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CASE REPORT

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Primary pulmonary Hodgkin's lymphoma mimicking rheumatoid arthritis-associated organizing pneumonia: A case report

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Abstract

Primary pulmonary Hodgkin's lymphoma (PPHL) is an extremely rare disease. The nonspecific clinical and radiological features render the diagnosis a great challenge. Here, we present a case of PPHL mimicking rheumatoid arthritis-associated organizing pneumonia.

KEYWORDS

Consolidation and nodules; lung biopsy; organizing pneumonia; primary pulmonary Hodgkin's lymphoma; rheumatoid arthritis

INTRODUCTION

Primary pulmonary Hodgkin's lymphoma (PPHL) is a malignant monoclonal lymphoid proliferative disease confined to the lung at the time of diagnosis or within 3 months thereafter, with Hodgkin and Reed–Sternberg (HRS) cells admixed with a heterogeneous population of non-neoplastic inflammatory cells.[1] The incidence of PPHL is far less common than that of Hodgkin's lymphoma (HL); 2 to 3 cases per 100,000 per year are reported.[2] Because the clinical and radiological features for PPHL are nonspecific, the diagnosis is always difficult, resulting in delays incurative treatment. Here, we report a case of PPHL with polyarthralgia and organizing pneumonia (OP)-like consolidation that was initially diagnosed as rheumatoid arthritis-associated OP.

CASE REPORT

A 61-year-old man with a 30-pack-a-year smoking history presented with chronic productive cough, intermittent fever, and arthralgia for 2 years and was admitted to our hospital in May 2019. The initial chest computed tomography (CT) scan in the local hospital showed multiple nodules and consolidations. His symptoms and pulmonary infiltrates typically improved after the administration of antibiotics or with low-dose corticosteroids. Over the 2 years, multiple episodes occurred with migratory lung consolidations. Drug abuse, occupational, and environmental exposures were denied.

On admission, crackles at the left lung base were evident on auscultation. Tenderness was noted at the proximal and distal interphalangeal joints. The wrist and knee joints were swollen and warm. The remainder of the physical examination was unremarkable. Laboratory examinations highlighted an elevated

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level of erythrocyte sedimentation rate (44 mm/h). Blood hemoglobin level, leukocyte count, platelet count, rheumatologic screening including anti-neutrophil cytoplasmic antibodies, tumor markers, and infection examination were all negative. Arterial blood gas analysis showed pH of 7.41, $PaCO_2$ 38.8 mm Hg, and PaO_2 75.4 mm Hg on room air. Pulmonary function test revealed a restrictive pattern with the total lung capacity of 74.9% predicted and diffusion of carbon monoxide (DLCO) of 70% predicted. Chest CT scan showed multiple consolidations and nodules, distributed along with the bronchial vascular bundle (Figure 1(a)). Bronchoalveolar lavage (BAL) on the right middle lobe retrieved lymphocytes of 56% and macrophages of 43%. Flow cytometry of lymphocytes in BAL detected abnormal phenotypic lymphocytes (CD3−/CD4+) at 27%. Neither smear nor culture of bronchoalveolar lavage fluid (BALF) revealed any pathogens. Transbronchial cryobiopsy was performed and pathologic examination showed OP. Additionally, polysynovitis were detected on ultrasound examination. As arthralgia getting worse, intramuscular diprospan (betamethasone 2 mg/betamethasone dipropionate 5 mg, every 2 weeks) was administered at consultation from the rheumatologist. Unexpectedly, the nodules and consolidation resolved significantly (Figure 1(b)), which cancelled our planned video-assisted thoracoscopic surgery (VATS) biopsy. He was discharged as the seronegative rheumatoid arthritis-associated OP with prednisone (30 mg, daily) and leflunomide (20 mg, daily) and was followed up regularly.

