INTERNAL MEDICINE

□ CASE REPORT □

Two Cases of Thymic Carcinoma Initially Presenting as Bone Metastasis: A Clinical Report and the Usefulness of CD5 Immunohistochemistry for Assessing Bone Lesions

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Abstract

Thymic carcinoma frequently spreads to the pleural space, regional lymph nodes, liver and lungs. However, an initial clinical presentation involving spinal or multiple bone metastases in patients with thymic carcinoma is extremely rare. We experienced two cases of thymic carcinoma that initially presented with spinal compression and severe pain due to multiple bone metastases, respectively. Both patients were histologically diagnosed with metastatic thymic squamous cell carcinoma based on the findings of specimens resected from the metastatic bone lesions. We herein describe the clinical courses of these cases and review the characteristics of bone metastasis of thymic carcinoma.

Key words: thymic malignancy, spinal compression, hemiparesis, chemotherapy, mediastinal tumor

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Introduction

Thymic carcinoma is a thymic epithelial neoplasm exhibiting cytological malignant features and a clinical course that tends to be much more aggressive than that of thymoma (1-4). Thymic carcinoma, located in the anterosuperior mediastinum, frequently spreads to the pleural space, regional lymph nodes, liver and lungs (1, 2). Regarding bone involvement, there are several case reports of the detection of spinal metastasis in the late phase of the clinical course in patients with thymic malignancies, including thymic carcinoid tumors (5-7). However, an initial clinical presentation with spinal or multiple bone metastases in patients with thymic carcinoma is extremely rare (8). In addition, due to the paucity of cases, there is little information about the diagnostic approach or treatment in clinical practice.

We herein describe two cases of thymic carcinoma that initially presented with spinal compression due to tumor spread into the intraductal space and severe pain due to multiple bone metastases, respectively. Both patients were diagnosed with metastatic thymic carcinoma based on the findings of immunohistochemical examinations of specimens resected from the metastatic bone lesions using a thymic carcinoma-specific marker, CD5.

Case Reports

Case 1

A 50-year-old woman presented with a three-year history of back pain. A paravertebral mass had been noticed on chest radiography and computed tomography (CT) performed during a medical examination conducted two years previously; however, the patient had not wished to undergo any further examinations. One month prior to the current ad-

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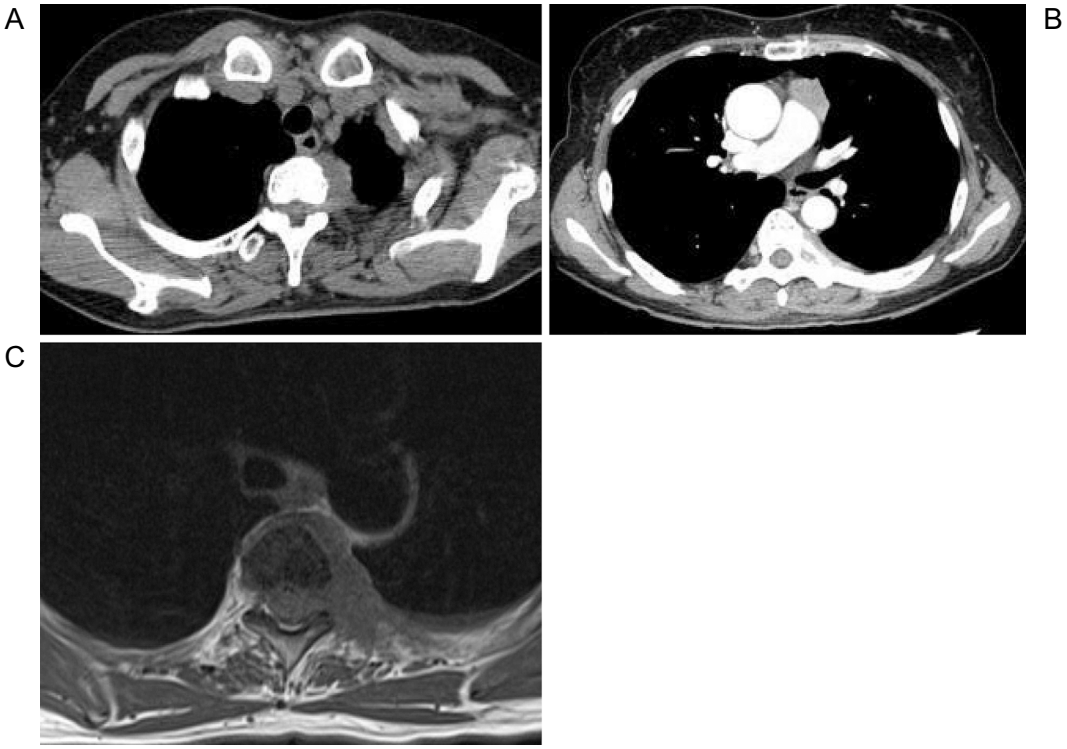

