnea on exertion was admitted to our hospital. Chest computed tomography (CT) revealed a mass in the anterior mediastinum with pericardial invasion. Histological examination with endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) led to the diagnosis of Masaoka stage IVa type B2 thymoma. For palliation, radiotherapy (32 Gy/16 fractions) and prednisolone (30 mg/day) were administered and tapered. After treatment, both the pericardial effusion and tumour size decreased. Combination therapy with steroids and radiotherapy may be effective for treating thymomas.

KEYWORDS

prednisolone, radiotherapy, steroid, thymoma

INTRODUCTION

A thymoma is a thymic epithelial tumour without cellular atypia. Surgical resection is advocated as the primary treatment for thymomas, which are slow-growing and often encapsulated tumours.[1] Systemic chemotherapy can be considered in patients with advanced disease or recurrence after primary therapy.[2] Initiating chemotherapy in elderly patients and those with a poor performance status (PS) is sometimes difficult.

Although radiation monotherapy and low-dose prednisolone therapy have been reported in some cases,[3,4] no case report on combination therapy using prednisolone and radiotherapy has been published yet. Herein, we report a case of Masaoka stage IVa type B2 thymoma that responded to combination therapy with prednisolone and radiotherapy.

CASE REPORT

An 86-year-old woman with leg edema and dyspnea on exertion was admitted to our hospital. Neuromuscular symptoms were not observed. Chest radiography revealed an enlarged cardiac silhouette and pleural effusion (Figure 1A). Enhanced computed tomography (CT) revealed pericardial effusion and a mass in the anterior mediastinum invading the pericardium (Figure 1B). Pericardial drainage was performed, and lymphocyte predominance and CYFRA levels were found elevated. Cytological examination of the pericardial and pleural effusions revealed no malignant cells. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) of the ostium of the left lower bronchus was performed for a mediastinal tumour (Figure 2A). Histological examination of EBUS-TBNA revealed thymic tissue with dense lymphocytic infiltration upon haematoxylin and eosin staining (Figure 2B). Thymic epithelial cells were positive for CK5/6 and CK AE1/AE3, but negative for CK5 (Figure 2C). CD5-positive lymphocytes infiltrated the thymoma (Figure 2D). The patient was diagnosed with an invasive thymoma (World Health Organization classification type B2), and the clinical stage was classified as IVa according to the Masaoka staging system. Chemotherapy was not administered, due to poor PS and dementia. The patient received radiotherapy (32 Gy/16 Fr) and medium-dose prednisolone (30 mg/day) as palliative therapy. Initially, radiotherapy was scheduled at 40 Gy/20 Fr; however, it was discontinued due to radiation esophagitis. Prednisolone was tapered

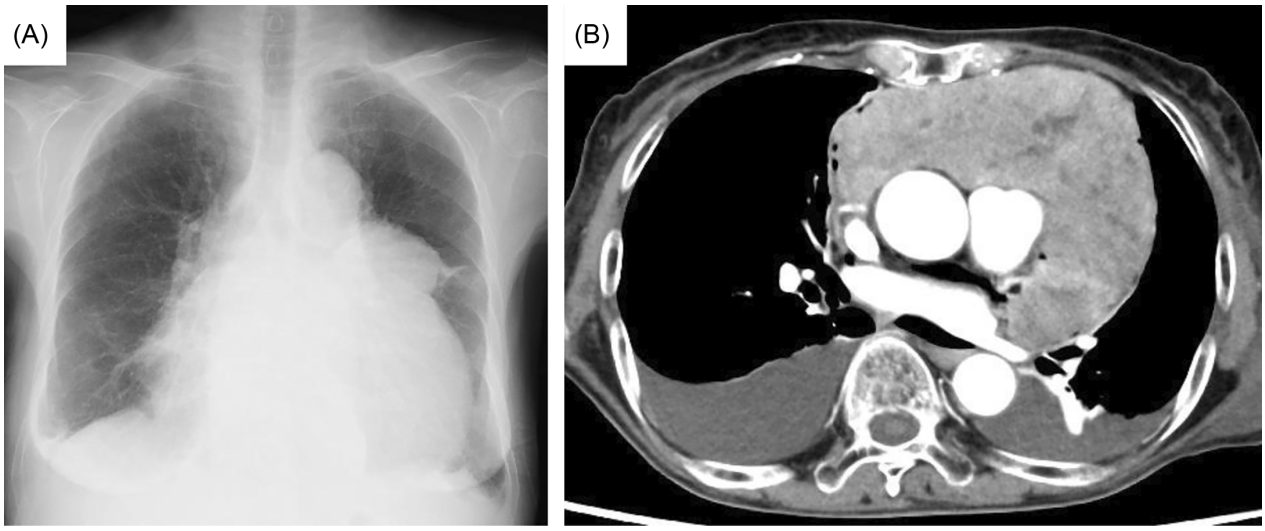

FIGURE 1 Chest x-ray and contrast-enhanced chest computed tomography (CT) findings on admission. (A) Chest x-ray showed cardiac enlargement. (B) Contrast-enhanced chest CT showed a mass in the anterior mediastinum with pericardial invasion. Pericardial effusion and bilateral pleural effusion were observed.