Four months later, new consolidation and nodules showed up on routine follow-up CT scan (Figure 1(c)). Further positron emission tomography-computed tomography (PET-CT) demonstrated increased F-fluorodeoxyglucose (FDG)-uptake of lung lesions to varying degrees, with a peak standard uptake value (SUV) of 6.5 in the superior right lower lobe, no lymphadenopathy or other abnormal uptake was found (Figure 2). The initial diagnosis was questioned. After a multidisciplinary discussion repeated lung biopsy was performed in the right upper and right lower lobes by VATS. Pathologic examination showed organizing nodules, and large atypical lymphoid cells of mono-, bi-, or multinuclei with prominent nucleoli, scattered in an abundance of lymphoid cells, neutrophils, histiocytes, and eosinophils background. Immunohistochemical staining revealed CD20−, CD3−, CD30+, PAX5+, OCT-2+, BOB.1- (Figure 3). Epstein-Barr virus encoded RNA was negative in in situ hybridization. Because there was no evidence of extra pulmonary involvement, a diagnosis of nodular sclerosing type of PPHL was established.

Eight cycles of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy were carried out. The patient was afebrile and arthralgia disappeared. Chest CT

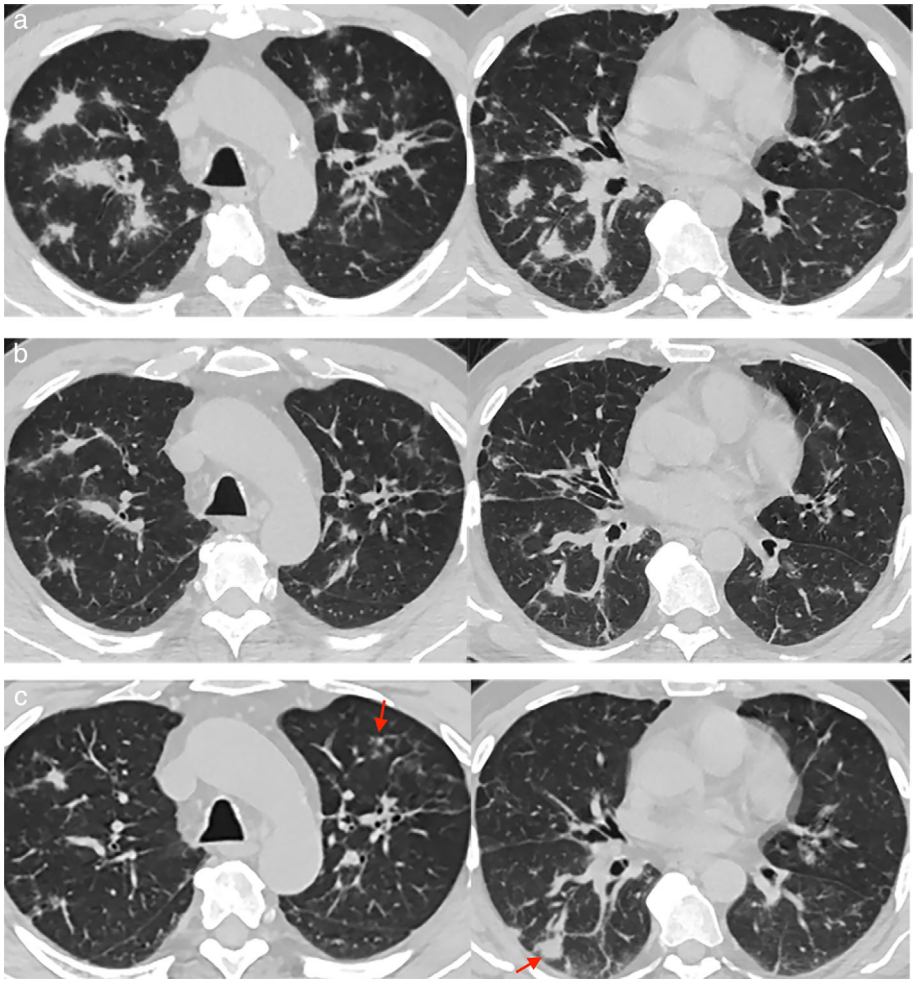

FIGURE 1 Images of chest CT scans during the disease course. (a) On admission, multiple consolidation and nodules are distributed along with the bronchial vascular bundle. (b) Absorption of the nodules and consolidation after the administration of diprospan. (c) Four months later, new consolidations and nodules reappear (arrow)

