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Case Report

Preoperative Proton Beam Therapy for Thymoma: A Case Report

Hideaki Kojima, MD,[1] Mitsuhiro Isaka, MD, PhD,[1] Masashi Nagata, MD,[1] Tsuyoshi Onoe, MD, PhD,[2] Shigeyuki Murayama, MD, PhD,[2] and Yasuhisa Ohde, MD, PhD[1]

We performed preoperative proton beam therapy for locally advanced thymoma and subsequently achieved complete resection. The patient was 31-year old woman, in whom chest computed tomography revealed a huge mass at the left anterior mediastinum. We diagnosed locally advanced type B3 thymoma. Because of the potential for complications to the lung and heart, definitive photon radiation therapy would have been difficult to administer. Therefore, we performed proton beam therapy, which could be administered within dose limitations. After proton beam therapy, the huge tumor had remarkably decreased in size. We were thereby able to achieve complete resection. As of 24 months after surgery, the patient has not developed any severe adverse events associated with proton beam therapy. Our experience suggests that preoperative proton beam therapy may be an effective modality for reducing tumor size, facilitating complete resection, and preventing toxicity of radiation therapy.

Keywords: proton beam therapy, thymoma, preoperative, locally advanced thymoma

Introduction

Achieving complete resection is the key to the treatment of thymoma.[1)] Masaoka stage I and II thymomas are generally managed with surgery and it is possible to perform complete resection. However, in cases of locally advanced thymoma (Masaoka stage III), complete resection requires extensive surgical resection, which has occasionally been difficult. It has been thought that the administration of preoperative radiation therapy (RT) might improve the rate of complete resection in patients with stage III thymomas.[2)] Yet, preoperative proton beam therapy (PBT) for thymoma has never been reported. Here, we describe a case of locally advanced thymoma that was completely resected after PBT.

Case Report

A 31-year old woman was admitted to our hospital with an anterior mediastinal tumor. She initially presented with chest pain, and chest computed tomography revealed a mass sized 17.0 cm × 10.4 cm × 9.7 cm (estimated volume: 768 cm^3) at the left anterior mediastinum (**Fig. 1**). Computed tomography-guided needle biopsy yielded a pathological diagnosis of type B3 thymoma. The large mass invaded the left upper lobe and mediastinal fat tissue, and had broad contact with the main pulmonary artery to the left pulmonary artery and chest wall (**Fig. 1**). The final clinical diagnosis was Masaoka stage III thymoma. Complete resection might not have been achieved by pneumonectomy and extensive resections of the neighboring organs. Furthermore, considering the patient's age and the future possibility of pregnancy, it was preferred that

[1]*Division of Thoracic Surgery, Shizuoka Cancer Center, Sunto-gun, Shizuoka, Japan*
[2]*Division of Proton Therapy, Shizuoka Cancer Center, Sunto-gun, Shizuoka, Japan*

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Corresponding author: Hideaki Kojima, MD. Division of Thoracic Surgery, Shizuoka Cancer Center, 1007 Shimonagakubo, Nagaizumi-cho, Sunto-gun, Shizuoka 411-8777, Japan
Email: h.kojima@scchr.jp

