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CASE REPORT

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Primary pulmonary diffuse large B-cell lymphoma presenting multiple nodules mimicking metastasis: A case report

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Abstract

Primary pulmonary diffuse large B-cell lymphoma is a rare entity. We describe a case of pulmonary lymphoma with multiple nodules mimicking metastases in a treated patient with rheumatoid arthritis. A 73-year-old man was diagnosed with rheumatoid arthritis at the age of 30. He was treated with leflunomide. He was followed up for a nontuberculous mycobacterial infection. He underwent percutaneous coronary intervention for acute myocardial infarction at the age of 70. In April 2022, routine follow-up revealed new-onset multiple nodules on chest computed tomography (CT). A position emission tomography/CT scan with 18F-fluorodeoxyglucose showed a low-high maximum standardized uptake value by multiple nodules. Pathologic examination of a video-assisted thoracic surgical biopsy revealed pulmonary diffuse large B-cell lymphoma. Systemic chemotherapy with rituximab, cyclophosphamide, vincristine, and prednisolone reduced and eliminated multiple nodules. Pulmonary lymphoma should be considered as a differential diagnosis in the case of multiple nodules on a chest CT.

KEYWORDS
diffuse large B cell, multiple lung nodules, primary pulmonary lymphoma

INTRODUCTION

Primary pulmonary lymphoma (PPL) is an extremely rare clonal lymphoproliferative lung disease, accounting for <1% of lymphomas and approximately 3%–4% of all extranodal lymphomas.[1] Patients with PPL constitute a heterogeneous group. Diffuse large B-cell lymphoma (DLBCL) is accounting for >10% of PPLs.[1] Radiologically, they can present as consolidation, infiltration, masses, and nodules with nonspecific findings.[2] Here, we report our experience with a case of PPL-DLBCL detected as multiple pulmonary nodules and masses mimicking metastasis. The cause of multiple nodules of the lung in the elderly is mostly metastasis. In our case, the images suggested metastatic lung disease; however, the final diagnosis was a PPL. Sometimes, rare malignancies may result in a better prognosis than common lung malignancies. Histological diagnosis of lung lesions is important.

CASE REPORT

A 73-year-old man was followed up for a nontuberculous mycobacterial infection in acute care hospital. He underwent percutaneous coronary intervention for acute myocardial infarction at the age of 70. He presented with rheumatoid arthritis (RA) and was treated with leflunomide for 40 years. He was a former smoker (1 pack/day between the ages of 20 and 45 years). He underwent a routine chest X-ray every 2 months and chest computed tomography (CT) every year. Chest CT revealed new multiple lung nodules with no hilar/mediastinal lymph node swelling (Figure 1A–D). 18-F-labelled

