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Mediastinal Malignant Lymphoma Difficult to Diagnose: A Patient Report

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We report a 58-year-old man who suffered from shortness of breath on exertion with wheezing. A chest enhanced computed tomography (CT) scan showed an irregular tumor in the middle mediastinum involving the right main pulmonary artery, vena cava superior and right main bronchus. Transbronchial lung biopsy and endobronchial ultrasound-guided transbronchial needle aspiration yielded no evidence for a pathological diagnosis of malignancy. We employed mediastinoscopy, which led to a diagnosis of lymphoid reactive change. 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) scan revealed a high FDG uptake in the tumor lesion. Because the CT scan and FDG-PET findings led to a marked suspicion of malignancy, we decided to attempt biopsy by a video-assisted thoracoscopic surgery (VATS) approach. Flow cytometry showed a monoclonal pattern, and the final diagnosis was mediastinal follicular lymphoma both pathologically and immunohistologically. The patient achieved a complete remission by following chemotherapy. Low-grade malignancy type of lymphoma such as follicular lymphoma that generally contains small-cell components often presents a diagnostic challenge and the VATS approach was effective for the diagnosis of such type of mediastinal lymphoma.

Key words: follicular lymphoma; malignant lymphoma; mediastinal tumor

Low-grade malignancy type of lymphoma often presents a diagnostic challenge (Jaffe, 2009). We report a case of mediastinal follicular lymphoma which could not be diagnosed employing bronchoscopic or mediastinoscopic biopsy, but was finally diagnosed using thoracoscopic biopsy, with a review of the literature.

Patient Report

A 58-year-old man experienced exertional dyspnea and wheezing, and visited a local hospital. Chest X-ray showed right hilar enlargement, and he was referred to our department. The serum C-reactive protein was slightly high, at 2.07 mg/dL, the tumor marker Sialyl Lex-i antigen was high, at 52 U/mL, and other tumor markers were within normal limits. Chest X-ray showed an ill-defined mass in the right hilum, accompanied by secondary pneumonia in the right lung field. The chest enhanced computed tomography (CT) scan (Fig. 1) revealed a tumor about 9 by 5 cm extending from the middle mediastinum to the right hilum, involving the right main pulmonary artery, superior vena cava and right main bronchus, becoming a conglomerate mass with lymph nodes. Bronchoscopic biopsy of the tumor extending from the mediastinum to the

Abbreviations: CD, cluster of differentiation; CT, computed tomography; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; FDG-PET, 18F-fluorodeoxyglucose-positron emission tomography; VATS, video-assisted thoracoscopic surgery

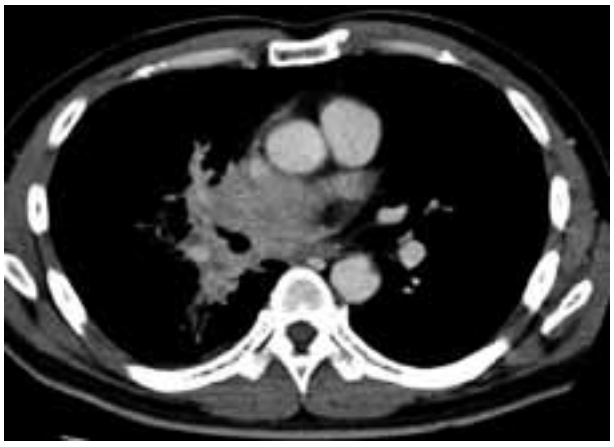

Fig. 1. Chest CT scan shows an irregular tumor about 9 × 6 cm in size in the middle mediastinum expanding to the right hilum involving the right main pulmonary artery, vena cava superior and right main bronchus. CT, computed tomography.

right hilum did not show a clearly abnormal mass lesion in the lumen, but the angle of the bifurcation between the middle lobar branch and inferior main bronchus was dull. Biopsies from the orifices of the right B5, B6 and B8 bronchi revealed no malignant lesions. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsies of the subcarinal lymph node and right main bronchus lymph node also showed no malignant findings. Re-bronchoscopy identified edema and stenosis at the orifice of the right B6 bronchus. Biopsies of the spurs at the orifices of B6 and B7 bronchi showed the infiltration of small lymphocytes, which was considered difficult to diagnose. Since the chest CT findings raised a strong suspicion of a malignant tumor, mediastinoscopic biopsy was performed on a grayish-white, enlarged pretracheal lymph node. Frozen-section examination revealed no epithelial components, thus excluding malignant tumors such as lung cancer, and leading to a suspicion of malignant lymphoma. However, the degree of lymphocytic atypia was slight, and the results of flow cytometry indicated a benign lesion, which led to the only diagnosis of a reactive lymph node. 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) showed a high FDG uptake in the tumor extending from the middle mediastinum to the right hilum, with maximum standardized uptake values of 11.55 in the early phase and 13.23 in the delayed phase. Since these findings raised a strong suspicion of a malignant tumor, we decided to perform a thoracoscopic biopsy. Thoracoscopy revealed an ill-defined, whitish tumor diffusely invading from the pulmonary hilum to the middle mediastinum (Fig. 2). From the tumor, we took a biopsy sample about 4 by 2 cm. Histopathological

