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Case Report

Idiopathic Lymphocytic Interstitial Pneumonia

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Abstract

Idiopathic lymphocytic interstitial pneumonia (LIP) is a rare benign lymphoproliferative lung disease that is characterized by the infiltration of lymphocytes, plasma cells, and other lymphoreticular cells along the interstitium and alveolar septa, which lead to serious consequences. It may be accompanied by other diseases or can be idiopathic. This study presents a patient with complaints of cough and shortness of breath who was diagnosed with idiopathic LIP on the basis of radiographic and lung biopsy findings.

Keywords: Idiopathic, lymphoproliferative, pneumonia

Introduction

Lymphocytic interstitial pneumonia (LIP) is a lung disease characterized by collection of lymphocytes in response to various peribronchial and interstitial warnings. LIP may be associated with several diseases, such as Sjögren's syndrome, HIV, and Epstein–Barr virus. However, it may also be idiopathic. Once diagnosed, approximately 33–50% of patients die within 5 years; also, about 5% of cases turn into lymphoma (1). The aim of this study was to analyze the clinical, radiologic, and pathologic characteristics of idiopathic LIP and to discuss the diagnosis and treatment progression reported in the current literature.

Case Report

A 67-year-old female patient admitted with complaints of weakness, loss of appetite, weight loss (14 kg in 5 months), cough, and sputum for 6 months. On physical examination, the blood pressure was 110/70 mm Hg, pulse 84/min, respiratory rate 20/min, body temperature 36.7°C, and oxygen saturation 97% in room air. There were fine mid-inspiratory crackles in both lung bases. There was no hepatosplenomegaly on abdominal examination, and two lymph nodes of approximately 1 cm were found in the bilateral cervical chain on neck examination. The patient had hypertension and diabetes. Laboratory tests revealed the following: leukocytes, 27000/mm^3; neutrophil, 15400/mm^3; lymphocyte, 10500/mm^3; monocytes, 1400/mm^3; hemoglobin, 10.5 g/dL; Hct 31.7%, MCV, 81.5 fL; platelets, 390000/mm^3. In the peripheral blood smear, 55.4% neutrophils, 37.9% lymphocytes, and 5% monocytes were found. Routine biochemistry tests revealed erythrocyte sedimentation rate, 117 mm/h; glucose, 196 mg/dL; BUN, 27 mg/dL; AST, 27 U/L; ALT, 42 U/L; LDH, 187 U/L; and ALP, 88 U/L. The viral serological markers anti-HCV, anti-HIV, and HBsAg were found to be negative. There was no bacterial or fungal growth on sputum culture. Acid-resistant bacilli examination performed three times in sputum was negative. Mild mitral insufficiency and mild tricuspid insufficiency were detected on transthoracic echocardiography. The extractable nuclear antigen profile performed to scan for collagen tissue diseases and other markers were detected as negative, and immunoglobulin, rheumatoid factor (RF), antinuclear antibodies, and anti-double-stranded DNA (anti-dsDNA) antibody levels were within normal limits. Hypercellular bone marrow (70–80%) was found, and lymphocyte ratio was 15%. Immunophenotyping of the bone marrow was consistent with splenic marginal zone lymphoma. A bone marrow biopsy performed for leukocytosis was evaluated as normal. In pulmonary function testing, the forced expiratory volume in 1 s (FEV_1) was detected as 1.13 L (64%), forced vital capacity (FVC) as 2.15 L (56%), FEV_1/FVC as 95%, diffusing lung capacity for carbon monoxide (DLCO) as 2.5 mL/mm Hg/min (13%), and DLCO corrected for alveolar volume (DLCO/VA) as 1.17 mL/min/mmHg/L (26%). Bilateral consolidated opacities were found on posteroanterior chest radiograph (Figure 1). In thoracic computed tomography (CT), specifically in bilateral lung parenchyma, many nodular opacities were found the largest of which were in the left upper

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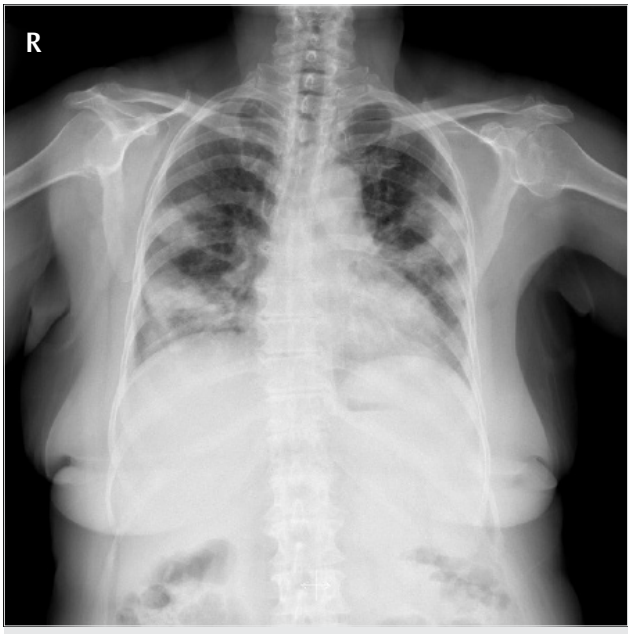

