INTERNAL MEDICINE

□ CASE REPORT □

Mantle Cell Lymphoma Mainly Involving Thoracic Lesions: Two Case Reports

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Abstract

Most mantle cell lymphoma patients show remarkable disseminated disease at the initial diagnosis. We describe two cases of mantle cell lymphoma mainly involving thoracic lesions at the initial presentation of the disease. The clinical presentations were right hilar lymphadenopathy in one case and right pleural thickness in the other. The diagnosis of mantle cell lymphoma was confirmed by immunohistochemistry, including CD5, CD 20, and cyclin D1, and the presence of t(11 ; 14)(q13 ; q32) by fluorescence *in situ* hybridization. These thoracic manifestations at the initial diagnosis should be taken into consideration for the clinical spectrum of mantle cell lymphoma.

Key words: hilar lymphadenopathy, R-CHOP, chemotherapy, non-Hodgkin lymphoma

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Introduction

Mantle cell lymphoma (MCL) is a distinct type of B-cell non-Hodgkin lymphoma characterized by t(11 ; 14)(q13 ; q32) and cyclin D1 overexpression (1-3). The affected patients are mainly middle-aged or older, and they often present with advanced stage disease (Stages III-IV), frequently involving multiple extranodal sites (2-5). Patients with MCL frequently show bone marrow, spleen, and gastrointestinal involvement (4-6). However, thoracic involvement is extremely rare, and little information has been reported regarding the clinical manifestations at the initial presentation (7). We report here two cases of mantle cell lymphoma presenting with thoracic lesions; one was hilar lymphadenopathy and the other showed pleural and chest wall involvement.

Case Report

Case 1

A 72-year-old man with history of pneumoconiosis was admitted to our hospital because of an abnormal shadow on chest computed tomography (CT) scans detected during a health examination. The abnormal shadow was a swollen lymph node in the right hilum (Fig. 1A). He was a heavy smoker (Brinkman index 1000), and he had a history of exposure to asbestos. He had been asymptomatic, including no B symptoms (night sweats, fever, or loss of weight). Physical examination revealed no superficial lymph node swelling or hepatosplenomegaly. A nuclear gallium scan revealed unusual high intensity uptake in the only lymph node of the right hilum. Laboratory studies showed slightly elevated LDH 240 IU/L (normal: 115-245) and soluble IL-2 receptor 832 U/mL (normal: 145-519), while the other findings were normal. Endobronchial ultrasound-guided transbronchial needle aspiration was performed for the lymph node in the

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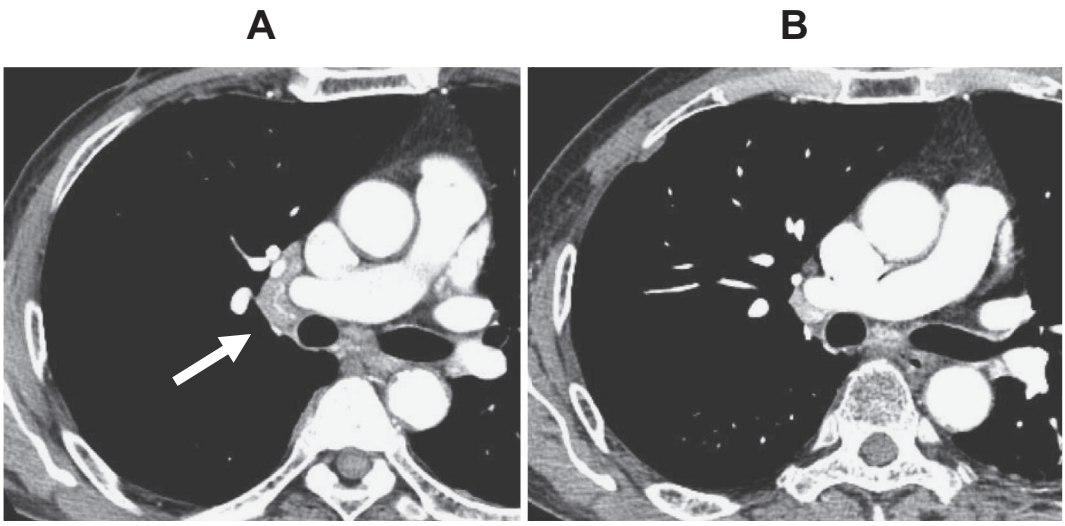