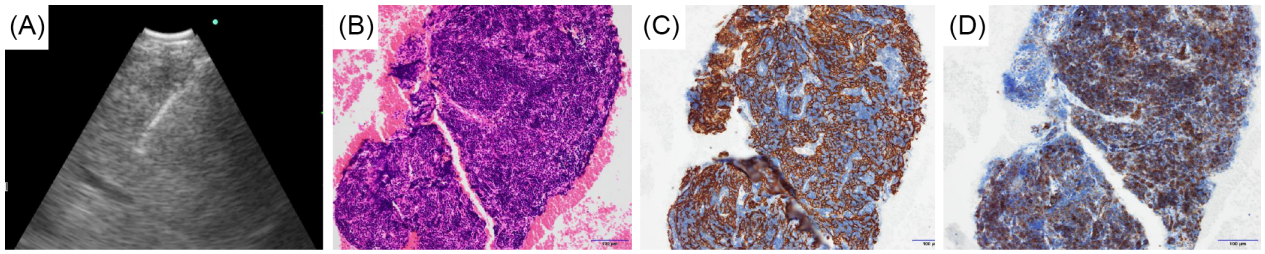

FIGURE 2 Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and histological findings. (A) EBUS-TBNA of mediastinal tumour performed at the ostium of left lower bronchus. (B) Histological specimen obtained by EBUS-TBNA (haematoxylin and eosin staining, 200×). (C) Immunocytochemical staining for CK5/6 (200×) and (D) CD5 (200×).

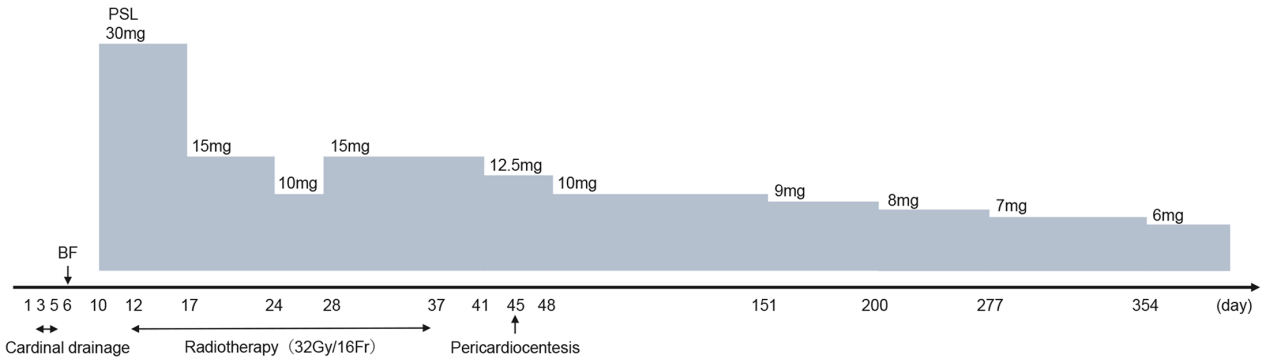

FIGURE 3 Clinical course. Radiotherapy (32 Gy/16 Fr) and a medium-dose (30 mg/day) prednisolone were administrated. Radiotherapy was discontinued due to radiation esophagitis. Pericardial effusion was increased when prednisolone was tapered from 15 mg to 10 mg, therefore the dose was increased back to 15 mg and then tapered gradually. BF: Bronchofiberscopy; PSL: Prednisolone.

every 1–2 weeks (Figure 3). Pericardial effusion increased when prednisolone was tapered from 15 to 10 mg; therefore, the dose was increased back to 15 mg and then tapered gradually therefrom. Pericardiocentesis was performed 45 days after admission, and no increase in pericardial effusion was observed thereafter. After combination therapy with prednisolone and radiotherapy, CT revealed a remarkable decrease in tumour size, pericardial effusion, and pleural effusion (Figure 4). After 45 days of admission, the pericardial effusion changed from lymphocyte predominance to monocyte

