



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).

References

1. Suster S, Rosai J. Thymic carcinoma. A clinicopathologic study of 60 cases. *Cancer* **67**: 1025-1032, 1991.
2. Hsu CP, Chen CY, Chen CL, Hsu NY, Wang JH, Wang PY. Thymic carcinoma. Ten years' experience in twenty patients. *J Thorac Cardiovasc Surg* **107**: 615-620, 1994.
3. Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. *Ann Thorac Surg* **76**: 878-884, 2003.
4. Yano M, Sasaki H, Yokoyama T, et al. Thymic carcinoma 30 cases at a single institution. *J Thoracic Oncol* **3**: 265-269, 2008.
5. Georgy BA, Casola G, Hesselink JR. Thymic carcinoid tumors with bone metastases. A report of two cases. *Clin Imaging* **19**: 25-29, 1995.
6. Rao KC, Jhaveri HS, Gellad FE. Carcinoid tumor with intradural spinal metastases. *J Comput Tomogr* **12**: 258-260, 1998.
7. Nagel SJ, Hughes G, Ugokwe KT, Prayson RA, Krishnaney AA. Spinal carcinoid metastasis with dural invasion. *World Neurosurg* **2011** **76**: 478.e7-478.e11, 2011.
8. Liu T, Qiu G, Tian Y. Thymic carcinoma with primary spine metastasis. *J Clin Neurosci* **18**: 840-842, 2011.
9. Masaoka A, Monden Y, Nakahara K, Tanioka T. Follow-up study of thymomas with special reference to their clinical stages. *Cancer* **48**: 2485-2492, 1981.
10. Ruffini E, Detterbeck F, Van Raemdonck D, et al; European Society of Thoracic Surgeons Thymic Working Group. Thymic carcinoma: a cohort study of patients from the European society of thoracic surgeons database. *J Thorac Oncol* **9**: 541-548, 2014.
11. Yoh K, Goto K, Ishii G, et al. Weekly chemotherapy with cisplatin, vincristine, doxorubicin, and etoposide is an effective treatment for advanced thymic carcinoma. *Cancer* **98**: 926-931, 2003.
12. Agatsuma T, Koizumi T, Kanda S, et al. Combination chemotherapy with doxorubicin, vincristine, cyclophosphamide, and platinum compounds for advanced thymic carcinoma. *J Thorac Oncol* **6**: 2130-2134, 2011.
13. Igawa S, Murakami H, Takahashi T, et al. Efficacy of chemotherapy with carboplatin and paclitaxel for unresectable thymic carcinoma. *Lung Cancer* **67**: 194-197, 2010.
14. Kondo K, Monden Y. Lymphogenous and hematogenous metastasis of thymic epithelial tumors. *Ann Thorac Surg* **76**: 1859-1864, 2003.
15. Tateyama H, Eimoto T, Tada T, Inagaki H, Hattori H, Takino H. Apoptosis, bcl-2 protein, and Fas antigen in thymic epithelial tumors. *Mod Pathol* **10**: 983-991, 1997.
16. Dorfman DM, Shahsafaei A, Chan JK. Thymic carcinomas, but not thymomas and carcinomas of other sites, show CD5 immunoreactivity. *Am J Surg Pathol* **21**: 936-940, 1997.
17. Hishima T, Fukayama M, Fujisawa M, et al. CD5 expression in thymic carcinoma. *Am J Pathol* **145**: 268-275, 1994.
18. Tateyama H, Eimoto T, Tada T, Hattori H, Murase T, Takino H. Immunoreactivity of a new CD5 antibody with normal epithelium and malignant tumors including thymic carcinoma. *Am J Clin Pathol* **111**: 235-240, 1999.

