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A case of pulmonary lymphoproliferative disorder presenting rapidly progressive respiratory failure

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Abstract

A 72-year-old woman presented with acute onset of shortness of breath and fatigue over several days, and was found to be in acute respiratory failure. Computed tomography of the chest revealed diffuse ground-glass opacities, crazy-paving, multiple nodules, and a large mass in the right lower lobe. She was diagnosed with B-cell lymphoma and a pulmonary lymphoproliferative disorder (PLD). PLD is known to present with a variety of radiographic patterns. The course of PLD is usually one of slow progression, and acute respiratory failure is a rare presentation. Physicians should be aware that acute respiratory failure can be caused by PLD.

Introduction

Pulmonary lymphoproliferative disorders (PLDs) are characterized by focal or diffuse infiltration of the lung by polymorphic mixtures of mature lymphocytes, histiocytes, and plasma cells [1–5].

PLD is known to be associated with various abnormal radiological changes in the lung, including multiple nodules, infiltrative and reticular shadows. It is often difficult to distinguish PLD from other lung infiltrative diseases such as pulmonary oedema, interstitial pneumonia, and acute respiratory distress syndrome. Since these other lung conditions are more common than PLD, physicians are often unaware of PLD. The progression of PLD is usually slow, and acute respiratory failure in PLD is very rare [6].

Here, we report a very rare case of acute respiratory failure caused by PLD.

Case Report

A 72-year-old female with a history of atrial fibrillation treated with ablation was admitted to our hospital with shortness of breath and fatigue for several days. She developed acute respiratory distress with a modified Medical Research Council dyspnoea scale grade of 5. On arrival at the hospital, her peripheral capillary oxygen saturation (SpO_2) was very low (≤75%), her arterial blood gas demonstrated a PaO_2 of 37 mmHg, $PaCO_2$ of 57.7 mmHg, HCO_3 of 17.6 mmHg, and pH of 7.1, and bilateral widespread pulmonary opacities were present on the chest radiography (Fig. 1A). She was treated initially for acute heart failure and was admitted to the intensive care unit. Computed tomography (CT) of the whole body revealed diffuse ground-glass opacity and partial crazy-paving appearance with multiple nodules across all the lobes of the lung and a large 50-mm-diameter mass in the right lower lobe. Bilateral pleural effusions, dilation of the inferior vena cava, adrenomegaly, and multiple rib fractures were also detected (Fig. 1B–E). Echocardiogram revealed no evidence of heart failure, suggesting that the bilateral pulmonary opacities were due to a non-cardiogenic cause. Blood examination indicated a slight elevation of liver aminotransferases (aspartate transaminase (AST): 85 IU/L (13–33 IU/L); alanine transaminase (ALT): 35 IU/L (6–27 IU/L)), lactate dehydrogenase (473 IU/L (119–

