Abstract. Thymic carcinoma is a rare neoplasm with a poor prognosis. We report the clinical course of a patient who received complete surgical resection after effective induction treatment. A 72-year-old woman with advanced thymic carcinoma (squamous cell carcinoma, stage IVb) was considered as nonresectable due to invasion of neighboring organs and mediastinal lymph node metastasis. Two cycles of chemotherapy, consisting of paclitaxel (180 mg/m²) plus cisplatin (80 mg/m²), combined with thoracic radiotherapy (total 54 Gy) were performed concurrently and complete radical resection could then be performed. She is currently alive and ambulatory and has remained disease-free for two years. This multimodal treatment may be a good treatment option for locally advanced thymic carcinoma.

Thymic carcinoma is a rare aggressive thymic neoplasm with a poor prognosis that was first reported by Shimosato et al. in 1977 (1). They analyzed eight cases of squamous cell carcinoma of the thymus and presented the concept of thymic carcinoma. Thirty years have passed since then and thymic carcinoma including thymic carcinoid separated by thymoma is now listed in the standard pathological classification of the World Health Organization (WHO) (2). Among thymic tumors, thymoma occurs with the greatest frequency followed by thymic carcinoma, whereas thymic carcinoid is exceedingly rare. Surgery is the mainstay of therapy in resectable cases. Multimodal approaches are playing an increasingly important role in subtotally resected or nonresectable cases, but there are no studies that have evaluated third-generation drugs or concurrent use of chemoradiotherapy because of the rarity of this tumor. This report describes a patient with nonresectable locally advanced thymic carcinoma in whom complete surgical resection was achieved after concurrent chemoradiotherapy.

Clinical Summary

The patient was a 72-year-old woman with no smoking history in whom an abnormal shadow was pointed out on chest images. She was admitted to our hospital for further examination and management of the shadow. Chest radiography demonstrated an enlarged mediastinal shadow on the right side (Figure 1A), while the thoracic CT scan demonstrated a large tumor (6.7 x 6.3 x 5.3 cm) invading the pericardium with multiple mediastinal lymph node metastases (Figure 1B). A diagnosis of thymic carcinoma (squamous cell carcinoma) was based on percutaneous CT-guided biopsy findings. Against the background of hyalinized connective tissue, atypical cell nests proliferated sporadically, and a few keratinizations were observed (Figure 2). Immunohistochemical staining of the tumor cells was positive for CD5, which is useful marker for thymic carcinoma (3). Although systemic workups did not detect any distant metastases, the patient was diagnosed in stage IVb according to the Masaoka staging system (4) because of mediastinal lymph node metastasis. Two cycles of chemotherapy consisting of paclitaxel (180 mg/m², 3 h) and cisplatin (80 mg/m², 1 h) on day 1 were administered every 3 weeks. She received thoracic radiotherapy (1.8 Gy x 30 fractions) in combination with concurrent chemotherapy. During treatment, grade 3 leukopenia and neutropenia developed, but not grade 3 or 4 non-hematological toxicities such as esophagitis or pneumonitis. Thoracic radiotherapy was interrupted for one week by hematological toxicities. The tumor size continued to decrease during and after treatment, and she achieved a partial response (37%
reduction in tumor diameter) (Figure 3). Subsequently, complete radical resection with lymphadenectomy via sternotomy could be performed five months after the start of induction treatment. The resected tumor still contained a few viable tumor cells and was mainly comprised of hyaline. The patient is still alive and ambulatory and has remained disease-free for two years.

Discussion

Thymic carcinoma is a rare aggressive neoplasm. In most cases, these lesions are found as advanced disease classified in stage III or IV of the Masaoka staging system. Although complete surgical resection is the main treatment for this tumor, it is not always achievable because of local invasion of neighboring organs or the presence of diffuse pleural or pericardial implants. The present patient was diagnosed as having advanced IVb stage with mediastinal lymph nodes metastasis and was considered nonresectable. Three prospective tri-modal regimens have been reported in thymic carcinoma (5-7). All of those performed induction chemotherapy, followed by surgery, and then post-operative radiotherapy, and have yielded overall survival rates of 78% for 10 years (6) or 79% for 7 years (7). Cisplatin is a key agent for chemotherapy against thymic tumors and was included in all of the reported regimens; adriamycin/ cisplatin/ vincristine/cyclophosphamide (ADOC) or cisplatin/ etoposide (5), cisplatin/epirubicin/etoposide or cisplatin/ adriamycin/cyclophosphamide (6), and adriamycin/ cisplatin/ cyclophosphamide/prednisone (7). Theoretically, induction chemotherapy with concurrent radiotherapy seems to be ideal for these cases similar to that in other malignancies; however, there is no information from prospective or retrospective studies and few case reports are available.

Paclitaxel is a new agent that induces excessive polymerization of tubulin, and has demonstrated clinical activity in a wide variety of malignancies, including ovarian, breast, head and neck, and lung cancer. Morio et al. (8) presented a case of stage IVb thymic carcinoma with lymph node metastasis and achieved complete resection after induction therapy with weekly paclitaxel plus cisplatin and concurrent radiotherapy (total 40 Gy). Another case of advanced thymic carcinoma treated with induction docetaxel, which is also a new agent classified as a taxan like paclitaxel, plus cisplatin and concurrent radiotherapy (total 40 Gy) also achieved complete resection (9). Therefore, we selected paclitaxel plus cisplatin with concurrent radiotherapy for induction treatment, although the supporting evidence is currently limited. We could not consider resection at the start of therapy, since the dose of radiation (total 54 Gy) was excessive for induction. Fortunately, this patient was able to undergo complete resection two months after completion of the induction therapy. The curability of the surgery was supported by her good status and she has remained disease-free for two years after treatment.
We encountered a case of a patient with advanced thymic carcinoma who was then able to undergo complete surgical resection after concurrent use of paclitaxel plus cisplatin chemotherapy and thoracic radiotherapy. This multimodal treatment may be a good treatment option for patients with locally advanced thymic carcinoma.

Figure 2. Pathological features of the percutaneous CT-guided biopsy specimen of mediastinal tumor.

Figure 3. Chest radiograph (A) and CT scan image (B) five months after chemoradiotherapy.
References


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