Primary Marginal Zone Lymphoma in the Posterior Mediastinum with Pleural Involvement

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Abstract

We herein report a case of primary marginal zone lymphoma (MZL) of the posterior mediastinum in an 84-year-old woman. Computed tomography of the chest showed a posterior mediastinal mass in the right thoracic paravertebral region with right pleural effusion. Pathological findings of a surgical biopsy from the posterior mediastinum, along with immunohistochemical and flow cytometric results, indicated MZL. The patient was treated with chemotherapy and radiation therapy for the mediastinal lesion and achieved complete remission. A relapse occurred 3 months after the initial treatment regimen. However, a second relapse has not occurred more than 2 years after second-line chemotherapy. This is the first case of MZL originating in the posterior mediastinum.

Key words: malignant lymphoma, posterior mediastinum, pleural effusion, marginal zone lymphoma, chemotherapy

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Introduction

Malignant lymphomas, including primary mediastinal large B-cell lymphoma and Hodgkin’s lymphoma, are one of the most common neoplasms encountered in the mediastinum. Malignant lymphoma presents as an anterior, superior, or middle mediastinal mass, in this order of frequency (1-3). Mediastinal malignant lymphomas mainly arise from a lymph node or the thymus, with anterior and middle mediastinal predilection. However, primary malignant lymphomas are extremely rare in the posterior mediastinum. In contrast, neurogenic tumors are the most common masses in the posterior mediastinum (4). Only three cases of primary high-grade lymphoma in the posterior mediastinum have been reported in the English literature (5-7). Low-grade B-cell lymphomas (LBGBCLs), including chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), follicular lymphoma, mantle cell lymphoma, lymphoplasmacytic lymphoma, and marginal zone lymphoma (MZL), have not been reported to occur in the posterior mediastinum. In the present report, we describe the first reported case of primary MZL of the posterior mediastinum.

Case Report

An 84-year-old woman, with a history of hypertension and mastectomy for breast cancer at 50 years of age, was incidentally found to have right pleural effusion on a chest radiograph by her family physician (Fig. 1A). The pleural effusion showed no remarkable changes for 4 months, and the patient was admitted to the National Hospital Organization Kinki-chuo Chest Medical Center for further evaluation. A physical examination revealed normal findings, except for...
Figure 1. A chest radiograph revealing slight pleural effusion on the right side (A). A chest CT image showing a homogenous lesion along the right paravertebral area in the posterior mediastinum and right pleural effusion (B and C). A coronal reconstruction image showing a spindle-shaped lesion that extended along the right paravertebral area from vertebrae 9 to 11 (D). Fluorodeoxyglucose (FDG)-positron emission tomography showing a FDG accumulation in the posterior mediastinal lesion in the paravertebral area without a FDG accumulation in any other regions (E, F).

Figure 2. Intraoperative findings of video-assisted thoracic surgery. A posterior mediastinal mass measuring 40 mm in diameter, with right pleural effusion but no pleural mass, was observed.

a postoperative scar from mastectomy. Laboratory findings showed a slight elevation of soluble IL-2 receptor (610 U/mL). No increase in the lymphoid cells was noted in the peripheral blood. Chest computed tomography (CT) showed a homogenous mass in the posterior mediastinum along the right side of the vertebral area with pleural effusion (Fig. 1B-D). No destruction of the vertebrae was noted. A fluorodeoxyglucose (FDG)-positron emission tomography-CT examination showed a FDG accumulation in the posterior mediastinal lesion in the paravertebral area from thoracic vertebrae 9 to 11, without a FDG accumulation in any other regions (Fig. 1E, F).