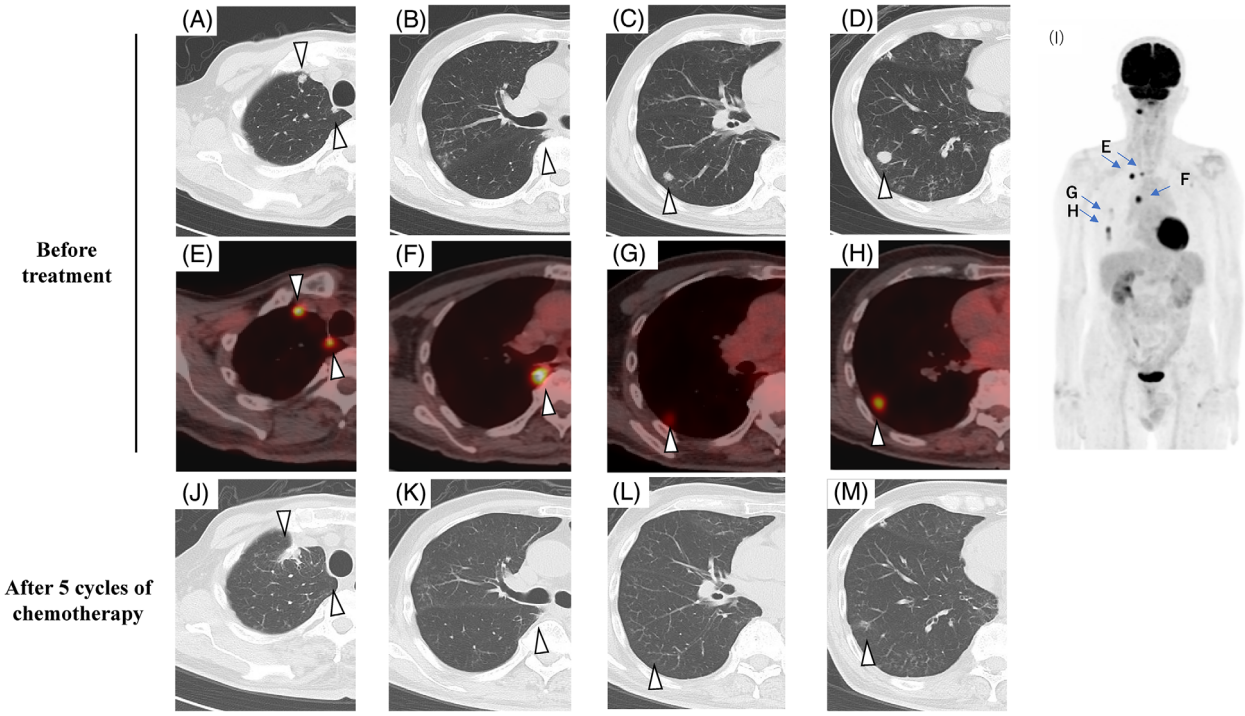

FIGURE 1 Computed tomography (CT) findings showed multiple pulmonary nodules in the right lung (white arrows) (A–D). 18F-labelled fluorodeoxyglucose (FDG) positron emission tomography (PET) revealed an abnormal accumulation of FDG in the multiple nodules in the right lung (white arrows) (E–H). The coronal image of whole-body PET revealed an abnormal accumulation of FDG in multiple nodules, and no abnormal accumulation of FDG in the hilar/mediastinal and superficial lymph nodes was observed (I). Chest CT findings after five cycles of chemotherapy showed a nodular shadow in the apex of the right lung as postoperative changes, and the other nodules had reduced or disappeared (J–M)

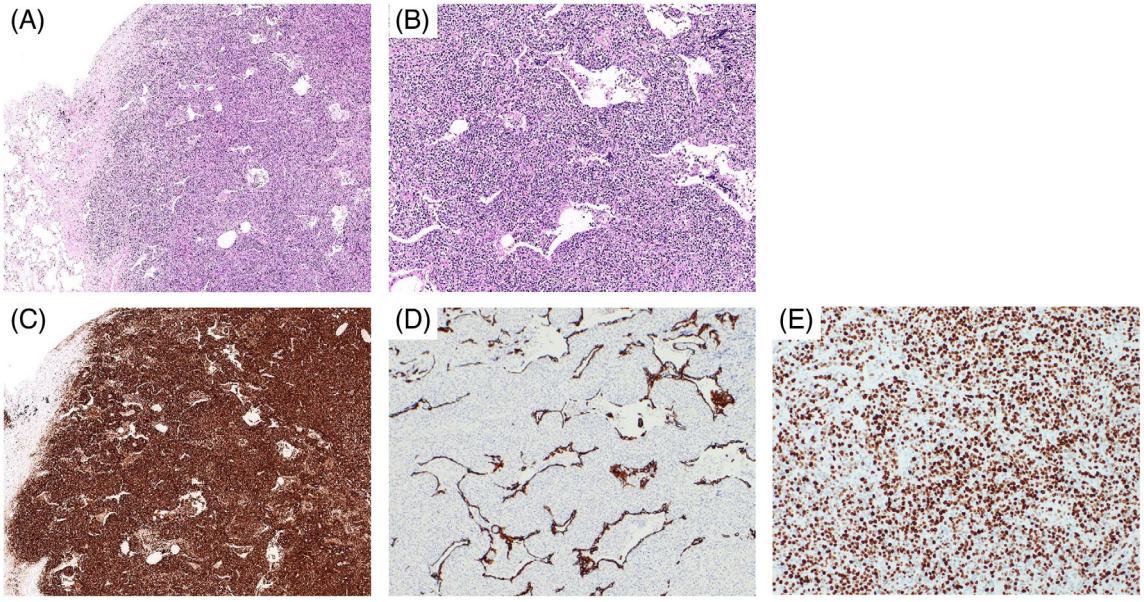

FIGURE 2 Histological images of the lung nodule obtained by partial resection at the apex of the right lung are shown. Haematoxylin–eosin staining showed diffuse and dense proliferation of monotonous lymphocytes ((A) × 25, (B) × 100). Immunostaining was positive for CD20 ((C) × 25) and negative for CAM5.2 ((D) × 40). The positive rate of Ki-67 was 60%–70% ((E) × 100)

fluorodeoxyglucose-position emission tomography/CT revealed the largest lung tumour to have a low–high maximum standardized uptake value (SUV) of max 1.7–11.8 (Figure 1E–H). Based on these radiological findings, metastatic lung disease from of extra-thoracic origin or metastasis from lung cancer and fungal infections were