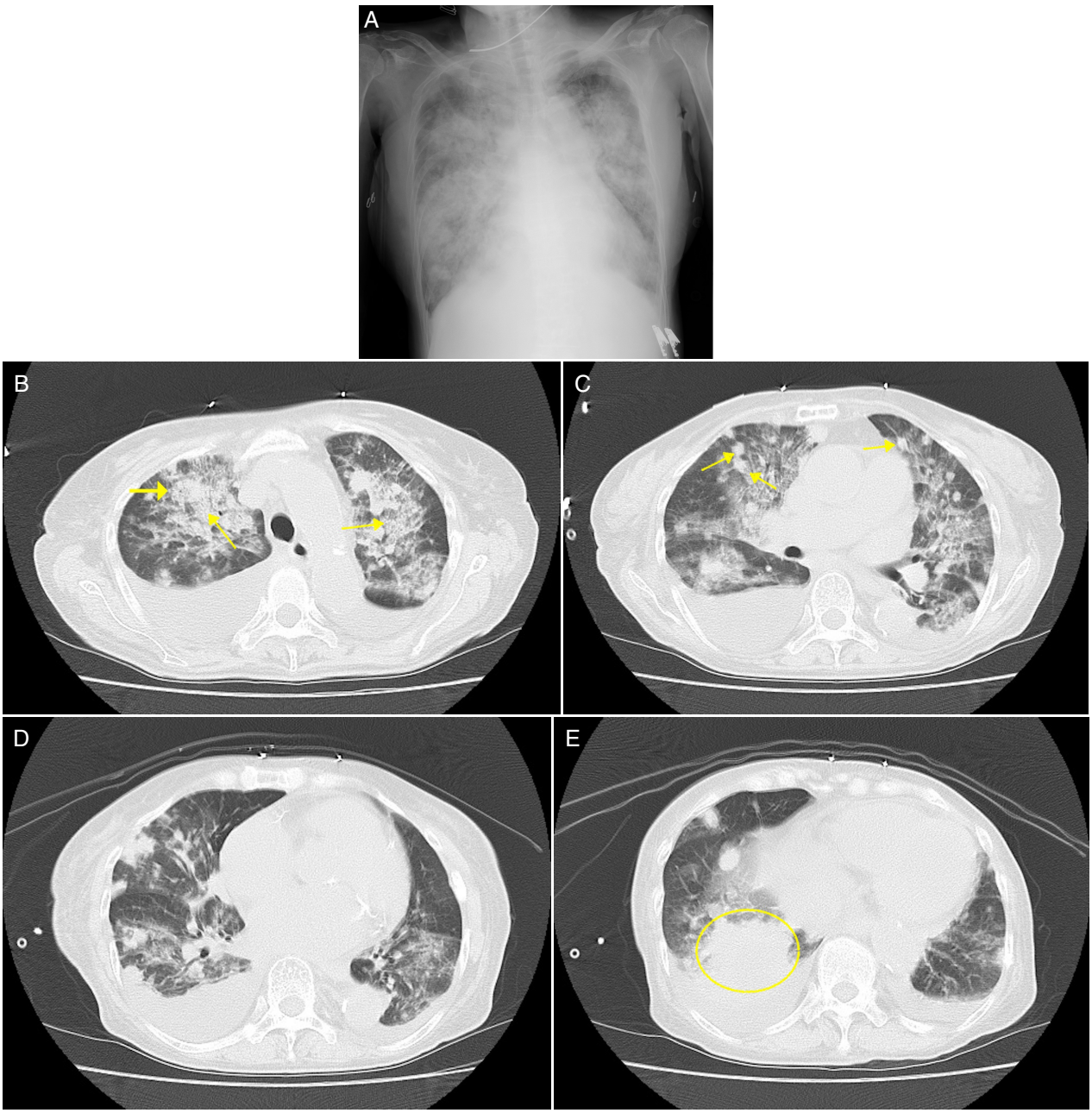

Figure 1. (A) Chest X-ray shows bilateral widespread pulmonary opacities with cardiomegaly. (B–E) Chest computed tomography shows massive ground-glass opacity and partial crazy-paving appearance with multiple nodules across all the lobes of the lung and a large mass in the right lower lobe. Bilateral pleural effusion and dilation of inferior vena cava are also seen. Yellow arrows and circles indicate region of interest. (B) Ground-glass opacity and partial crazy-paving appearance; (C) multiple nodules; (E) a large mass.

229 IU/L)), and C-reactive protein (8.41 mg/dL (<0.3 mg/dL)). White blood cell (WBC) count and renal function were normal (WBC: 7800/μL (3500–8500/μL); urinary nitrogen: 19 mg/dL (8–22 mg/dL); creatinine: 0.77 mg/dL (0.35–0.74 mg/dL)). Urinary antigen tests for *Streptococcus pneumoniae* and *Legionella*, and blood and sputum cultures were negative.

The revised working diagnosis was that of advanced lung cancer with lymphangitis carcinomatosa complicated by infection. She received steroid pulse therapy (1000 mg/day of methylprednisolone) and broad-spectrum antibiotics empirically. She was also administered non-invasive positive pressure ventilation for the severe acute respiratory failure. On day three of her admission,

