

High-dose Methylprednisolone with Chemotherapy for Invasive Thymoma: A Case Report

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Abstract. A case of invasive thymoma that responded well to the administration of a high-dose methylprednisolone with cisplatin and adriamycin is reported. A 63-year-old woman was admitted to our hospital because of dyspnea, chest oppression and edema of the face. Chest CT revealed a large mass in the anterior mediastinum with the opacification of superior vena cava. Biopsy specimens from the mass revealed a spindle cell thymoma, consisting of epithelial cells and lymphoid cells. A diagnosis of invasive thymoma was made and the patient was intravenously treated with a high-dose of methylprednisolone (1,000 mg on days 1-5 and 500 mg on days 6 and 7), cisplatin (80 mg/m² on day 1) and adriamycin (40 mg/m² on day 1). The treatment with three courses of this combined chemotherapy resulted in the improvement and regression of all clinical signs and symptoms. This case demonstrated that a high-dose methylprednisolone with cisplatin and adriamycin might be potentially effective for invasive thymoma.

Thymoma is one of the most common neoplasms of the mediastinum. This disease is a mixture of epithelial cells and lymphocytes, often T-cells and the malignant component is represented by the epithelial cells. Invasive thymoma, referred to as malignant thymoma, directly extends in all directions from the original site and penetrates the pleura, pericardium, or other mediastinal structures. The primary treatment of encapsulated thymoma is surgical resection. Patients with unresectable disease, however, potentially could benefit from systemic chemotherapy. There have been several reports demonstrating the responses to cisplatin-based combination chemotherapy (1-3), to octreotide as an octapeptide somatostatin analog (4), as well as to a daily corticosteroid therapy (5-7). In this report, a patient who had an invasive thymoma (Masaoka stage III) complicated with superior vena

cava (SVC) syndrome, which subsequently responded to a high-dose methyprednisolone with chemotherapy, is described.

Case Report

A 63-year-old woman was admitted to our hospital because of progressive dyspnea, chest oppression and edema of the face in May, 2001. One month before admission, the patient noticed breathlessness during exercise but not chest pain developed. Physical examination at admission revealed facial swelling and edema of the right upper extremity and decreased respiratory sounds on the right upper lung field. Muscle weakness was not recognized. The human chorionic gonadotropin and alfa-fetoprotein serum levels were both within normal range. The acetylcholine receptor antibody was negative.

The initial chest radiograph showed an air-space opacity in the right upper lung area that overlaid the right hilar region, a mass opacity in the left mid lung area and an enlarged cardiac silhouette (Figure 1). Chest computerized tomography (CT) scan examination disclosed a large mass (16 by 12 cm) in the anterior mediastinum, with the invasion of the adjacent pericardium, superior vena cava and aorta (Figure 2). This soft-tissue mass had areas of low attenuation, suggesting necrosis and the SVC was opaque. No signs of extrathoracic metastasis were seen in any organs. A microscopic view of the specimens obtained by the CT-guided needle biopsy showed a mixture predominantly of spindle cell proliferation and small lymphocytes (Figure 3).

A diagnosis of invasive thymoma (Masaoka stage III) complicated with SVC syndrome was made. On June 2001, the patient was intravenously treated with cisplatin (80 mg/m² on day 1), adriamycin (40 mg/m² on day 1) and methylprednisolone (1,000 mg on days 1-5 and 500 mg on days 6 and 7) for a total of three cycles. Her symptoms improved along with the dramatic decrease of the mass in the anterior mediastinum, as visualized by CT scan (Figure 4). In addition, radiation therapy was delivered in a dose of 45 Gy within 36 days. Although we recommend further surgical therapy for invasive thymoma, the patient refused the strategies of the operation. Three years later, the mass in the anterior mediastinum was observed to show a tendency for invasion of

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Figure 1. Chest radiograph. The initial chest radiograph shows a giant mass in the mediastinum. There is an air-space opacity in the upper left and the right lung.