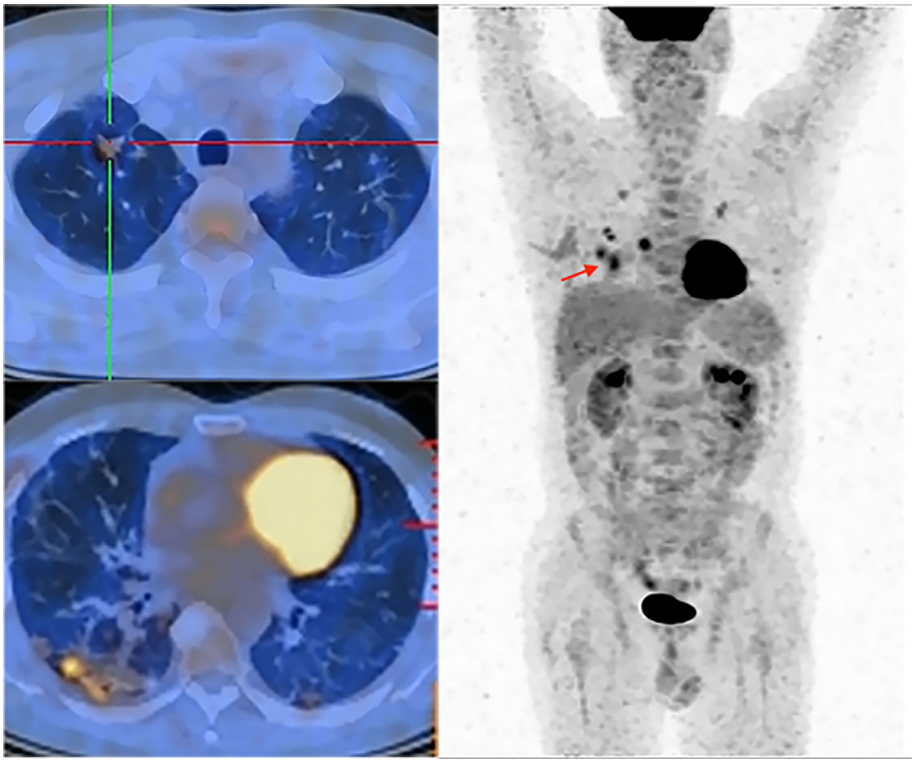

FIGURE 2 On PET-CT scan, F-fluorodeoxyglucose (FDG)-uptake of lung lesions increase to varying degrees, and the uptake is highest in the right lower lung (arrow), without lymphadenopathy and any other abnormal uptake