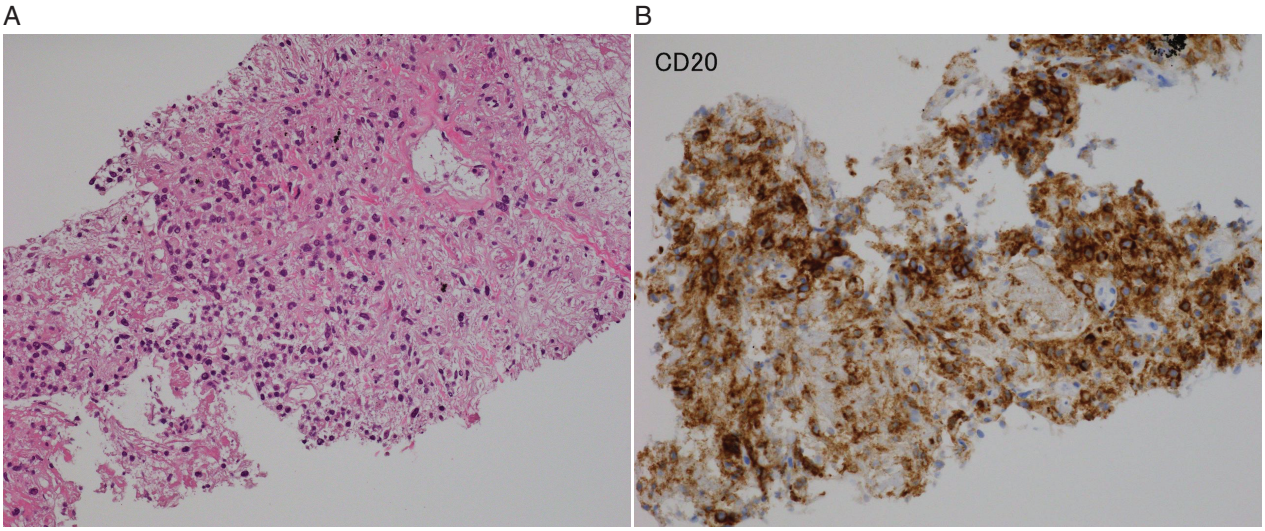

Figure 2. (A, B) Specimens taken by CT-guided biopsy reveal massive necrosis with atypical small oval cells spread across the whole field, which show positive staining for CD20 and negative staining for CD3, AE1/AE3, Cam2.5, p40, and TTF-1, suggesting malignant B-cell lymphoproliferation. (A, B) ×200; diameter of figure: 600 μm.

CT-guided lung biopsy was performed. The specimens from the lower lobe large 50-mm-diameter mass revealed B cell lymphoma (Fig. 2A, B). Since most of the tumour tissue that was obtained was crushed and necrotized, detailed immunostaining evaluation was difficult. The patient and family refused intubation and the patient died of progressive respiratory failure on day eight.

Discussion

In this case, specimens taken by CT-guided biopsy revealed primary pulmonary malignant lymphoma. Pulmonary lymphoproliferation caused fatal acute respiratory failure. PLD is known to cause a number of abnormalities on lung imaging such as multiple nodules, mass lesions, ground-glass opacity infiltrations, and multiple cysts [2–5]. Based on a previous review, PLD can be classified into two large categories [2,4]: benign or reactive spectrum and malignant type. The malignant type is subdivided into three categories: primary malignant PLD, secondary malignant PLD, and AIDS-related PLD. In accordance with the recent WHO classification, primary malignant PLD mainly consists of MALT lymphoma, diffuse large B-cell lymphoma, and lymphomatoid granulomatosis [7].

Our case was diagnosed to be primary malignant PLD as there was no typical axillary and inguinal lymphadenopathy or other lymphoid involvement on the CT scan. Although we could not make a precise pathological diagnosis of the type of B-cell lymphoma, the rapid progression of the lung infiltrations and respiratory failure suggested diffuse large B-cell lymphoma. Primary malignant PLD represents only 0.5% of all primary lung malignancies [2,7], and is usually detected incidentally during routine radiographic examinations [2,3,5]. Acute respiratory failure is known to be the leading cause for intensive care and has an overall mortality rate of 50% in patients with cancer [8]. However, acute respiratory failure due to PLD is rare. In a previous prospective study cohort of patients with various malignancies, only 8.8% of the patients developed acute respiratory failure due to PLD or suspected PLD [9].

Our case was confirmed to have diffuse large B-cell lymphoma based on histopathology and clinical manifestations. However, since most of the tumour tissue obtained was crushed and necrotized, further immunostaining could not be performed.

It is important to identify the cause of acute respiratory failure. As recent advancements in the treatment of respiratory failure can improve survival [10], arriving at a precise diagnosis is vital for the management of these patients. If the cause of the respiratory failure is advanced cancer, whether to intervene with an aggressive procedure remains a matter of dispute. Palliative care is a possible treatment option as it was in this case.

A precise diagnosis was critical for the management of this patient and a CT-guided biopsy of a large mass in close proximity to the pleura was sampled despite the patient being in severe acute respiratory failure. A previous study demonstrated that to identify the cause of acute respiratory failure in patients with cancer, non-invasive tests are not inferior to invasive procedures, such as bronchoscopy [9]. The choice of the procedure should be decided on a case-by-case basis.

In conclusion, this 72-year-old female with PLD due to B-cell lymphoma developed severe acute respiratory failure and survived only one week. Physicians should be aware that PLD can cause acute respiratory failure.

Disclosure Statement

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

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