Figure 1. **Chest computed tomography demonstrated a left posterior mediastinal mass expanding along the pleura (A) and an anterior mass (B). The left posterior mediastinal mass involved the thoracic vertebra on chest magnetic resonance imaging (MRI) (C).**

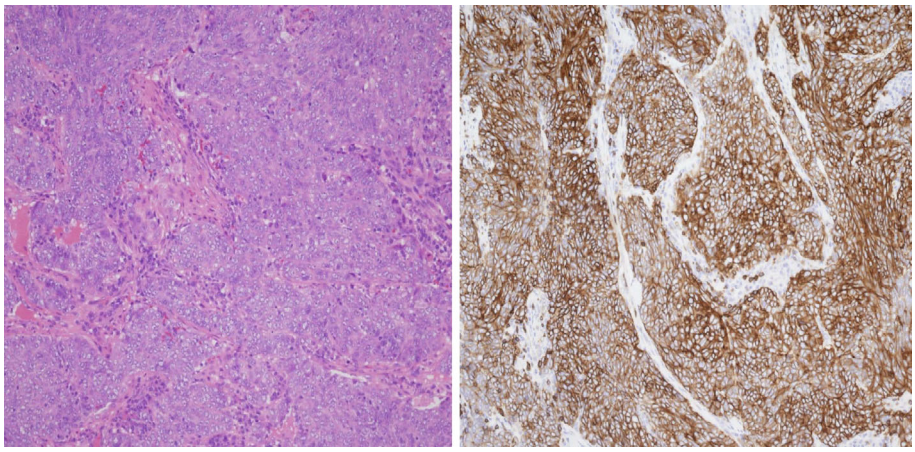

Figure 2. **The histological findings revealed squamous cell carcinoma (A). The tumor cells were positive for CD5 (B).**

mission, she developed progressive muscle weakness and numbness of the left leg. Chest CT demonstrated a left posterior mediastinal mass expanding along the pleura and an anterior mediastinal mass (Fig. 1A, B), while magnetic resonance imaging (MRI) revealed involvement of the mass in the thoracic vertebrae (Th3) (Fig. 1C). Laminectomy was performed to improve the leg paralysis, and the histopathological findings disclosed a diagnosis of squamous cell carcinoma, the tumor cells of which were positive for CD5 (Fig. 2). A tumor biopsy of the anterior mediastinum was also performed using video-assisted thoracic surgery, which pathologically confirmed the presence of thymic squamous cell carcinoma. Hence, the spinal involvement appeared to be due to direct invasion of the pleural spread of the thymic carcinoma; there were no other distant metastatic lesions. The patient therefore received chemotherapy with a combination of cisplatin (50 mg/m^2) and doxorubicin (40 mg/m^2) on day 1, vincristine (0.6 mg/m^2) on day 3 and cyclophosphamide (700 mg/m^2) on day 4 [cisplatin, doxorubicin, vincristine and cyclophosphamide (ADOC) chemotherapy]. Four cycles of ADOC chemotherapy and subsequent radiotherapy for Th2-5 were performed, and the chemotherapy