Figure 1. Pre-treatment posteroanterior chest radiograph
PA: postero- anterior

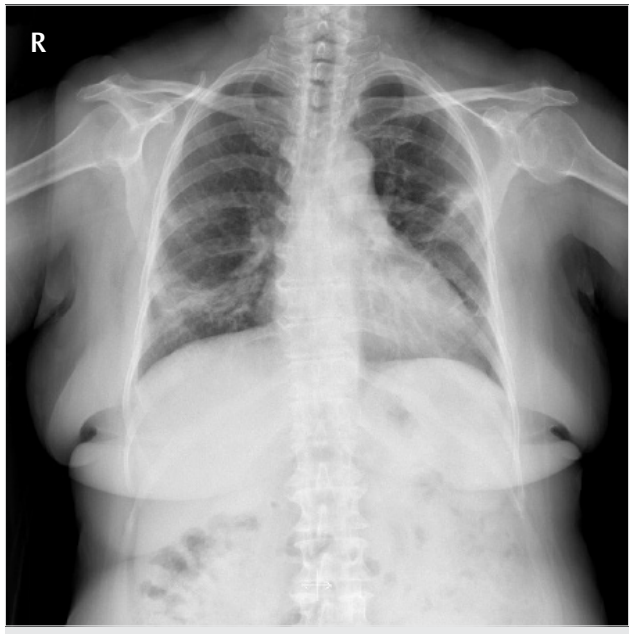

Figure 3. After treatment, decline in lesions on posteroanterior chest radiograph taken for control
PA: postero-anterior

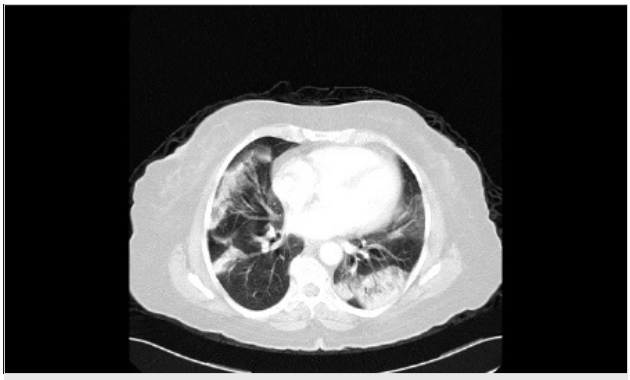

Figure 2. Pre-treatment thoracic computed tomography

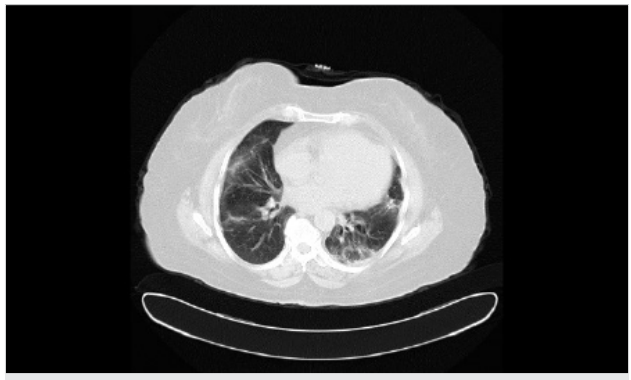

Figure 4. After treatment, thoracic computed tomography taken for control

lobe in the anterior segment, with a size of 3.5×2.5 cm and in the right lobe in the superior segment, 2 cm in diameter with irregular contours, with having air bronchograms and accompanying feeder vessels (Figure 2). In positron emission tomography/CT, many distributed irregular limited hypermethabolic mass lesions were detected in both lungs, the largest being in the right upper lobe inferolateral of 51×30 mm and in the left lower lobe posterobasal segment of 83×32 mm in diameter and with a mass appearance of ground-glass density. A fine-needle aspiration biopsy was taken from the lung lesion, but it was reported as insufficient material. Endobronchial pathology was not observed on fiberoptic bronchoscopy. The bronchoalveolar lavage fluid was evaluated to be consistent with marginal zone lymphoma in flow examination. Video-assisted thoracoscopic surgery (VATS) and left lung upper lobe wedge resection and pleural biopsy were performed on the patient. Histopathological and immunohistochemical findings were consistent with LIP. Because our patient did not have an underlying systemic disease with clinical and laboratory findings, 1 mg/kg steroid therapy was started with the diagnosis of idiopathic LIP and continued for 1 year in decreasing doses. During the follow-up, a significant improvement was seen in respiratory function and radiological findings (Figures 3, 4).