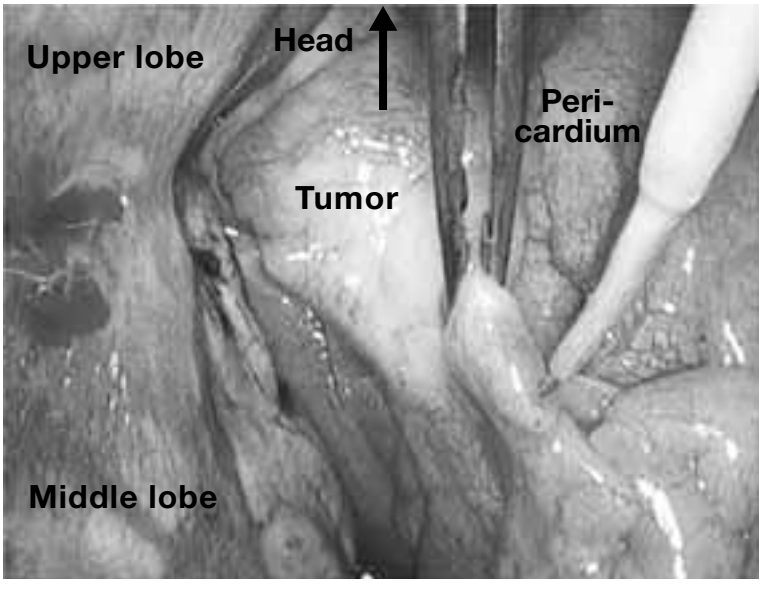

Fig. 2. Intraoperative findings. Biopsy of the middle mediastinal tumor.