Figure 1. **Chest computed tomography (CT) scan on admission (A) and after chemotherapy (B) in case 1. Chest CT scan showed a swollen lymph node in the right hilum before chemotherapy (arrow), and the lymphadenopathy disappeared after chemotherapy (B).**

right hilum, and the histological findings were consistent with MCL. Aspiration examination in bone marrow showed slight involvement, but other systemic examinations including upper and lower endoscopy revealed no involvement. Thus, the patient was diagnosed as MCL in stage IV and low-intermediate type in international prognostic index (IPI). He received 6 cycles of R-COP chemotherapy (rituximab, cyclophosphamide, vincristine, prednisolone) and the right hilum lymphadenopathy disappeared (Fig. 1B). He has remained well for over 4 years without any evidence of relapse.

Case 2

A 78-year-old man was referred to our hospital because of a subcutaneous tumor in the anterior chest wall. He underwent partial resection of the left lung (left S^{1+2}) 8 years previously, and right upper lobectomy was subsequently performed 3 years previously because of adenocarcinoma of the lung. He had been observed without any treatment of systemic chemotherapy or radiotherapy. He had noticed a tumor mass in the anterior chest wall 3 months previously, and the mass had gradually increased in size. At least, no abnormal findings were observed on the chest CT 6 months before the notification. Physical examination revealed a subcutaneous tumor measuring 8×6 cm in the anterior chest. Chest CT scans showed not only the subcutaneous tumor in the anterior chest, but also a tumor in the right pleura (Fig. 2A). Fluorine-18 fluorodeoxyglucose positron emission tomography showed abnormal uptake in both tumors with a maximal standardized uptake value of 7.4. The results of laboratory studies indicated an LDH level of 278 IU/L and soluble IL-2 receptor level of 652 U/mL. Percutaneous needle biopsy of the subcutaneous tumor in the anterior chest and then CT-guided percutaneous needle biopsy of the tumor in the right posterior chest wall was also performed. Both histological findings were identical and compatible with MCL. Systemic examination including bone marrow, upper and lower endoscopy revealed no evidence of disease in other organs (stage II and low-intermediate type in IPI). The patient received 6 cycles of R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone) and chest radiographic findings showed a complete response (CR) (Fig. 2B). However, the disease relapsed 8 months after the diagnosis in the anterior chest wall without any evidence of distant recurrence. The patient was treated again with 6 cycles of R-CHOP and second CR was achieved.

The histological findings in both cases are shown in Fig. 3 (case 1) and Fig. 4 (case 2). Histological examination of sections stained with Hematoxylin and Eosin showed diffuse proliferation of small- to medium-sized atypical lymphocytes. Immunohistochemical analysis showed that the lymphoid cells stained positive for CD20, CD5, and cyclin D1, but negative for CD3. Fluorescence *in situ* hybridization (FISH) using LSI IGH/CCND1 XT Dual-color Dual fusion probe detected fusion signals indicative of t(11 ; 14)(q13 ; q32) in both samples (Fig. 5).

Discussion

Here, we described two cases of MCL mainly involving thoracic lesions. Both cases showed typical histological and immunohistological findings of MCL, which were confirmed by the presence of t(11 ; 14)(q13 ; q32) on FISH.

