Lung parenchymal involvement of primary bone marrow follicular lymphoma: a rare case study

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Abstract
A 76-year-old man presented with shortness of breath. Computed tomography revealed ground-glass opacity and interlobular thickening in the right lower lobe. Blood examination showed elevated levels of white blood cell count and lymphocytes. Bone marrow aspiration revealed low-grade follicular lymphoma. Histopathological examination of the surgical lung biopsy from the right lower lobe demonstrated usual interstitial pneumonia and scattered aggregation of lymphocytes with poorly formed non-necrotizing granuloma. An 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET-CT) did not show intense uptake in areas other than the right lower lobe. We concluded that the granuloma in the lung was presumed to be a sarcoid reaction associated with bone marrow follicular lymphoma, and the intense 18F-FDG uptake in the right lower lobe might have been due to a sarcoid reaction. Immunohistochemistry or other genetic examinations are important even if 18F-FDG uptake on PET-CT seems to be a false-positive because of the possibility of a sarcoid reaction.

Introduction
Follicular lymphoma is generally an indolent B-cell lymphoproliferative disorder that commonly presents with systemic lymphadenopathy. Although rare, follicular lymphoma that arises primarily from the bone marrow has been reported [1].

Case Report
A 76-year-old man presented with a 1-year history of shortness of breath. Chest radiograph and computed tomography revealed ground-glass opacity and interlobular thickening in the right lower lobe with minimal mediastinal lymphadenopathy (Fig. 1A–C). Blood examination showed elevated levels of haemoglobin (17.5 g/dL), white blood cell count (16,300 per mm3) with 69.5% lymphocytes, and sialylated carbohydrate antigen KL-6 at >1220 U/mL (normal range, <500 U/mL). With a consideration of interstitial lung disease, bronchoalveolar lavage (BAL) combined with transbronchial lung biopsy (TBLB) was performed. Bone marrow aspiration was likewise performed to rule out malignant lymphoma.

BAL fluid from the right lower lobe showed lymphocytic predominance, a CD4/CD8 ratio of 1.18, and culture that was negative for Mycobacterium tuberculosis complex. The TBLB material from the right lower lobe showed minimal infiltration of lymphocytes and buds of granulation tissue within the centrilobular air spaces, resulting in a histological diagnosis of organizing pneumonia. However, examination of the bone marrow aspirate revealed nodular infiltration of uniform small- to medium-sized lymphocytes (Fig. 2A, B). On immunohistochemistry, these lymphocytes were positive for CD20, CD10, and BCL-6 but were negative for CD5, CD23, BCL-6, cyclin D1, CD138, and MUM-
1. This immunohistochemical pattern of bone marrow lymphocytes suggested low-grade follicular lymphoma. We performed video-assisted thoracoscopic surgery for a more definite diagnosis. Histopathological examination of the surgical lung biopsy from the right lower lobe demonstrated usual interstitial pneumonia (UIP), characterized by a patchwork pattern of fibrosis, architectural distortion, honeycomb changes, fibroblastic foci, and scattered aggregation of lymphocytes (Fig. 2C, D), with poorly formed non-necrotizing granuloma (Fig. 2E, F). Typical follicular growth pattern was occasionally observed in some lung parenchymal structures, but immunohistochemical staining of the lymphocytes was positive for cell-surface CD10, CD20, and BCL-2 and negative for CD5 and cyclin D1 (Fig. 2G–I). Southern blotting analysis revealed IgH/JH reconstruction with B lymphocytic monoclonality.

Figure 1. (A) Chest radiograph showed a reticular shadow in the right lower area. (B) and (C) Chest computed tomography shows ground-glass opacity and interlobular thickening in the right lower lobe with mediastinal lymphadenopathy. (D) 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET-CT) does not show intense uptake in areas other than the right lower lobe.

Figure 2. (A) and (B) There is nodular infiltration of uniform small- to medium-sized lymphocytes in the bone marrow. (C) and (D) Low- and high-magnification photomicrographs of the surgical lung biopsy specimen from the right lower lobe show scattered aggregation of lymphocytes. (E) and (F) Low- and high-magnification photomicrographs of the surgical lung biopsy specimen from the right lower lobe show poorly formed non-necrotizing granuloma. Immunohistochemical staining of the lymphocyte was positive for cell surface (G) CD10, (H) BCL-2, and (I) CD20. HE, haematoxylin and eosin staining.
An 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET-CT) did not show intense uptake in areas other than the right lower lobe.

Discussion

The granuloma in the lung was presumed to be a sarcoid reaction associated with malignant lymphoma because there were no systemic lesions, and tuberculosis was not likely [2]. Sarcoid reaction was reported to be a possible cause of false-positive 18F-FDG PET-CT results in oncology patients [3]. The intense 18F-FDG uptake in the right lower lobe might have been due to a sarcoid reaction because there was no significant uptake in the bone marrow, despite the presence of lymphoma cells. Cases of UIP with pulmonary sarcoidosis are rare [4], and UIP and sarcoidosis have distinct pathological features [5]; therefore, we concluded that the patient had both UIP and sarcoid reaction to follicular lymphoma. The final diagnosis was primary bone marrow lymphoma with involvement of the pulmonary parenchyma and concomitant UIP. In conclusion, we presented a rare case of primary bone marrow follicular lymphoma that infiltrated the lung parenchyma. In cases suspected to be malignant lymphoma, immunohistochemistry or other genetic examination is important even if 18F-FDG uptake on PET-CT seems to be false-positive because of the possibility of a sarcoid reaction.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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