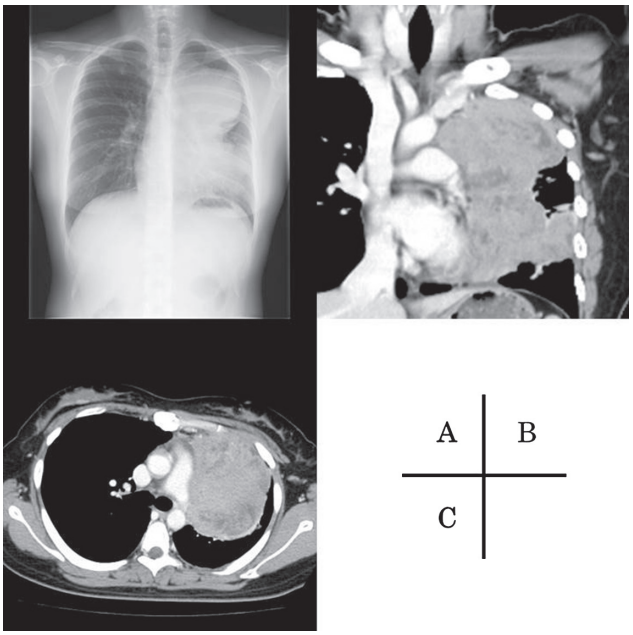

Fig. 1 Radiographic findings of the tumor before proton beam therapy. (**A**) Chest radiography showed a large anterior mediastinal tumor. (**B, C**) Chest computed tomography revealed a mass sized 17.0 cm × 10.4 cm × 9.7 cm at the left anterior mediastinum. The large mass invaded the left upper lobe and mediastinal fat tissue.

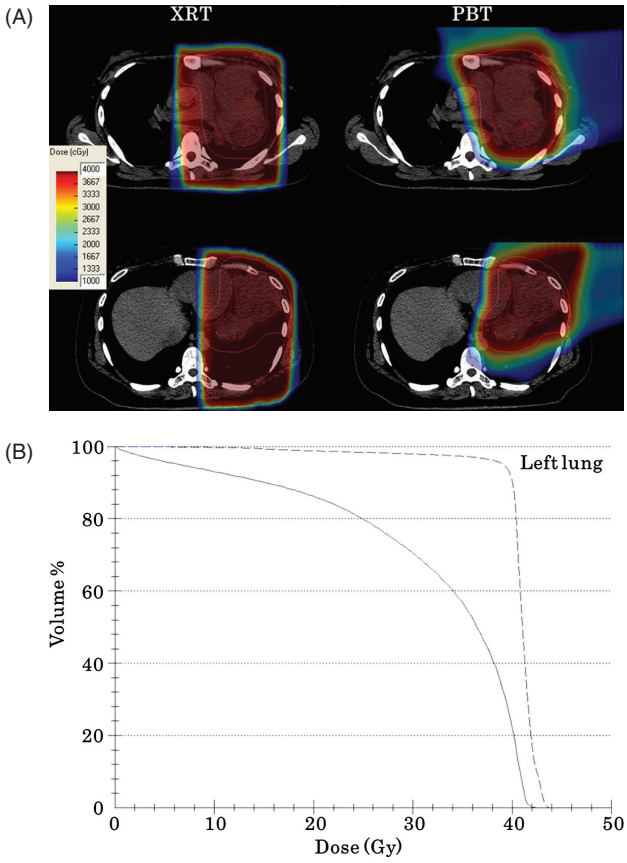

Fig. 2 (**A**) Colorwash isodose distribution for photon radiation therapy and proton beam therapy. The GTV is outlined by the red line, and the PTV is outlined by the pink line. (**B**) Dose-volume histogram of the left lung for proton beam therapy (solid line) and photon radiation therapy (dotted line). XRT: photon radiation therapy; PBT: proton beam therapy; GTV: gross tumor volume; PTV: planned target volume

pneumonectomy and chemotherapy be avoided. Definitive photon (X-ray) RT (XRT) of 60 Gy using 3-dimensional conformal RT would have been difficult to administer because of the potential for complications to the lung (V20: over 35%) and heart (mean dose: 45 Gy). We therefore selected definitive PBT, because it could be administered within dose limitations. Considering a plan for possible surgery at a later point, a PBT plan was initially developed to deliver 40 Gy (RBE) (Relative Biological Effectiveness (RBE) = 1.1) to the planned target volume in 20 fractions. **Figure 2A** shows the colorwash isodose distributions for XRT and PBT. **Figure 2B** shows the dose-volume histograms for the left lung. Compared with XRT, PBT reduced the mean dose to the left lung by 8 Gy. In practice, it took 29 days to complete the planned PBT regimen. After 40 Gy (RBE) PBT, the large tumor decreased in size to 11.5 cm × 8.8 cm × 6.7 cm (estimated volume: 268 cm^3) (**Fig. 3**). We judged that complete resection was possible without pneumonectomy, and the treatment strategy was changed from definitive PBT to surgery. We performed thymectomy and extensive resection of the left upper lobe of the lung, phrenic nerve, and pericardium, which were removed completely via median sternotomy on the 42nd day after the start of PBT. PBT did not result in any technical difficulties during surgery. Pathology revealed a stage II, type A thymoma with microscopic negative margins. As of 24 months after surgery, the patient has not developed any severe adverse events of PBT.