MCL frequently involves multiple extranodal sites and presents with advanced stage disease at the initial diagnosis (2-6). Thus, we speculate that thoracic involvement may parallel disease progression and reflect advanced MCL systemically. Indeed, there were a few case reports of thoracic lesions as a relapsed site or as one of the multiple localizations of the MCL (2, 8). However, little information is available about the prevalence of thoracic involvement in the in-

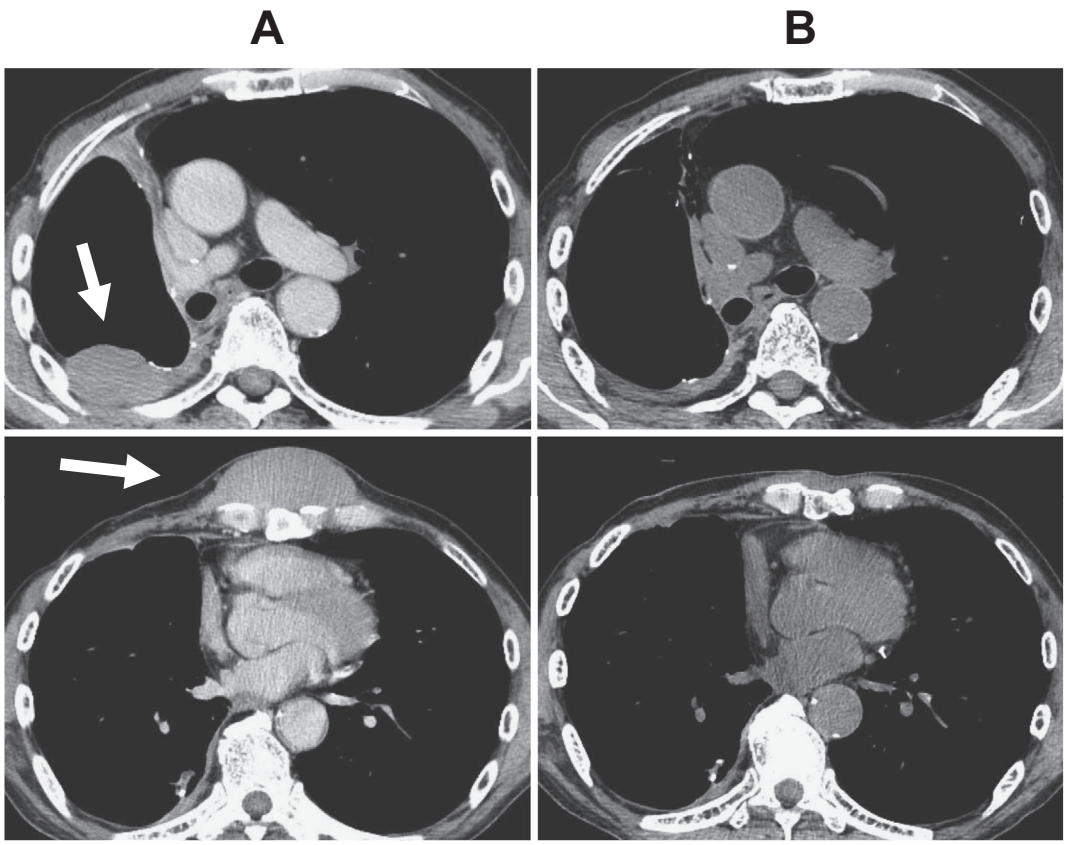

Figure 2. **Chest computed tomography (CT) scan on admission (A) and after chemotherapy (B) in case 2. Chest CT scans showed a subcutaneous tumor in the anterior chest wall and a tumor on the right pleura before chemotherapy (A). Both tumors disappeared after chemotherapy (B).**

itial presentation of MCL. Ianotto et al (7) described a case of MCL initially presenting acute dyspnea with single tracheal localization. Thus, we would like to emphasize that as thoracic involvement at initial presentation of MCL is uncommon, clinicians, especially chest physicians, should consider the possibility of various modes of presentation in MCL.