A needle biopsy of the posterior mediastinal lesion showed monotonous proliferation of small lymphoid cells, which were suspected to be LGBCL. A surgical biopsy was subsequently performed for the diagnostic confirmation. A biopsy of the posterior mediastinal lesion was carried out by video-assisted thoracic surgery under general anesthesia. Intraoperative findings showed a posterior mediastinal mass measuring 40 mm in diameter, with right pleural effusion but no pleural mass (Fig. 2). Hematoxylin and Eosin-stained sections of the resected posterior mediastinal mass revealed diffuse proliferation of small to medium sized lymphoid cells with somewhat irregular nuclear outlines and a moderate amount of pale to clear cytoplasm (Fig. 3A, B). Mitotic figures were not prominent. Hassall corpuscles were not identified in the sections. Immunohistochemistry revealed that the lymphoid cells were positive for CD20 (Fig. 3C), CD79a, and bcl-2, but negative for CD3 (Fig. 3D), CD5, CD10, CD21, CD23 (Fig. 3E), CD43, cyclin D1, bcl-6,
SOX11, and CXCR3. No meshwork of CD21/CD23-positive dendritic cells was observed in the lesion, and there was colonization of germinal centers (Fig. 3E). The proliferation index was very low (MIB-1 index was 5%) (Fig. 3F). In addition, a flow cytometric analysis showed the following results: CD3: 27.1%, CD4: 23.8%, CD5: 36.7%, CD8: 5.6%, CD10: 8.9%, CD20: 72.2%, CD23: 1.2%, κ: 3.1%, λ: 69.2%, CD56: 1.0%, CD30: 0.1%, and CD103: 0.6%. The analysis also revealed immunoglobulin light-chain restriction. Molecular genetic findings with Southern blotting demonstrated clonal immunoglobulin gene rearrangement. However, no API2-MALT1 gene fusion was noted using the fluorescence in situ hybridization method. The morphological and immunohistochemical findings were consistent with a diagnosis of MZL. Atypical lymphoid cells were observed in the pleural effusion as well as the posterior mediastinum. However, aspiration cytology of the bone marrow showed negative results for malignancy. The CT findings and FDG-positron emission tomography-CT examination did not show any abnormal findings except for the posterior mediastinal lesion. Thus, we diagnosed the case as primary MZL in the posterior mediastinum.

The disease was localized to the posterior mediastinum and right pleura. The patient was treated at Sakai City Medical Center with 4 courses of the R-THP-COP regimen, comprising cyclophosphamide, pirarubicin, vincristine, prednisolone, and rituximab. Subsequently, radiation therapy for the mediastinal lesion was added to the treatment regimen. The soluble IL-2 receptor concentration declined to a normal level (417 U/mL). The patient achieved complete remission; however, relapse occurred in the paravertebral area of the 9th vertebra and right lung 3 months after radiation therapy with elevation of the soluble IL-2 receptor concentration (858 U/mL). The patient was then treated using chemotherapy with etoposide and sobuzoxane for 2 months; the soluble IL-2 receptor level again declined to a normal level (434 U/mL), and complete remission has been achieved for more than 2 years as of the time of this report.

Discussion

In this report, we describe the first case of primary MZL in the posterior mediastinum. The patient was treated with chemotherapy and radiation therapy for the mediastinal lesion and achieved complete remission. A relapse occurred 3 months after initial treatment. The patient has not experienced another relapse for more than 2 years after completing second-line chemotherapy.

This case was diagnosed as LGBCL according to the morphological findings, a low MIB-1 index (8), immunoglobulin light-chain restriction, and clonal immunoglobulin gene rearrangement. Masses composed of small lymphocytes with a predominantly diffuse growth pattern are also seen in lymphoplasmacytic lymphoma, mantle cell lymphoma, and CLL/SLL. In our case, the pathological findings differed from those observed in these disease types. Lymphoplasmacytic lymphoma, which is associated with Waldenstrom macroglobulinemia, shows monomorphic lymphoplasmacytic

Figure 3. Pathological findings from a surgical biopsy. A low-power view of a Hematoxylin and Eosin staining section revealing diffuse proliferation of lymphoid cells (A). A high-power view showing that the tumor cells consisted of small to moderate sized lymphoid cells with somewhat irregular nuclear outlines and a moderate amount of pale to clear cytoplasm (B). The tumor cells were positive for CD20 (C) and negative for CD3 with slight infiltration of non-neoplastic T-cells (D). The tumor cells were negative for CD23. However, CD23-positive follicular dendritic cells were also observed in residual follicles with colonization of germinal centers (E). The MIB-1 index of the tumor cells was approximately 5%, as indicated by immunohistochemistry for Ki-67 (F).
proliferation with Dutcher bodies and typically affects the bone marrow with less common involvement of the lymph nodes. Mantle cell lymphomas usually co-express CD43 and CD5, and cyclin D1 protein is reliably detected in the nuclei (9). Nearly all cases of CLL/SLL co-express CD43 and CD5 antigens (10), but are often only focally positive or even negative for CD23 (11). However, in the present case, the tumor cells were negative for CD5 by immunohistochemistry, whereas flow cytometric analyses indicated a slight increase in CD5-positive cells. It is possible that a subset of tumor cells weakly expressed CD5. CD5 is aberrantly expressed in 8.6% of cases of nodal MZL (12); therefore, this result does not contradict the findings of nodal MZL. Thus, our pathological findings, along with the results of the immunohistochemical and flow cytometric analyses, ruled out these diagnoses and indicated MZL.