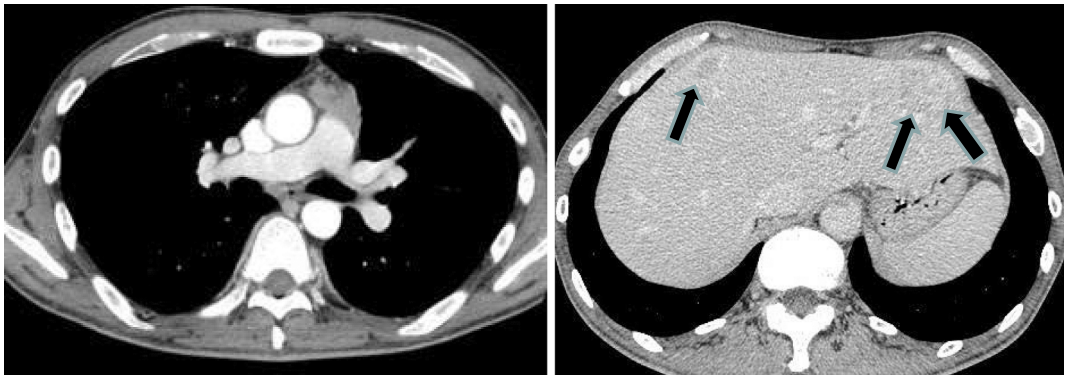

Figure 3. **Chest computed tomography showed abnormal masses in the anterior mediastinum (A) and liver (B).**

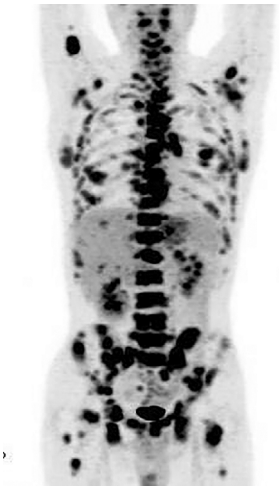

Figure 4. **^{18}F-Fluorodeoxy glucose positron emission tomography (FDG-PET) disclosed an abnormal uptake in multiple bone and lymph node lesions, including the masses in the anterior mediastinum and liver.**

and radiotherapy resulted in stable disease. Although slight right hemiparesis persisted, she has experienced no serious problems in her activities of daily living (ADLs), and she has remained well for approximately 1.5 years since the diagnosis.

Case 2

A 49-year-old man presented with a six-month history of low back pain and arthralgia. He had been admitted to a local hospital due to progressive pain. A physical examination performed at the time revealed no specific findings, although his performance status was 2 [Eastern Cooperative Oncology Group (ECOG) classification]. In addition, chest CT revealed abnormal masses in the anterior mediastinum and liver (Fig. 3), and ^{18}F-fluorodeoxy glucose positron emission tomography (FDG-PET) showed a positive uptake in multiple bone lesions, including the mediastinal and hepatic tumors (Fig. 4). A bone marrow biopsy of the ilium was subsequently performed, and the histological findings revealed squamous cell carcinoma with tumor cells positive for CD5 (Fig. 5). Morphine therapy was therefore initiated for pain, followed by the administration of ADOC chemotherapy. Although a partial response was achieved after four cycles of ADOC chemotherapy and the dose of morphine was reduced, the patient died 10 months after the initial chemotherapy due to disease progression.

Discussion

We herein described two cases of thymic carcinoma initially presenting with spinal cord compression and multiple bone metastases, respectively. According to the classification of Masaoka et al. (9), both patients had advanced disease with bone metastases (stage IVb). Neither patient had any respiratory symptoms resulting from the primary thymic carcinoma and were diagnosed based on the findings of histological specimens obtained from the metastatic bone lesions. Similar to that observed in the present cases, Liu et al. (8) described a case of thymic carcinoma in which the patient initially developed spinal metastasis and cord compression. However, the onset of initial clinical manifestations related to bone involvement is extremely rare in patients with thymic carcinoma. Therefore, clinical physicians should be aware of the possibility of initial bone involvement in this group.

Based on the database of the European Society of Thoracic Surgeons (ESTS), 47 of 229 thymic carcinomas showed recurrence after surgical intervention, among which three patients developed bone metastasis (10). In addition, Yano et al. (4) reported 30 cases of thymic carcinoma at various stages and identified one patient who developed bone metastasis during the clinical course of the tumor. Hence, bone metastasis is usually recognized parallel to disease recurrence after surgery or progression during follow-up and/or in the late stage of the disease.