Discussion

Regarding PBT for thymoma, only one report has described postoperative therapy.[3] To the best of our knowledge, the current report provides the first description of preoperative PBT for thymoma. Previously, Onuki et al. reported that preoperative RT effectively reduced tumor size, thus facilitating complete resection of stage III thymoma.[2] Considering the present case, even with

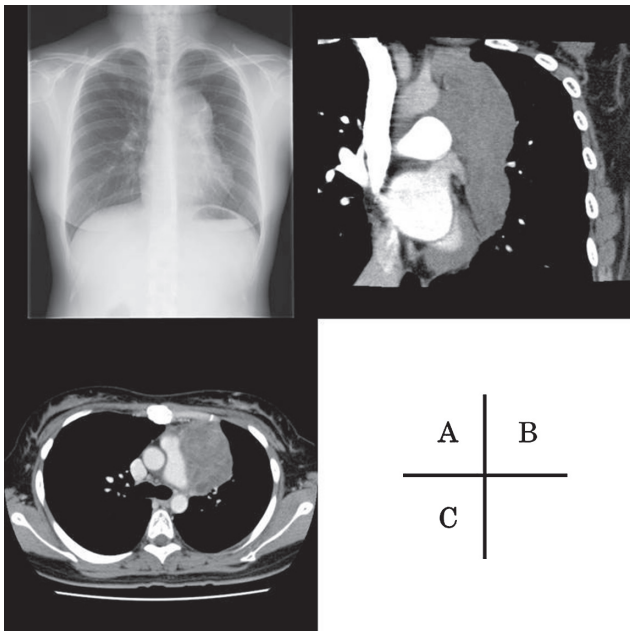

Fig. 3 Radiographic findings of the tumor after proton beam therapy. (**A**) Chest radiography showed that the tumor had significantly decreased in size. (**B, C**) The tumor was reduced in size to 11.5 cm × 8.8 cm × 6.7 cm.

the most conformal photon radiation technique, the mean dose to the organs at risk would have been quite high. Due to the physics of an X-ray, many beams are required to irradiate a deep, large tumor using XRT, thereby increasing the irradiation of healthy tissues and organs. On the other hand, proton particles enter the body, deposit most of their energy in the final portion of their trajectory, and then stop (this behavior is known as the Bragg peak). Therefore, PBT allows fewer beams to be used, which spares normal tissues and organs. Komaki and Gomez recommended PBT (if available) for cases of thymic malignancies treated with definitive RT.[4] As compared with XRT, PBT reduced the mean dose to the left lung by 8 Gy in our case. As a result, we were able to perform PBT safely and achieved complete resection without any severe adverse events.

In this case, histological change was observed after preoperative PBT. Onuki et al. reported this phenomenon as radiation-induced histological change, which was prominent in type B1 and type B2 thymomas.[2] This change seems to result from the different radioresponses of the tumor epithelial cells and lymphocytes.[2] However, it is also possible for small biopsy specimens to be inconsistent with the surgical specimen because of tumor heterogeneity.

One disadvantage of PBT is that it is more affected by respiratory motion and heartbeat in comparison with XRT. Because there have been few reports of PBT for thymoma, its effectiveness remains generally unknown. We need to accumulate more data on PBT for thymoma to validate its benefits.

Conclusion

Our experience suggests that preoperative PBT may be an effective modality for reducing tumor size, facilitating complete resection, and preventing RT toxicity. PBT should be considered in similar cases with huge thymoma, in whom there are concerns regarding the toxicity associated with RT.

Disclosure Statement

There are no conflicts of interest to declare.

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