Discussion

Lymphocytic interstitial pneumonia is a form of interstitial pneumonia characterized by intense and diffuse lymphocytic infiltration of alveolar septa, and its incidence is not known. Its etiology may be associated with immunological diseases (AIDS, Sjögren's syndrome, etc.) or viral infections (HIV, Epstein–Barr) (2). Underlying secondary diseases, such as immune deficiency and connective tissue diseases, take an important place among the reasons for LIP, and idiopathic LIP is seen less frequently (3, 4). There were no symptoms or clinical findings associated with collagen tissue disease or HIV in our patient. Most patients with LIP are female, and the symptoms begin between the ages of 40 and 70. When diagnosed, the majority of patients have respiratory symptoms. Progressive dyspnea and dry cough are the most common symptoms, and fever, night sweats, and weight loss are the systemic symptoms that are seen less frequently. Clubbing is the physical examination finding that is often seen, and peripheral and mediastinal lymphadenopathy and splenomegaly are rarely seen (1). Our patient had complaints of cough, sputum, weakness, weight loss, and fever, which began 6 months previously.

The laboratory findings in LIP vary according to concomitant diseases. Serum dysproteinemia is seen in approximately 80% of pa-

tients. Polyclonal hypergammaglobulinemia is seen most often (5). Incidence of lymphoproliferative malignancy is higher in patients with hypogammaglobulinemia or monoclonal gammopathy (6).

In the studies by Takata et al. (6) and Kurosu et al. (7), it is reported that RF in the serum, anti-dsDNA antibodies, cancer antigen 19-9 elevation, and an increase in globulin and lymphocyte levels might occur. In our patient, the tumor marker CA 19.9 was found to be high, but hyperglobulinemia and autoantibody positivity was not detected. Features of malignancy were not detected in gastroscopy, colonoscopy, and abdominal CT examinations made for the investigation of gastrointestinal system.

In LIP, the most common findings in high-resolution chest CT are reported to be a ground-glass appearance, centrilobular nodules, small nodules under the pleura, bilateral reticular, and reticulonodular opacities in the lower lung zones on a chest radiograph. Other imaging findings associated with LIP are the presence of bronchovascular branch thickening, interlobular septal thickening, air cysts, and lymphadenopathy (7). Consolidated bilateral opacities on the chest radiograph of our patient were observed in the radiological findings. In thoracic computed tomography (CT), specifically in bilateral lung parenchyma, many nodular opacities the largest of which were in the left upper lobe in the anterior segment with a size of 3.5 x 2.5 cm and in the right lobe in the superior segment 2 cm in diameter with irregular contours, and having air bronchograms and feeder vessels accompanying were monitored.

Lymphoid infiltrates consisting of lymphocytes, histiocytes, plasma cells, type II pneumocytes hyperplasia and alveolar macrophages constitute the histopathological features of lymphoid interstitial pneumonia (8). Only cases with common alveolar septal infiltration are classified as LIP in the definition of American Thoracic Society (ATS) / European Respiratory Society (ERS) (3). This can be seen in non-necrotizing giant cell granulomas in pathological examination. When transbronchial or endobronchial biopsies taken as bronchoscopic are insufficient for diagnosis, it is required to take an open or thoracoscopic biopsy (1). A fine needle aspiration biopsy was taken from the lung lesion, but it was reported as insufficient material. An endobronchial pathology was not observed in fiberoptic bronchoscopy. Bronchoalveolar lavage fluid was evaluated to be consistent with marginal zone lymphoma in flow examination. Left lung upper lobe wedge resection and pleural biopsy were performed on the patient through VATS. Histopathological and immunohistochemical findings were consistent with the lymphoid interstitial pneumonia. Histopathological findings of lymphoma are malignant lymphocytes in monoclonal feature. Furthermore, a small amount of fibrosis is a clue in favor of indicating lymphoma. Immunophenotyping can be made in cases for which a diagnosis cannot be made (9). In our patient, pulmonary lymphoma was excluded with histopathological findings.

Steroids and immunosuppressants can be used in the treatment of LIP. A steroid treatment dose is recommended between 0.75 mg/kg/day and 1 mg/kg/day but should not exceed 100 mg/kg/day for 8–12 weeks or until the clinical condition becomes stabilized. When the clinical situation becomes stabilized, the dose is gradually reduced up to 0.25 mg/kg/day. Showing symptomatic and radiological improvement, 50–60% of patients respond to steroids (1). In their study, Uslu et al. (10) used steroids in LIP treatment and significant benefits were observed. After diagnosis, steroid therapy was started in our patient. After steroid treatment, a decrease in clinical complaints, a significant increase in pulmonary function tests, and radiological improvement were observed in the follow-up. Recurrence was not observed in the follow-ups.

Conclusion

The diagnosis of idiopathic LIP, which is also covered in quite a few cases in the literature, could be made according to the results of the clinical, radiological, and pathological approaches. In the chest radiograph and computed tomography, with the differential diagnosis of bilateral, diffuse, and nodular opacity and ground-glass density with the air bronchograms and consolidation, LIP should also be considered. Although idiopathic LIP usually responds well to steroids, we emphasize that it may lead to progressive respiratory failure and therefore should be followed closely.

Informed Consent: Written informed consent was not received due to the retrospective nature of this study.

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