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Case report

Anti-synthetase syndrome presenting as cryptogenic organizing pneumonia

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ABSTRACT

Interstitial lung disease (ILD) is a unique group of lung diseases that can be associated with inflammatory conditions, such as polymyositis-dermatomyositis (PM-DM). Presentation of PM-DM with ILD is not uncommon but clinical and radiological features can be similar to other conditions (e.g. atypical pneumonia) and can be challenging to diagnose. Delayed diagnosis of PM-DM can be associated with progression of pulmonary involvement and potentially increase morbidity. We report a patient presenting with pulmonary symptoms who had positive anti-Jo-1 antibodies and cryptogenic organizing pneumonia features on biopsy, which is a rare reported finding.

1. Introduction

There are a number of etiologies associated with interstitial lung disease (ILD).[1] ILD has been recognized as an early presentation of polymyositis-dermatomyositis (PM-DM) with frequency as high as 65%.[2] ILD in PM-DM is associated with a high rate of morbidity and mortality.[2] We report a case of a patient with dyspnea, cough, and intermittent fever in the setting of positive anti-Jo-1 antibodies, who was subsequently documented to have ILD on lung biopsy.

2. Case report

A 52 year-old man who was previously healthy and a non-smoker presented to an outside facility with cough, progressive dyspnea and fevers. He was empirically treated for suspected community acquired pneumonia with intravenous Ceftriaxone and Levofloxacin. A diagnostic bronchoscopy with bronchioalveolar lavage sampling was unrevealing. Because of poor therapeutic response, progression of shortness of breath, and hypoxemia, the patient was transferred to our institution for further evaluation and management.

The patient's social history included a recent business trip to Bangkok and Tokyo, but he denied any specific environmental or infectious exposures. He denied weight loss, previous pulmonary symptoms, muscle weakness, joints swelling and rashes. Initial vital signs revealed that he was febrile to 38.8 °C, blood pressure of 170/72 mmHg, and hypoxic with oxygen saturation in the low 80 s on 3 liters per minute (LPM) of oxygen by nasal cannula. Physical examination was remarkable for bilateral inspiratory crackles and otherwise unrevealing.

Laboratory evaluation was remarkable for leukocytosis of $9.3 \times 10^3/mm^3$ with an elevated fraction of eosinophils 0.85% (normal 0.05–0.5%), an elevated sedimentation rate of 43 mm/1 h (normal 0–22 mm/1 h), an elevated C-reactive protein of 21.8 mg/L (normal $\leq$ 8.0 mg/L) and creatinine kinase of 740 U/L (normal 52–336). Urine analysis was normal; no myoglobin was seen. Spirometry was consistent with a restrictive pattern (FVC 38% predicted). Repeat chest computed tomography (CT) demonstrated a progressive and bilateral scattered consolidative appearing infiltrates (Fig. 1). Given the recent travel and eosinophilia, an extensive infectious disease evaluation was performed, which was unrevealing.

A subsequent video-assisted thoracic surgery (VATS) lung biopsy showed patchy organizing pneumonia and diffuse mixed inflammatory infiltrates involving interstitial septa and alveolar spaces (Fig. 2). Subsequent serologies revealed slight increase in antinuclear antibody to 2.2 (normal < 1.0 units) with increased anti-Jo-1 antibody of 2.2 (normal < 1.0 units); other extractable

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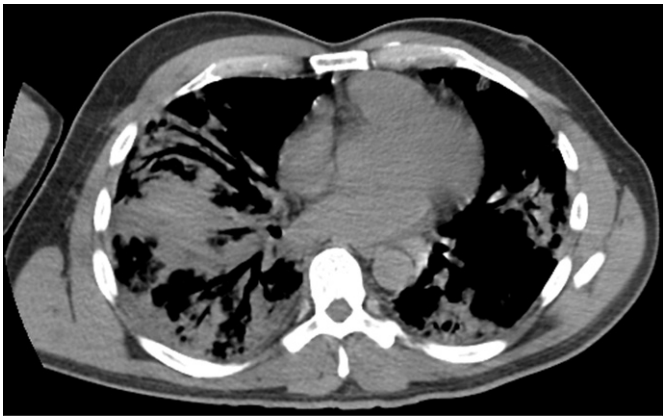

Fig. 1. CT of the lungs shows bilateral scattered consolidative appearing infiltrates.

nuclear antibodies, rheumatoid factor, and anti-neutrophil cytoplasmic antibodies were not detected. Due to concern for an underlying autoimmune process, electromyography was pursued and was consistent with a proximal inflammatory myopathy. Magnetic resonance imaging of the lower extremities showed marked intramuscular edema, which was compatible with the clinical diagnosis of myositis. He also underwent muscle biopsy, which showed a slight inflammatory myopathy and mild denervation atrophy. The patient was not on any medication, including statin therapy, that would cause myositis.