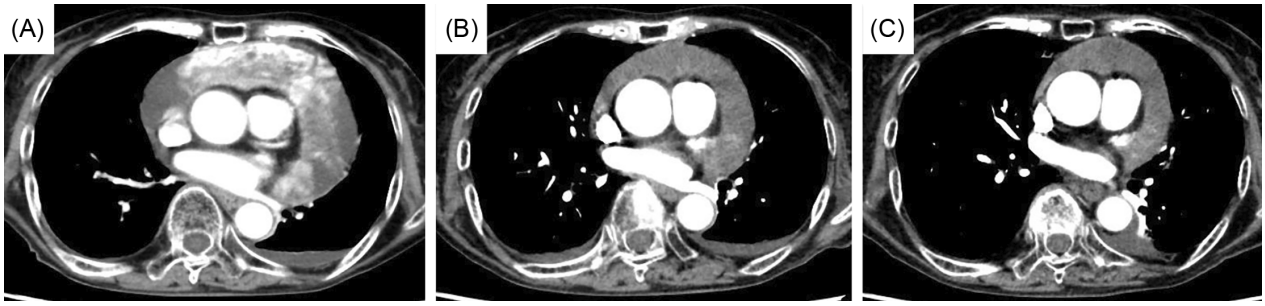

FIGURE 4 Contrast-enhanced chest computed tomography (CT) findings after treatment. The CT scans showed reduction in tumour size, pericardial effusion, and bilateral pleural effusion, respectively. (A) Chest CT on day 45. (B) Chest CT on day 122. (C) Chest CT on day 240.

predominance, and CYFRA decreased. Prednisolone was gradually tapered off during follow-up as an outpatient and treatment is still ongoing.

DISCUSSION

Although multimodal therapy is recommended for patients with advanced or recurrent thymomas, the detailed treatment strategy remains controversial. Previous reports had demonstrated that thymomas are sensitive to systemic chemotherapy,[2,5–7] whereas several other reports have shown that corticosteroids, as a single-drug treatment, are also effective for thymomas.[4,8–11] Hanibuchi et al. demonstrated that low-dose prednisolone is effective for treating invasive type B3 thymomas.[4] Kobayashi et al. reported that steroid pulse therapy induced thymoma regression in 8 of 17 patients with advanced thymoma (ORR = 47.1%),[8] and indicated a partial response in all 5 patients with type B1 thymoma and in 3 of 6 patients with type B2 thymoma. In our case, the patient's family refused chemotherapy due to poor PS and dementia, and we decided to use steroid therapy to alleviate the symptoms.

The glucocorticoid receptor (GR) is expressed in both the epithelial cells and lymphocytes of thymomas. The number of GR sites is much greater in lymphoepithelial thymomas than in pure epithelial thymomas.[10] Furthermore, multivariate analysis revealed that GR expression was associated with better prognosis in patients with surgically resected thymomas and thymic carcinomas.[11] High doses of corticosteroids, such as steroid pulse therapy, induce apoptosis of neoplastic thymic epithelial cells and lymphocytes in thymomas.[12] The reduction in tumour size after steroid pulse therapy was shown to be accompanied by a remarkable reduction in $CD4^{+}$ 8+ double-positive immature lymphocytes, indicating that tumour size reduction of thymomas could be partly explained by the reduction in the bulk of these lymphocytes.[8] Types AB, B1, and B2 tumours retain the ability to induce CD4 + CD8+ double-positive cells at a level comparable to that of normal thymic cortical epithelial cells.[13] Type B2 thymomas contain many immature T-cells, and neoplastic thymic epithelial cells express steroid receptors. Therefore, in our case, even medium doses of prednisolone might have resulted in tumour regression.

Radiotherapy is a non-surgical modality, and the ORR of radiotherapy alone, sequential chemoradiation, and concurrent chemoradiation have been reported to be 43.8%, 50%, and 87.5%, respectively.[3] In our case, for therapeutic effects, radiotherapy was added to steroid therapy, and the tumour shrank as a result. Owing to extensive pericardial invasion and the risk of constrictive pericarditis,[14] radiotherapy was initiated at 40 Gy. Although radiation esophagitis occurred during the combination therapy, no other adverse event was observed. The patient had dementia, and overall radiotherapy was terminated early when she developed a reduced appetite due to radiation esophagitis. We believe that combination therapy is well-tolerated and may be a treatment option for thymoma.

Here, we reported a case of type B2 thymoma that was successfully treated with steroids and radiotherapy. The case suggested that combination therapy with prednisolone and radiotherapy could be one of the treatment options for elderly patients with locally advanced thymomas.

AUTHOR CONTRIBUTIONS

Miho Fujiwara and Hiromi Watanabe wrote the manuscript, which was reviewed by all co-authors. All authors have approved the final version for submission.