considered differential diagnoses. The patient was evaluated for extra-thoracic primary cancer. Contrast-enhanced CT of the abdomen and esophagogastroduodenoscopy revealed no malignant sites (Figure 1I). He was referred to our tertiary hospital. The patient was clinically asymptomatic. The patient's temperature was 36.5°C; his heart rate was 72 bpm; and his blood pressure was 110/60 mmHg. There was no skin rash or superficial lymphadenopathy. Laboratory findings revealed a white blood cell count of 5700/μL (neutrophils 53%, lymphocytes 15%, monocytes 27%, and eosinophils 2%), a haemoglobin level of 11.9 g/dL, a normal lactate dehydrogenase level of 203 U/L, and an extremely elevated soluble interleukin-2 receptor level of 2496 U/mL. For the histological diagnosis, a video-assisted thoracic surgical (VATS) biopsy of the nodule in the apex of the right lung was performed. Histopathological examination (haematoxylin–eosin staining) showed diffuse infiltrates of medium-to-large atypical lymphocyte-like cells (Figures 2A, B). Immunohistochemistry showed positive results for B-cell lymphoma 2 and cluster of differentiation (CD) 20 (Figure 2C) but negative results for cytokeratin 5.2 (Figure 2D), CD3, CD10, CD21, and cyclin D1. The Ki-67 labelling index was 60%–70% (Figure 2E). Based on these findings, DLBCL stage IE was diagnosed as the staging classification used for these extranodal lymphomas.[3]

Systemic chemotherapy with rituximab, cyclophosphamide, vincristine, and prednisolone was administered. After four cycles, vincristine was avoided for peripheral neuropathy. After five cycles, a chest CT scan showed that the multiple nodules were reduced and disappeared (Figure 1J-M).

DISCUSSION

PPL is defined as clonal lymphoid proliferation affecting one or both the lungs.[1] Primary non-Hodgkin lymphoma of the lung is very rare, accounting for only 0.4% of malignant lymphomas.[3] Here, we have reported a case of DLBCL presenting with multiple nodules mimicking metastases during leflunomide therapy for RA. The clinical description of PPL is nonspecific, and 37.5% of patients are asymptomatic. Cough (46%) and dyspnea (23%) are frequent pulmonary symptoms.[3] In this case, the patient was asymptomatic and multiple nodules were newly detected by routine chest imaging of a nontuberculous mycobacterial infection. Patients with RA do not have higher overall incidence of malignancies, but lymphoma is significantly more frequent.[4] Significant risk factors for lymphoma were reported to be the use of methotrexate (MTX) or tacrolimus and higher age.[4] Specifically, MTX has been used as a key drug in the treatment of RA.MTX was not given all at once in this case. The patient was administered leflunomide since the age of 30 years. Leflunomide has not been reported as a risk factor for malignancy. Chest CT showed multiple nodules. Imaging findings suggested metastatic tumours and fungal infections as differential diagnoses. The radiographic findings of PPL are nonspecific. High-resolution CT of the chest revealed solitary nodules, multiple nodules, masses, infiltrates, and consolidation.[3] Clinical and misdiagnosed analysis of PPL was reported in a retrospective study of 19 cases,[5] wherein 68.4% of patients were misdiagnosed as having pneumonia, lung cancer, or tuberculosis before final diagnosis. The time between initial diagnosis and subsequent diagnosis ranges from 0.5 months to 2 years, with the median being 6 months.[5] In this case, contrast-enhanced CT of the abdomen and esophagogastroduodenoscopy revealed no malignant sites. To the best of our knowledge, no reports on PPL being found incidentally after surgical resection are available. The diagnosis of PPL is challenging, as the symptoms are generally nonspecific. The radiological manifestations of PPL also vary considerably. CT-guided or transbronchial biopsy is usually inconclusive. Generally, VATS biopsy and thoracotomy leads to the final diagnosis.

Although a tissue biopsy was needed for diagnosis, the patient did not have superficial lymphadenopathy. In this case, PPL was diagnosed using an invasive VATS biopsy. The treatment options include surgery or radiotherapy for localized tumours and chemotherapy for multiple/diffuse involvement.[2] In this case, as multiple lung nodules were detected, we selected chemotherapy. Chemotherapy had a high level of effectiveness. The prognosis of primary pulmonary non-Hodgkin's lymphoma varies because of the heterogeneous groups of patients. The median period to mortality was reported as 7 years, with the 3-year overall survival rate being 86% and the 5-year overall survival rate being 57%–75%.[2] Rare malignancies can sometimes have a better prognosis than common lung malignancies. Physicians should make every effort to achieve a histological diagnosis even if an invasive biopsy was performed.

AUTHOR CONTRIBUTIONS

Nobuhiro Fujioka and Yoshiro Kai wrote the manuscript. All authors contributed to editing the manuscript and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this article.Further enquiries can be directed to the corresponding author.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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