However, little information is available regarding the prevalence of bone metastasis at the time of diagnosis in patients with thymic carcinoma, especially those with ad-

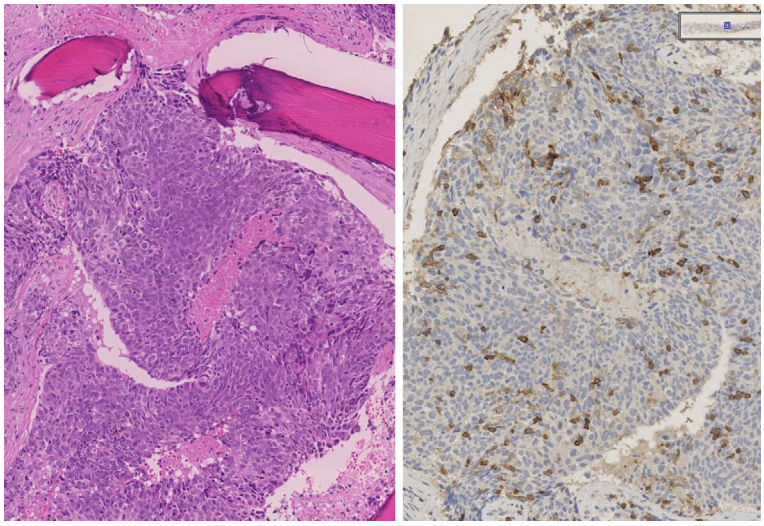

Figure 5. The histological findings revealed squamous cell carcinoma (A). The tumor cells were positive for CD5 (B).

vanced and metastatic thymic carcinoma. Yoh et al. (11) summarized 12 cases of advanced and unresectable thymic carcinoma treated with cisplatin, vincristine, doxorubicin and etoposide chemotherapy, among which one patient presented with bone metastasis prior to the commencement of therapy. We previously summarized the cases of 34 patients with advanced and unresectable thymic carcinoma treated at our institute (12). All patients were diagnosed based on histology of the primary lesion, and six of the subjects were found to have bone metastasis, including one patient with pain related to the involved bone site. Therefore, we speculate that bone involvement is not uncommon in cases of advanced thymic carcinoma and it is thus necessary to check for the presence of bone involvement in thymic carcinoma patients throughout their clinical course.

Although only a limited number of patients have been analyzed to date, the reported median survival time among patients with advanced and unresectable thymic carcinoma is 21.3-46.0 months (11-13). In the current case 2, ADOC chemotherapy was effective, achieving a partial response; however, the patient survived for only one year, which is shorter than that observed in other reports (11-13). Several studies of patients with thymic carcinoma have indicated that patients with hematogenous metastasis at the time of the initial diagnosis have a significantly poorer prognosis than those with lymphogenous metastasis (3, 14). Further case studies are therefore needed to clarify whether bone metastasis is a clinical prognostic factor.

In case 1, paralysis of the right leg continued after laminectomy. However, the myelopathy remained stable, and the patient was able to maintain her ADLs by herself. Based on the findings of a report by Liu et al. (8) and our experience, we consider spinal surgery to be preferable in patients with thymic malignancy exhibiting progressive myelopathy. If possible, complete surgical resection of the primary tumor remains the treatment of choice for maintaining ADLs, and several reports have suggested that thymic carcinoma is sensitive to chemotherapy (11-13). Although the response to chemotherapy or radiotherapy was classified as stable disease in case 1, we believe that the administration of adjuvant therapy after laminectomy may result in local control and the maintenance of ADLs.

The histological diagnoses in the present cases were made based on the findings of samples obtained from metastatic bone sites. In general, primary organs demonstrating histological findings of squamous cell carcinoma include the lungs, esophagus and head and neck. In the present cases, immunohistological examinations using CD5 were useful for confirming the primary site in the thymus. CD5, first recognized in subsets of lymphocytes (15), is also detected in cases of thymic carcinoma, but not thymoma or other malignant tumors (16-18). Several studies have focused on the CD5 expression in patients with squamous cell carcinoma in various malignant organs and found negative findings, except for thymic carcinoma (16-18). Therefore, CD5 is useful for making the differential diagnosis between thymic carcinoma and metastatic squamous cell carcinoma at various primary sites. In cases of cancer of unknown origin, particularly that involving the histological type of squamous cell carcinoma, CD5 immunostaining should be performed in clinical practice.

In summary, the present cases suggest that thymic carcinoma exhibits a variety of clinical features and should be considered in the differential diagnosis in patients who initially present with spinal or multiple bone metastases. Immunohistochemistry using CD5 should be performed to confirm the differential diagnosis of squamous cell carcinoma.

The authors state that they have no Conflict of Interest (COI).

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