A diagnosis of anti-synthetase syndrome was made, and treatment started with high dose methylprednisolone (500 mg twice a day for three days) and cyclophosphamide (one time dose of 1000 mg IV). Subsequently, his fever, cough and breathing markedly improved, with tapering of the immunosuppressive medication doses.

3. Discussion

Myositis associated with ILD may present with ILD preceding the myositis or at any time during the disease course.[3] Surgical lung biopsies in patients with ILD associated anti-synthetase syndrome may show different histological features including nonspecific interstitial pneumonia (NSIP), diffuse alveolar damage (DAD), usual interstitial pneumonia (UIP), or cryptogenic organizing pneumonia (COP).[5] The prevalence of these histological features varies between reports.[4–6]

Anti-synthetase syndrome is a systemic autoimmune syndrome characterized by the presence of anti-aminoacyl tRNA antibodies (anti-ARS antibodies) accompanied by a constellation of clinical findings including PM-DM, ILD, “mechanic” hands appearance and Raynaud’s phenomenon. Anti-ARS antibodies in PM patients are strongly associated with the presence of ILD.[2,3,7] Anti-histidyl-tRNA synthetase (anti-Jo-1) antibody was the first of the anti-ARS antibodies to be discovered and is one of the most commonly reported auto-antibodies in patients with PM.[8–10] ILD is a common early manifestation in patients with anti-Jo-1-positive PM-DM.[11] Indeed, respiratory symptoms may be the presenting symptoms in up to 61% of patients with PM-DM.[7]

Previous studies have described an acute versus chronic form of ILD associated with PM-DM. Our patient’s presenting symptoms were respiratory in nature and the CT scan demonstrated consolidation, consistent with the acute form of PM-DM associated ILD.[4] Our patient’s case uniquely demonstrates how the diagnosis of anti-synthetase syndrome may be not clinically apparent on history or physical exam, but may appear upon further diagnostic evaluation. This case also highlights the importance of considering a broad differential diagnosis for suspected infectious pneumonia cases that are not responding to standard antibiotic regimens. Prompt diagnosis and appropriate therapy for those cases can prevent disease progression and improve patient outcome.

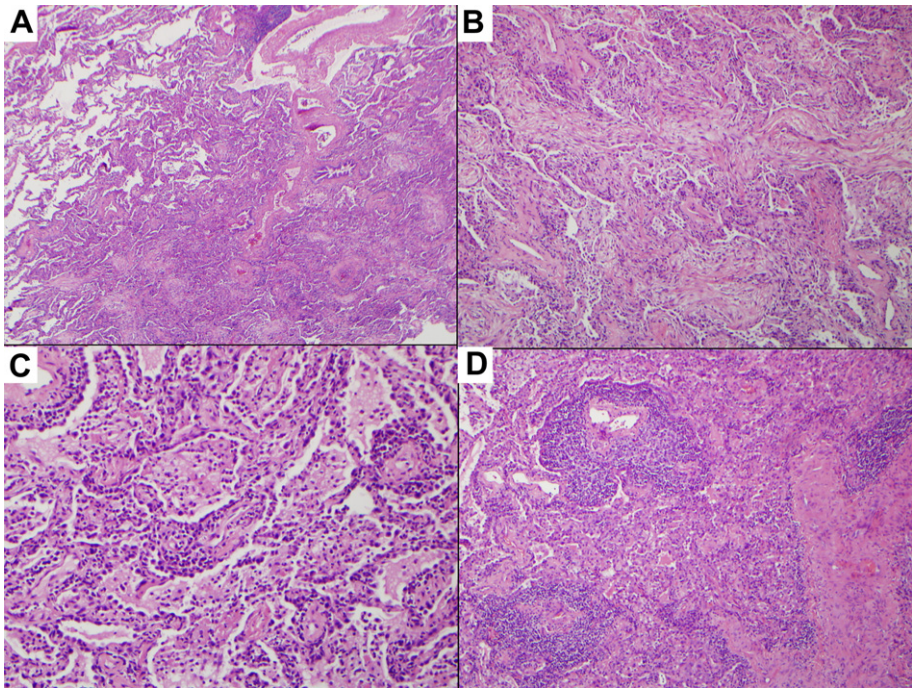

Fig. 2. Patchy foci of confluent organizing pneumonia (A: hematoxylin and eosin staining, 40× original magnification) characterized by intraalveolar polypoid fibroblastic proliferation (B: hematoxylin and eosin staining, 200×). Adjacent lung with interstitial and intraalveolar lymphoplasmacytic infiltration (C: hematoxylin and eosin staining, 200×) and areas of benign lymphoid hyperplasia (D: hematoxylin and eosin staining, 100×).

Conflict of interest

None.

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