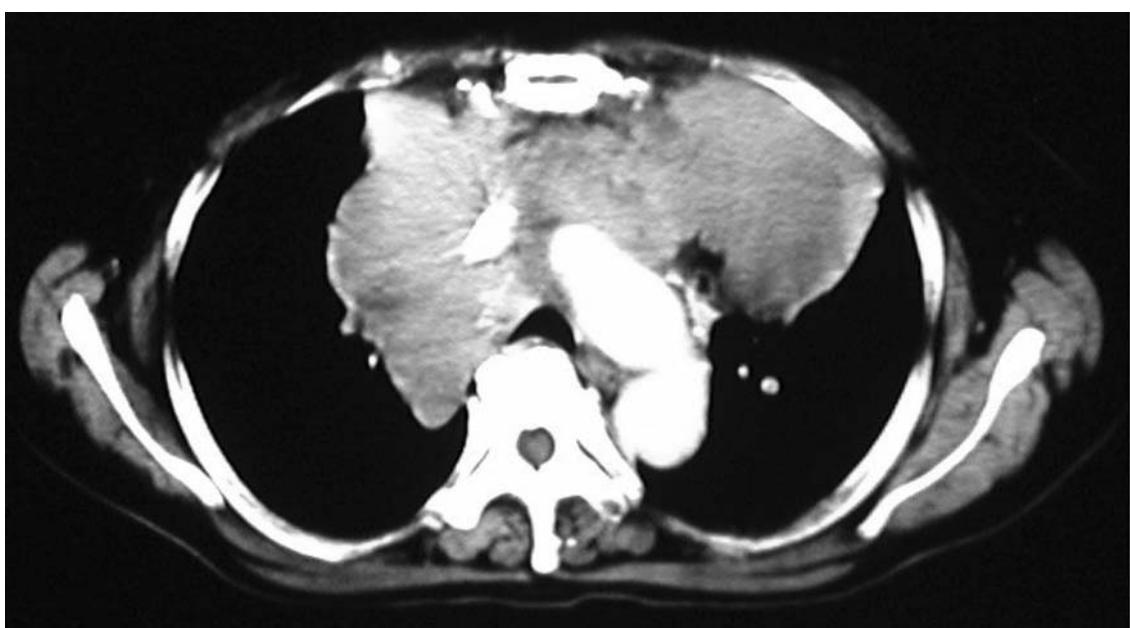


Figure 2. CT scan of the thorax. The initial CT scan of the thorax shows a large mass with low attenuation foci that suggests necrosis. The mass extended to the aorta and the opacification of the superior vena cava was decreased by the mass.

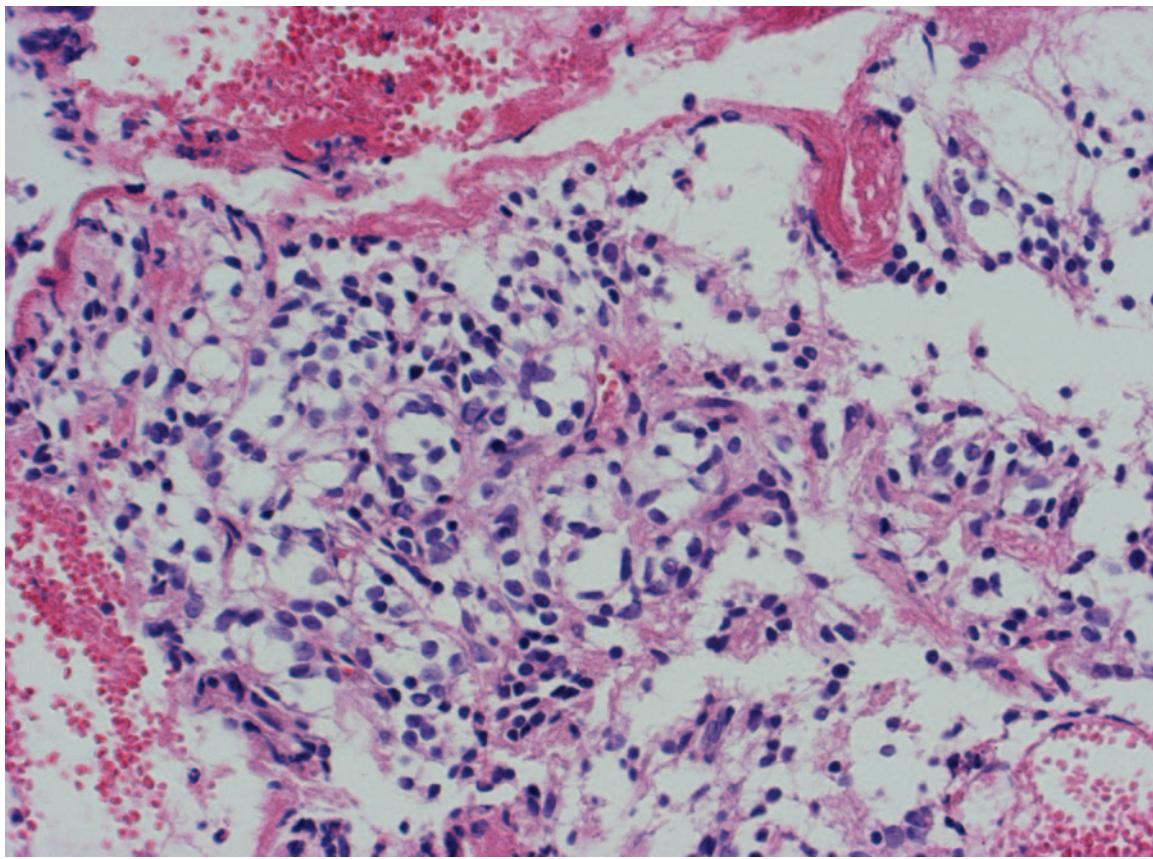


Figure 3. Biopsy specimen of mediastinal mass (hematoxylin and eosin). A proliferation of spindle cells and an infiltration of small lymphocytes were observed. 400X.

the left pulmonary artery. Therefore, we added one course of this combination chemotherapy was added and resulted in the decrease of the mass. The patient remained symptom-free for four years up to the present time, without any complication such as myasthenia gravis, erythroid hyperplasia, or hypogammaglobulinemia.