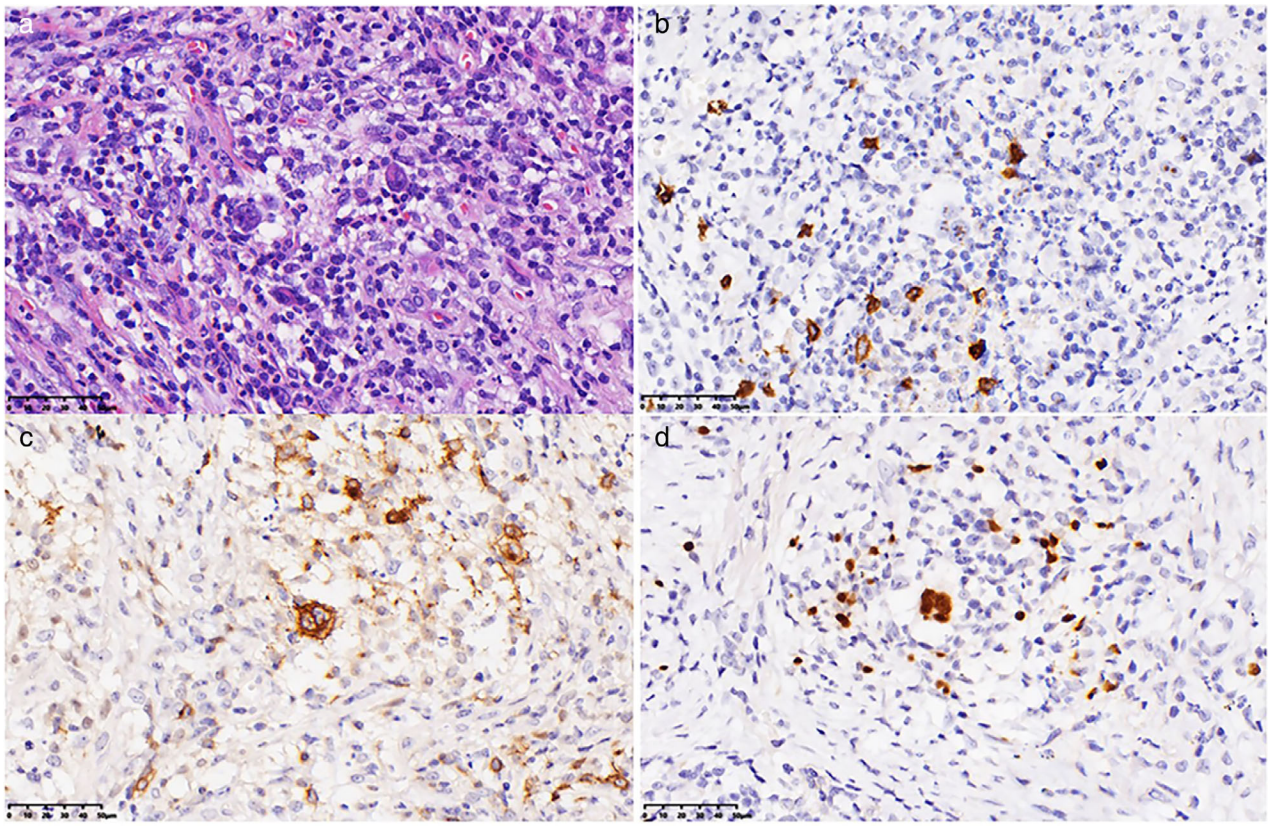

FIGURE 3 (a) Hematoxylin and eosin (H&E) staining demonstrating large atypical lymphoid cells (H&E, 400×). (b) Immunohistochemistry staining negative for CD20 (400×). (c) Immunohistochemistry staining positive for CD30 (400×). (d) Immunohistochemistry staining positive for PAX5 (400×)