ACKNOWLEDGMENTS

We would like to thank the patient and her family. We are grateful to Dr. Yoko Shino for the helpful discussions.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

ORCID

Miho Fujiwara https://orcid.org/0009-0009-3790-4373
Yuki Takigawa https://orcid.org/0000-0003-0613-0423

REFERENCES

1. Okumura M, Miyoshi S, Takeuchi Y, Yoon HE, Minami M, Takeda SI, et al. Results of surgical treatment of thymomas with special reference to the involved organs. J Thorac Cardiovasc Surg. 1999;117:605–13. https://doi.org/10.1016/s0022-5223(99)70343-0
2. Chahinian AP, Bhardwaj S, Meyer RJ, Jaffrey IS, Kirschner PA, Holland JF. Treatment of invasive or metastatic thymoma: report of eleven cases. Cancer. 1981;47:1752–61. https://doi.org/10.1002/1097-0142(19810401)47:7<1752::aid-cncr2820470705>3.0.co;2-c
3. Wang CL, Gao LT, Lv CX, Zhu L, Fang WT. Outcome of nonsurgical treatment for locally advanced thymic tumors. J Thorac Dis. 2016;8:705–10. https://doi.org/10.21037/jtd.2016.01.79
4. Hanibuchi M, Saijo A, Mitsuhashi A, Kajimoto T, Kitagawa T. A rare case of invasive thymoma presented a dramatic response to low-dose prednisolone as a single-drug therapy. J Med Invest. 2021;68:396–9. https://doi.org/10.2152/jmi.68.396
5. Fornasiero A, Daniele O, Ghiotto C, Piazza M, Fiore-Donati L, Calabró F, et al. Chemotherapy for invasive thymoma. A 13-year experience. Cancer. 1991;68:30–3. https://doi.org/10.1002/1097-0142(19910701)68:1<30::aid-cncr2820680106>3.0.co;2-4
6. Yokoi K, Matsuguma H, Nakahara R, Kondo T, Kamiyama Y, Mori K, et al. Multidisciplinary treatment for advanced invasive thymoma with cisplatin, doxorubicin, and methylprednisolone. J Thorac Oncol. 2007;2:73–8. https://doi.org/10.1097/JTO.0b013e31802bafc8
7. Loehrer PJ, Kim K, Aisner SC, Livingston R, Einhorn LH, Johnson D, et al. Cisplatin plus doxorubicin plus cyclophosphamide in metastatic or recurrent thymoma: final results of an intergroup trial. the eastern cooperative oncology group, southwest oncology group, and southeastern cancer study group. J Clin Oncol. 1994;12:1164–8. https://doi.org/10.1200/JCO.1994.12.6.1164
8. Kobayashi Y, Fujii Y, Yano M, Sasaki H, Yukiue H, Haneda H, et al. Preoperative steroid pulse therapy for invasive thymoma: clinical experience and mechanism of action. Cancer. 2006;106:1901–7. https://doi.org/10.1002/cncr.21875
9. Yano T. Treatment strategy for thymoma. Establishment of treatment strategy and prognosis. Nagoyaichiritu Daigaku Igakukai Zasshi. 2010;51:159–64. (in Japanese).
10. Ranelletti FO, Iacobelli S, Carmignani M, Sica G, Natoli C, Tonali P. Glucocorticoid receptors and in vitro corticosensitivity in human thymoma. Cancer Res. 1980;40:2020–5.
11. Mimae T, Tsuta K, Takahashi F, Yoshida A, Kondo T, Murakami Y, et al. Steroid receptor expression in thymomas and thymic carcinomas. Cancer. 2011;117:4396–405. https://doi.org/10.1002/cncr.26061
12. Tateyama H, Takahashi E, Saito Y, Fukai I, Fujii Y, Niwa H, et al. Histopathologic changes of thymoma preoperatively treated with corticosteroids. Virchows Arch. 2001;438:238–47. https://doi.org/10.1007/s004280000333
13. Okumura M, Miyoshi S, Fujii Y, Takeuchi Y, Shiono H, Inoue M, et al. Clinical and functional significance of WHO classification on human thymic epithelial neoplasms: a study of 146 consecutive tumors. Am J Surg Pathol. 2001;25:103–10. https://doi.org/10.1097/00000478-200101000-00012
14. Hikosaka Y, Yano M, Otsuka S, Sasaki H, Moriyama S, Okuda K, et al. Post-irradiation constrictive pericarditis following thymoma treatment: a report of two cases. Gen Thorac Cardiovasc Surg. 2015;63:413–5. https://doi.org/10.1007/s11748-013-0302-9

How to cite this article: Fujiwara M, Watanabe H, Takigawa Y, Goda M, Shiraha K, Inoue T, et al. Successful treatment of type B2 thymoma with steroid and radiotherapy. Respirology Case Reports. 2024;12(8):e70006. https://doi.org/10.1002/rcr2.70006