Discussion

Thymoma is a tumor originating within the epithelial cells of the thymus. The major constituents of the epithelial cells have defined histological subtypes of thymoma, which also contain admixtures of lymphocytes. Clinically, thymoma is a neoplasm of the anterior mediastinum with interesting biological and therapeutic potential. Much is unknown regarding the genetic alteration that leads to the development of thymoma and the unique association with paraneoplastic syndromes, such as myasthenia gravis, hypogammaglobulinemia and pure red cell aplasia. Previous trials conducted for the treatment of invasive thymoma have demonstrated that thymomas are tumors sensitive to chemotherapy (8, 9). For patients with unresectable or advanced thymoma, systemic chemotherapy has been used

widely. Fornasiero *et al.* reported that the ADOC regimen (cisplatin, doxorubicin, vincristine and cyclophosphamide) yielded a response rate of 90% and a median survival of 1.25 years (10). In an intergroup trial, the PAC regimen, consisting of cisplatin, doxorubicin and cyclophosphamide, produced a 50% objective response rate in 30 patients with metastatic or locally progressing recurrent thymoma ($n=29$) or thymic carcinoma ($n=1$) (11). These observations led to the development of multimodality therapy for the treatment of patients with advanced thymoma.

Corticosteroids were widely known to have been a useful drug for the treatment of thymoma. Single case reports of response to corticosteroids alone have been reported, primarily in cases of lymphocytic thymoma (7, 12). Furthermore, interesting case reports about the effectiveness of corticosteroids on thymoma were published. Palmieri *et al.* documented that a patient with red cell aplasia and heavily pretreated thymoma achieved a durable complete remission, when treated with high-dose octreotide plus prednisone (13). In addition, Tiseo *et al.* reported one case in which the addition of prednisone on prolonged octreotide treatment achieved a complete remission of malignant thymoma (14). These reports

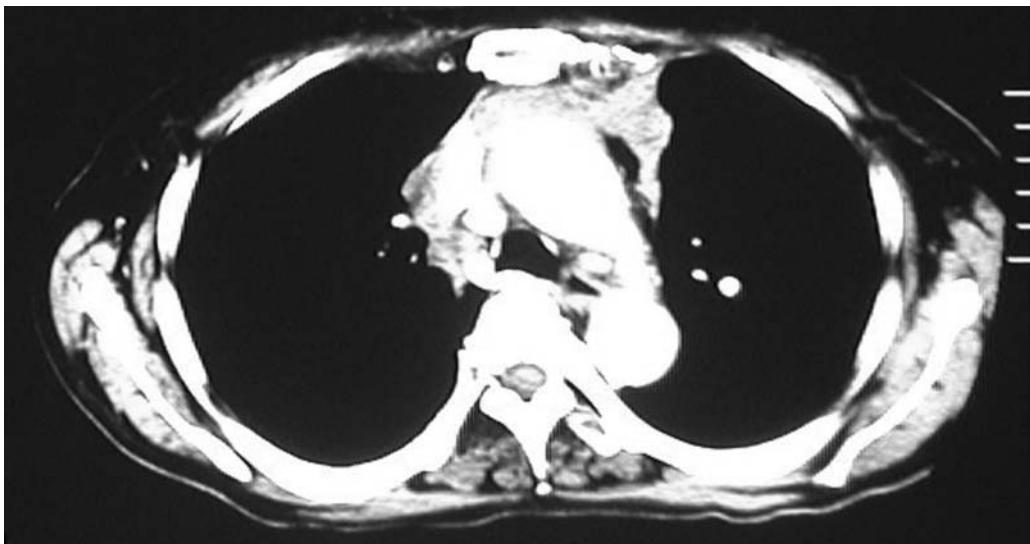


Figure 4. CT scan of the thorax after chemotherapy. The CT scan shows a dramatic decrease in the size of the anterior mediastinum mass as well as resolved SVC syndrome, and the mass effect of the aorta disappeared after high doses of methylprednisolone containing cisplatin and adriamycin for three cycles.

indicated that the response had been due to the apoptotic effects of corticosteroids, mainly on the lymphocyte component of the mass. On the other hand, it was recently shown that high doses of corticosteroids, such as methylprednisolone 1,000 mg/day for three or four days, induced the apoptotic indices of epithelial cells (15). These findings suggested that corticosteroids cause degenerative changes in the epithelial cells, as well as lymphocytes in thymoma. In our case, although we could not investigate the pathological change after the chemotherapy, high-dose methylprednisolone with chemotherapy might affect the lymphocytic components and the neoplastic thymic cells in invasive thymomas.

The primary treatment of invasive thymoma is chemotherapy followed by surgical excision and/or radiation therapy. In the present case, the infiltration of vena cave superior made radical extirpation of the tumor impossible. We suggest that high-dose methylprednisolone with chemotherapy may be potentially effective for invasive thymoma regardless of the histological findings.

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