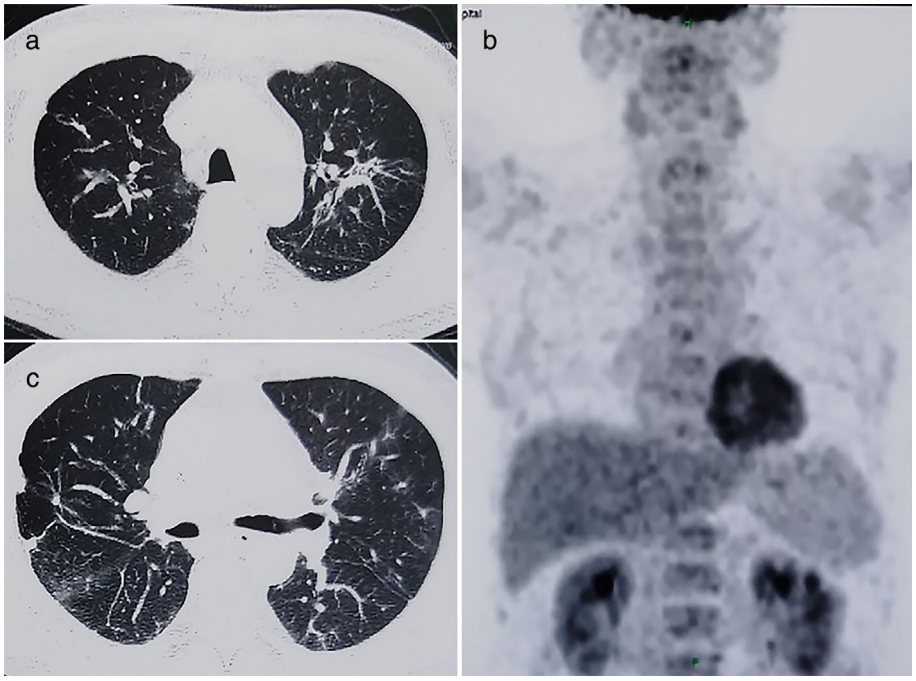

FIGURE 4 After chemotherapy, chest CT and PET-CT show that the nodules and consolidations are completely resolved

and PET-CT showed complete resolution of multiple nodules and consolidations (Figure 4).

DISCUSSION

PPHL is a rare visceral Hodgkin disease, comprised of 1.5%–2.4% of primary pulmonary lymphomas, which shows a slight female preponderance (F: M = 1.4: 1) and bimodal age distribution (<35 and >60 years).[3,4] Clinically, most of the PPHL patients present with unspecific respiratory symptoms, such as cough, hemoptysis, chest pain, and dyspnea, whereas others can also manifest as fever, night sweats, weight loss, or be asymptomatic.[5] Intermittent fever and arthralgia as the predominant symptom of PPHL are quite rare. When suggestive features such as lymphadenopathy and hepatosplenomegaly are absent at the initial time, these patients may be misdiagnosed with rheumatoid arthritis as in our patient. Autoimmune paraneoplastic disorders have been described in lymphoma.[6] We speculate that polyarthralgia may result from host response to tumor antigens and cytokine-driven synovial inflammation.[7] Reed–Sternberg cells could secrete a variety of inflammatory cytokines and chemokines, of which interleukin (IL)-1, IL-6, and tumor necrosis factor α (TNF-α) are particularly associated with arthritis, explaining the initial clinical manifestation mimicked rheumatic disease.[6]

The diagnosis of PPHL depends on the morphology and immunohistochemistry confirmation. The typical pathology is characterized by the appearance of HRS cells with polymorphous inflammatory infiltration. In our case, the patient was at first misdiagnosed as seronegative rheumatoid arthritis-associated OP based on polyarthralgia, pathology of cryobiopsy, and initial response to steroids. OP is associated with many different diseases and exposures. Only one case noting OP with biopsy as the presentation of PPHL has been reported.[8] OP may be an inflammatory response to underlying HL that was likely missed because of a sampling error of transbronchial cryobiopsy. Another possibility is that OP represents a paraneoplastic harbinger of PPHL, which may precede the clinical manifestation of lymphoma a few months later.[9]

Moreover, immunohistochemistry provides the definitive diagnosis in histopathologically indistinct cases. PPHL tumor cells are positive for CD15, CD30, Pax5, and rarely CD20, and negative for T-cell markers.[10] However, expression of a single T cell antigen (e.g., CD4) may occasionally be seen and related to adverse outcome.[10] Correspondingly, abnormal phenotypic lymphocytes (CD3−/CD4+) of BAL were detected using flow cytometry in our patient, which has not been reported previously. This indicates that flow cytometry of BAL could be a potential clue to differentiate pulmonary lymphoid neoplasms.

In conclusion, polyarthralgia with migratory consolidations that partially responded to corticosteroids might be the major presenting manifestations of PPHL. Awareness should be raised that PPHL should be considered as a differential diagnosis of atypical OP concomitant with rheumatic symptoms.

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DISCLOSURE

The authors have no conflicts of interest to declare.

INFORMED CONSENT

Written informed consent for the publication of clinical details and clinical images was obtained from the patient.

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