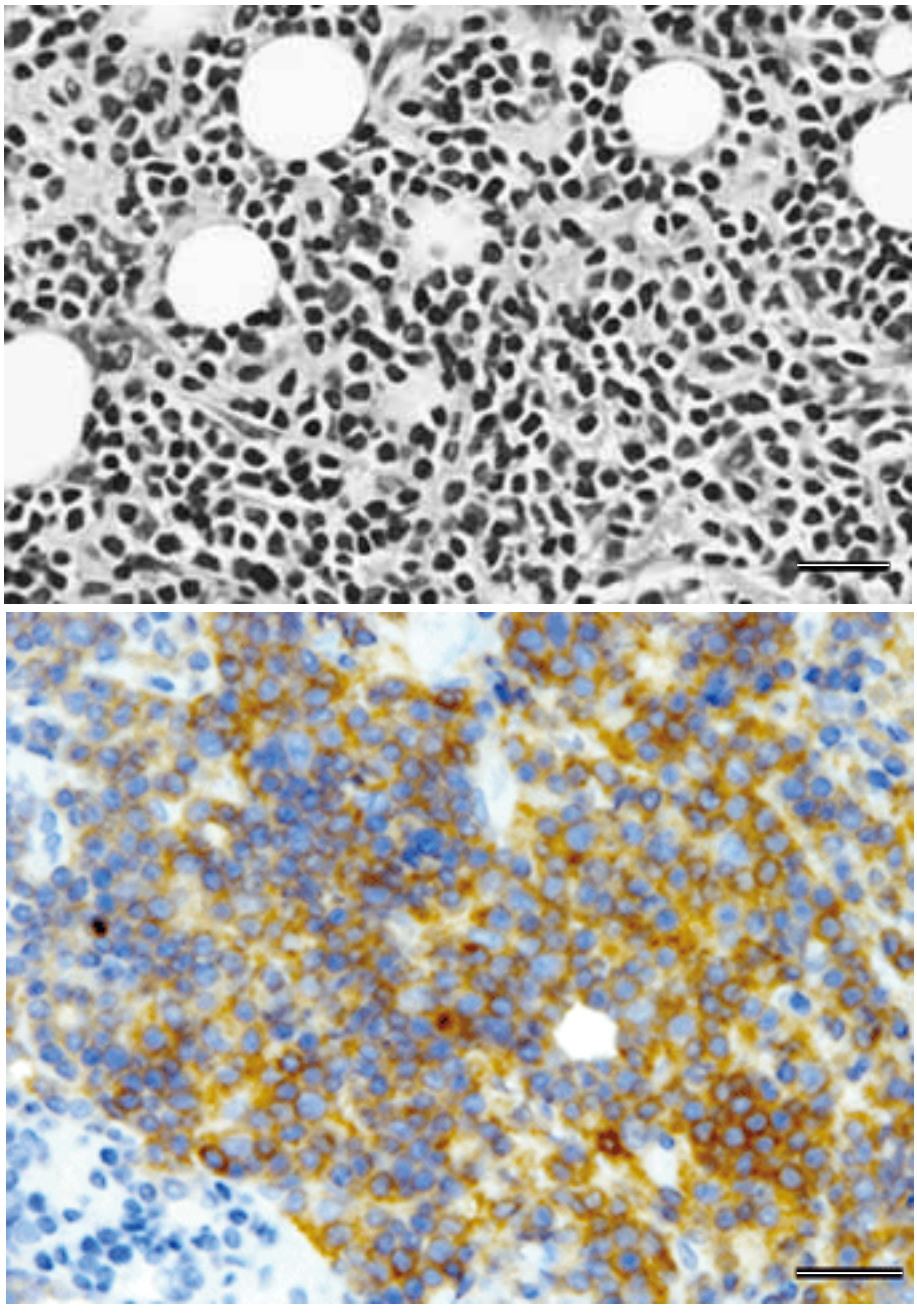

Fig. 3. Histopathological findings.
a: Pathological findings. The biopsy specimen shows monotonous proliferation with small-sized atypical lymphocytes (hematoxylin and eosin staining). Bar = 50 μm.
b: Immunohistchemical findings. Malignant cells are positive for CD 10. Bar = 50 μm.

examination revealed many small atypical lymphocytes (Fig. 3a), which showed monoclonality on flow cytometry. Immunohistochemically, the lymphocytes were positive for cluster of differentiation (CD)10 (Fig. 3b), CD20, CD79α and B-cell lymphoma 2, weakly positive for CD5, only partially positive for CD23 and negative for CD3 and cyclin D1, leading to a final diagnosis of B-cell follicular lymphoma. The patient received six courses of chemotherapy (rituximab, cyclophosphamide, doxoru-

bicin, vincristine and prednisolone). At present, 13 months after complete remission, he remains free of recurrence.

Discussion

Although the World Health Organization classification of malignant lymphomas was revised in 2008, it is still overly complicated, and the details of treatment vary greatly from one subtype of lymphoma to another. Farmer and coworkers reported that malignant lymphoma must be diagnosed more accurately and precisely than any other diseases, but that the diagnosis of malignant lymphoma in small tissue samples was difficult (Farmer et al., 2007). As they stated, this is because the histological structure is most important for the distinction of lymphomas, such as follicular lymphoma and diffuse large B-cell lymphoma, derived from germinal center cells, and because follicular lymphoma generally contains small-cell components, but does not have characteristic immunophenotypes (Farmer et al., 2007). EBUS-TBNA biopsy worked as the decisive method in diagnosing mediastinal follicular lymphoma in a patient (Inoue et al., 2010); however, it is clear that some cases present diagnostic challenges (Jaffe, 2009).

In the present patient, imaging suggested the possibility of mediastinal metastatic lung cancer and a malignant mediastinal tumor. We performed both multiple bronchoscopic and mediastinoscopic biopsies, but were unable to make a diagnosis. If biopsies provide adequate tissue, follow-up is an option. However, considering that patients with malignant lymphoma may present a diagnostic challenge, we finally performed thoracoscopic surgery. If the tumor is located in the middle mediastinum, thoracotomy or thoracoscopic biopsy is useful for diagnostic purposes (Toba et al., 2008). They suggested that performing thoracoscopic biopsy initially may be advisable. In the present patient, a definitive diagnosis was made after re-evaluating the histological diagnosis based on the results of flow cytometry. This case made us re-recognize the difficulty of diagnosing low-grade malignant type of lymphoma and the importance of consultation with pathologists.

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