MCL is an aggressive B-cell lymphoma, accounting for 5%-10% of all non-Hodgkin lymphomas (2). A definitive diagnosis of MCL is made based on appropriate immunohistochemical staining. In general, primary pulmonary lymphoma represents only 0.4%-3% of extranodal non-Hodgkin lymphomas (9, 10) and 0.5%-1.0% of primary pulmonary malignancies (9, 11). Thus, malignant lymphoma in pulmonary origin itself is very rare. Furthermore, low-grade B-cell lymphoma, *e.g.*, mucosa-associated lymphoid tissue (MALT) non-Hodgkin lymphoma, is the most frequent disease among thoracic malignant lymphomas (9, 10, 12), which requires quite different therapeutic strategies and shows a better prognosis compared with other types of non-Hodgkin lymphoma. MCL initially presenting with thoracic involvement is more unusual in thoracic non-Hodgkin lymphomas. Radiographic and clinical findings are not useful for distinguishing MCL from other non-Hodgkin lymphomas (3, 4, 12). Furthermore, with regard to prognosis, the 5-year survival rate in MCL is <30%, which is significantly less than for other small B-cell lymphomas (2-5). Thus, the presence of MCL in thoracic diseases should be considered and distinguished histologically from other types of non-Hodgkin lymphoma in patients with suspected malignant lymphoma.

Case 1 had a history of pneumoconiosis and an exposure to asbestos and developed MCL. Although an increased risk of the exposure to these dusts, especially asbestos, for a development of non-Hodgkin's lymphoma was speculated (13), Seidler et al (14) recently reported no statistically significant association between cumulative asbestos exposure and the risk of any lymphoma subtypes including MCL. Thus it is likely that only asbestos is unrelated to the development of MCL in case 1, but the possible risk of simultaneous coexistences of a history of heavy smoker and pneumoconiosis in case 1 remains unclear.

We speculated that the origin of MCL in the first case was the right hilar lymph node, but the primary disease site in the second case was unclear. In a review of 34 patients with malignant lymphoma involving the pleura detected by pleural biopsy, Vega et al (15) found that 6 cases could be considered to have primary pleural lymphoma. As such primary pleural lymphoma was reported previously, we speculated that the right pleura could have been the site of origin of MCL in the second case. Indeed, Hatzibougias et al (16) reported a case of MCL that developed from the pleura. The