Previously reported cases of lymphoma in the posterior mediastinum were all high-grade subtypes. These include Burkitt lymphoma, diffuse large B-cell lymphoma, and diffuse B-cell lymphoma with prominent mitotic cells and necrotic foci, which would now be diagnosed as diffuse large B-cell lymphomas according to the WHO classification of 2008 (Table) (5-7). Our finding of a primary LGBCL in the posterior mediastinum indicates that low-grade lymphomas, including MZL, should therefore be considered in the differential diagnosis of masses in the posterior mediastinum. Therefore, malignant lymphoma, including MZL, should be considered in the differential diagnosis of masses in the posterior mediastinum.

The authors state that they have no Conflict of Interest (COI). Shigeki Shimizu and Yasushi Inoue contributed equally to this work.

References
1. Strollo DC, Rosado-de-Christenson ML, Jett JR. Primary mediastinal tumors: part II. Tumors of the middle and posterior mediastinum. Chest 112: 1344-1357, 1997.
2. Shrivastava CP, Devgarha S, Atlawat V. Mediastinal tumors: a clinicopathological analysis. Asian Cardiovasc Thorac Ann 14: 102-104, 2006.
3. Dubail D, Niyaruhiira I, Boschaerts T, Locuifer JL, Barthel J, Barroy JP. Primary mediastinal tumors. Acta Chir Belg 94: 215-221, 1994.
4. Duwe BV, Sterman DH, Musani AI. Tumors of the mediastinum. Chest 128: 2893-2909, 2005.
5. Ando K, Motonaga R, Shirakusa T, Eimoto T. Malignant lymphoma of the posterior mediastinum with transverse myelopathy. Thoracic Cardiovasc Surg 37: 58-60, 1989.
6. Takamizawa A, Koizumi T, Fujimoto K, et al. Primary malignant lymphoma in the posterior mediastinum. Respiration 71: 417-420, 2004.
7. Chaari Z, Charfi S, Bentati A, Ayadi I, Abid H, Frikha I. Primary Burkitt lymphoma in the posterior mediastinum. Asian Cardiovasc Thorac Ann 23: 1110-1112, 2015.
8. Nakamura S, Akazawa K, Yao T, Tsumeyoshi M. A clinicopathologic study of 233 cases with special reference to evaluation with the MIB-1 index. Cancer 76: 1313-1324, 1995.
9. Cheuk W, Wong KO, Wong CS, Chan JK. Consistent immunostaining for cyclin D1 can be achieved on a routine basis using a newly available rabbit monoclonal antibody. Am J Surg Pathol 28: 801-807, 2004.
ferentiation of B-cell non-Hodgkin’s lymphomas of small lymphocytes. Mod Pathol 11: 1046-1051, 1998.
11. DiRaimondo F, Albitar M, Huh Y, et al. The clinical and diagnostic relevance of CD23 expression in the chronic lymphoproliferative disease. Cancer 94: 1721-1730, 2002.
12. Jaso JM, Yin CC, Wang SA, et al. Clinicopathologic features of CD5-positive nodal marginal zone lymphoma. Am J Clin Pathol 140: 693-700, 2013.
13. Inagaki H, Chan JK, Ng JW, et al. Primary thymic extranodal marginal-zone B-cell lymphoma of mucosa-associated lymphoid tissue type exhibits distinctive clinicopathological and molecular features. Am J Pathol 160: 1435-1443, 2002.
14. Bar-Ziv J, Barki Y, Itzchak Y, Mares AJ. Posterior mediastinal accessory thymus. Pediatr Radiol 14: 165-167, 1984.
15. Bhatnagar S, Pradhan R, Shastri P, Shenoy P. Accessory thymus in posterior mediastinum. J Indian Assoc Pediatr Surg 13: 140-141, 2008.

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