Anterior Mediastinal Lymphoma Arising after Resection of an Invasive Thymoma and Immunosuppressive Therapy for Complicated Myasthenia Gravis

Kohei Hashimoto, MD,1 Hirohisa Horinouchi, MD, PhD,1 Takashi Ohtsuka, MD, PhD,1 Mitsutomo Kohno, MD, PhD,1 Yotaro Izumi, MD, PhD,1 Yuichiro Hayashi, MD PhD,2 and Hiroaki Nomori, MD, PhD1

We present the case of a 56-year-old woman with an anterior mediastinal tumor who has past history of myasthenia gravis and invasive thymoma. Furthermore, she had superior vena cava syndrome that was caused by a rapidly growing tumor. A biopsy proved diffuse large B-cell lymphoma. After 8 courses of chemotherapy, remission of the lymphoma was achieved. Because a second primary malignancy, including lymphoma, can occur in patients with thymoma, a biopsy is necessary for tumors located in the anterior mediastinum, particularly in patients with a history of treatment for thymoma, to distinguish between recurrence and a second primary malignancy.

Keywords: mediastinal tumor, thymoma, second malignancy

Introduction

The incidence of a second primary malignancy is higher in patients with thymoma than in healthy individuals.1–4 Therefore, in the case of a tumor that develops at anterior mediastinum after resection of thymoma, distinguishing between recurrence of thymoma and a second primary malignancy is necessary. Here, we report the case of a tumor diagnosed by needle biopsy as non-Hodgkin’s lymphoma (NHL) that occurred in the anterior mediastinum 4 years after resection of an invasive thymoma. Complete remission was achieved by chemotherapy.

Case Report

A 56-year-old Japanese woman presented with dyspnea and edema of the face and upper limb. Four years ago, she had been treated for an invasive thymoma and ocular-type myasthenia gravis. The thymoma had been resected with an extended thymectomy (Fig. 1a). The pericardium and the right upper lobe had been involved by tumor and had been resected together with the thymoma. Disseminated lesions within the right thorax were also observed. The tumor was pathologically diagnosed as a type B2 thymoma according to the WHO classification (Fig. 1b), and was classified as stage IVa according to Masaoka’s classification. Postoperative radiation therapy was administered to the right hemithorax with 15 Gy, to the whole mediastinum with 20 Gy, and to the primary site with 10 Gy. Eighteen months after the surgery, a disseminated tumor of diameter 2 cm was observed at the diaphragm on follow-up CT and was treated by radiation therapy with 50 Gy. Thirty-four months after the surgery, another disseminated tumor appeared in the right thorax, and this was treated by surgery; the pathological diagnosis of this tumor type B2 thymoma. After the surgery, the patient...
experienced a myasthenic crisis; thus, she was treated with 5 cycles of plasmapheresis and steroid-pulse therapy that resulted in remission. After that, she was administered cyclosporin (20 mg/day), prednisolone (20 mg/day), and pyridostigmin bromide (120 mg/day).

Forty-five months after the first surgery, she complained of dyspnea and edema of the face and upper limb. CT showed an anterior mediastinal mass of diameter 8 cm that occluded both brachiocephalic veins (Fig. 2a and 2b). Because of the rapidly worsening symptoms, a stent was inserted into the left brachiocephalic vein, which resulted in a prompt improvement of symptoms. Because of the fast growth of the tumor in reference to the most recent CT finding, recurrence of thymoma was unlikely; a CT-guided needle biopsy was performed that diagnosed the tumor as a diffuse large B-cell lymphoma (Fig. 2c and 2d).

The lymphoma was treated with a combination of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP regimen). After the first course of the treatment, the size of the tumor decreased considerably, and the symptoms disappeared (Fig. 3a and 3b). The patient was in complete remission after 8 courses of the chemotherapy.

Discussion and Conclusion

Several epidemiological studies have shown that second primary malignancies are sometimes associated with the long-term clinical course after diagnosis of a thymoma. The risk of NHL was reported to increase with a long period after the diagnosis of thymoma, with a standardized incidence ratio of 7.1 in patients with thymoma against the general population. However, anterior mediastinal tumors that appear after the resection of an invasive thymoma are usually considered a recurrence of thymoma.

While the mechanism underlying an increased risk of a second malignancy after treatment of thymoma is unknown, the speculated mechanism is that abnormally functioning T cells that arise in association with the thymoma either induce or fail to control B-cell proliferation. This could subsequently lead to NHL. Similarly, a much higher NHL risk is associated with more severe T-cell dysfunction, as observed in acquired immunodeficiency syndrome (AIDS) or after organ transplantation, and in patients with autoimmune conditions. In addition to the presence of the thymoma itself, immunosuppressive therapy for myasthenia gravis could also influence the development of lymphoma in the present case, as is mentioned in the previous report by Engels. Impaired surveillance function of the T-cell caused by immunosuppressive agents is thought to lead to B-cell proliferation and subsequently to the development of B-cell lymphoma.

In this case, the needle biopsy diagnosed the tumor as NHL; however, if the biopsy had not been conducted, the patient would have not received treatment for the NHL. Therefore, for patients with anterior mediastinal tumors who had a past history of treatment for thymoma, the possibility of de novo generation of a diffuse large B cell lymphoma should be recognized and a biopsy should be performed.

Disclosure Statement

We have no financial or other interest in the manufacture or distribution of the device from the manufacturer.
Fig. 2  Enhanced CT scan obtained on admission and histological findings of the biopsied specimen of the B-cell lymphoma. (a) An anterior mediastinal mass with a diameter of 8 cm involved the great vessels and caused stricture of the jugular veins. (b) A pericardial effusion and left pleural effusion were also observed. (c) At a high magnification, diffusely infiltrating atypical cells with darkly stained, irregularly shaped, and enlarged nuclei were observed (hematoxylin eosin stain). (d) The tumor cells showed positive CD20 immunostaining. The proliferated tumor cells were also positive for leukocyte common antigen and CD79a antibodies but negative for pancytokeratin and CD5, CD10, and CD30 antibodies. (not shown).

Fig. 3  Plain CT scan showing the lymphoma after 1 course of R-CHOP. (a) The mass was obviously decreased, (arrow: the stent inserted into the left brachiocephalic vein). (b) Disappearance of the left pleural and pericardial effusion.
References