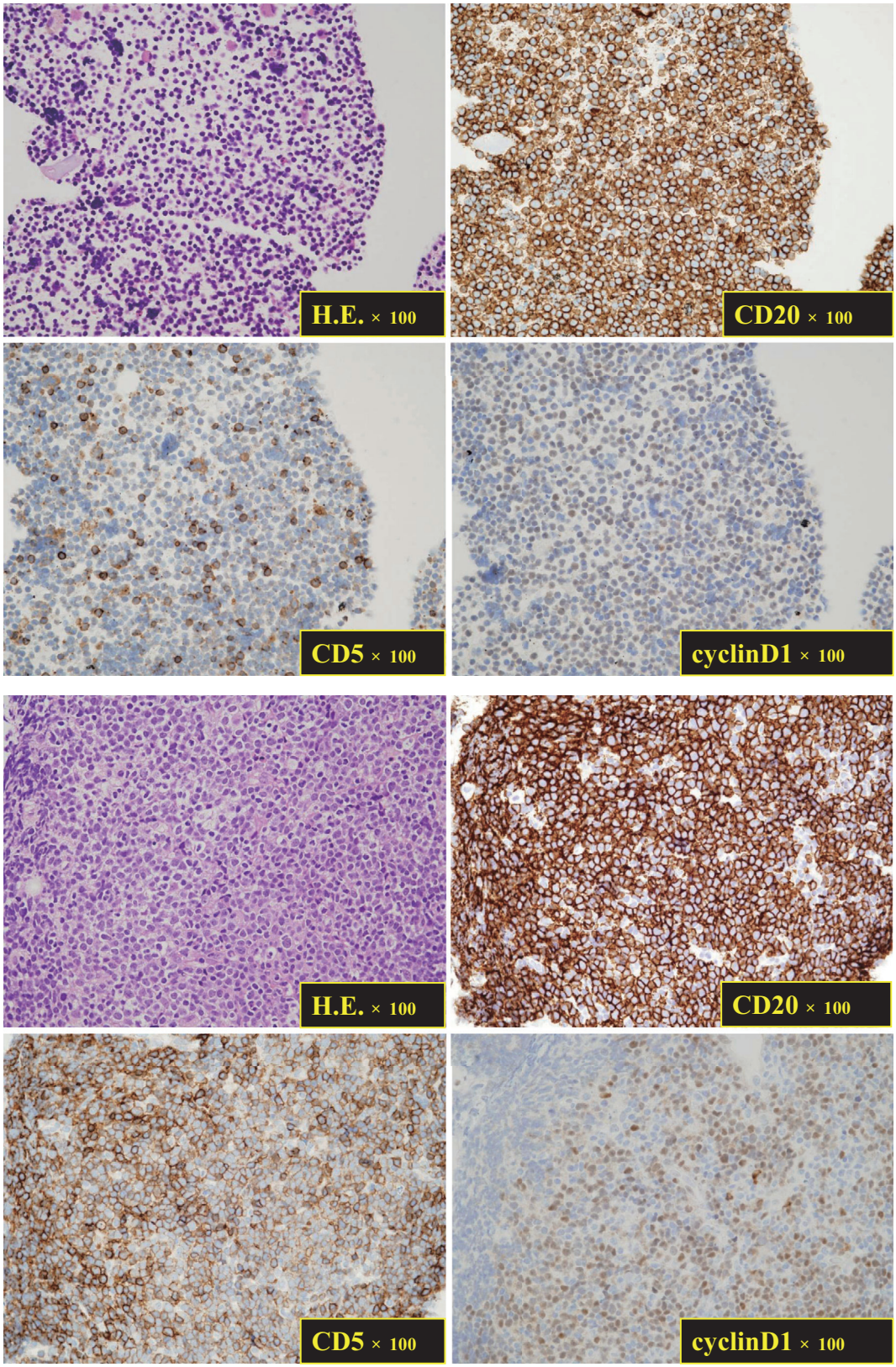

Figure 3 and 4. **Pathological findings are shown in Figure 3 (case 1) and Figure 4 (case 2). Histological examination of sections stained with Hematoxylin and Eosin staining showed diffuse proliferation of small- to medium-sized atypical lymphocytes. Immunohistochemical analyses showed that the lymphoid cells stained positive for CD20, CD5, and cyclin D1 in both cases.**

disease was discovered incidentally during an operation for pneumothorax.

In general, the clinical course of MCL patients is aggressive with an overall survival rate of around 3-4 years. In addition, Yatabe et al (17) analyzed the clinical characteristics of MCLs with and without cyclin D1 overexpression and re-

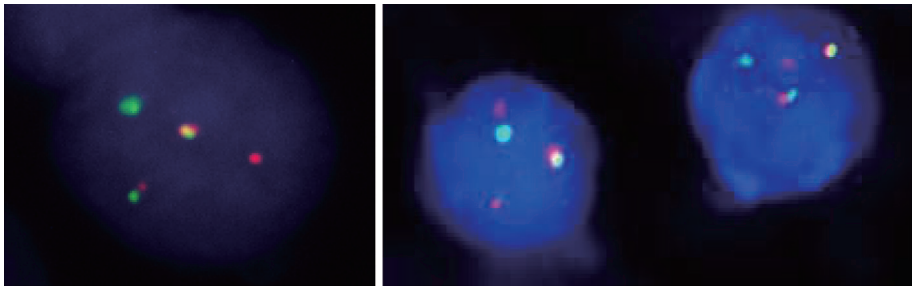

Figure 5. **Fluorescence *in situ* hybridization (FISH) showed the presence of *t*(11;14)(q13;q32) as the only abnormality. 11q13; LSI CCDN/MYEOV (orange spectrum), 14q32; LSI IGH as (green spectrum).**

ported that cyclin D1-positive MCL showed significantly poorer survival than cyclin D1-negative MCL. The first patient in the present study has remained well for over 4 years without any signs of relapse, but the second patient showed early relapse. The second patient showed CR with salvage chemotherapy, but new therapeutic strategies may be needed.

In summary, we presented two cases of MCL mainly involving thoracic lesions. Thoracic MCL seems to show nonspecific clinical and radiographic manifestations compared to other non-Hodgkin lymphomas. Based on the observations in these two cases, thoracic MCL should be recognized immunohistologically from other thoracic malignant lymphomas and malignancies. As mantle cell lymphoma initially presenting with thoracic lesions is rare, further clinical experience is required to identify the features of such cases.

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

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