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Case Report

Antisynthetase syndrome-related organizing pneumonia: A case report

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Antisynthetase syndrome is a rare multisystem disease. Lung involvement is usually manifested by interstitial lung disease of different histologic subtypes that may occur either before, simultaneously or after the development of dermatomyositis/ polymyositis. We report a rare case of a 39-year-old female who presented with organizing pneumonia as the first manifestation of antisynthetase syndrome. Physicians are advised to keep low threshold of suspicion and to screen for this disease even in the absence of connective tissue manifestations.

Keywords: Antisynthetase, Organizing pneumonia

INTRODUCTION

Antisynthetase syndrome (AS) was described in 1990, and consists of a group of symptoms that often occur in association with antibodies against aminoacyl-tRNA synthetase (Marguerie et al., 1990). Clinical presentation can include myositis, polyarthritis, fever, mechanic's hands, Raynaud phenomena, and interstitial lung disease (ILD) (Shinjo and Levy-Neto, 2010). ILD is the clinical hallmark of AS, and is regarded as mandatory for the diagnosis of AS by most practitioners (Jan and Øyvind, 2011). The Antisynthetase Syndrome).

Different histological subtypes of ILD have been described in association with AS. Non-specific interstitial pneumonia (NSIP) is the most common. This is followed by usual interstitial pneumonia (UIP) and diffuse alveolar damage. Organizing pneumonia is a less frequently reported form of ILD (Xing et al., 1999; Haydour et al., 2012). Herein, we report a case of organizing pneumonia secondary to AS. We aim to increase physicians' awareness of this rare condition.

CASE REPORT

A 39-year-old female patient presented with fever, shortness of breath, dry cough, and joint pain in her proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, and reported having experienced dyspnea on exertion for 3 months. There was no history of skin rash, oral ulcer, photosensitive rash, or dysphagia, but she had a history of proximal muscle weakness, and reported weakness when standing from a sitting position and when dressing herself. Nevertheless, she had no diplopia or swallowing complaints. She was a housewife and a non-smoker, with no animal or noxious environmental exposure. Other aspects of a systemic review were unremarkable.

Examination results were temperature 38 degrees, pulse 110 beats/min, blood pressure 116/73 mm Hg, heart rate 110 bpm, respiratory rate 18 breaths/min, and oxygen saturation 94% while breathing room air. The patient was in a semi-sitting position and not in respiratory distress, and there was no skin pigmentation, rash, or lymphadenopathy. Chest examination revealed fine crepitation throughout her lungs, but predominantly at their bases. Musculoskeletal examination revealed a

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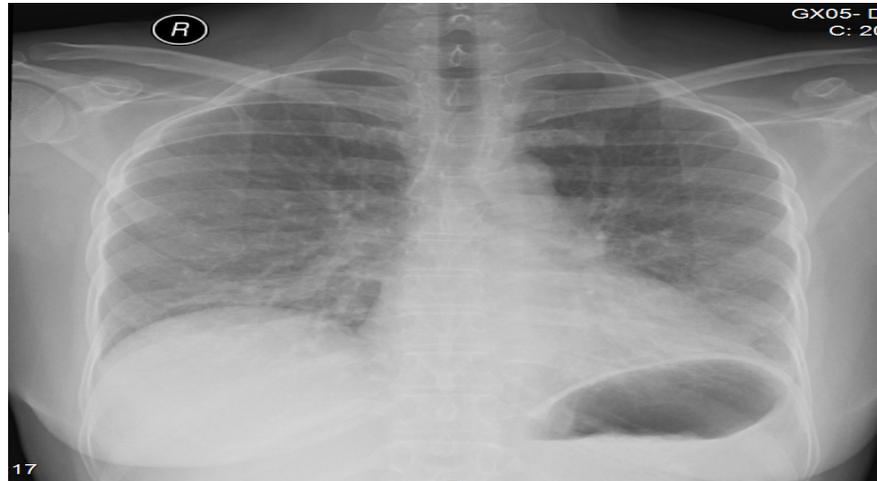


Figure 1. Chest x ray showed bilateral lower lobe predominant reticular opacities with preserved lung volume.



Figure 2. High-resolution chest computed tomography showing bilateral scattered patchy ground-glass opacities (red arrows) and consolidations (black arrows) are seen, with basilar and peribronchovascular predominance.

full range of motion in her joints, no deformity of her PIP or MCP joints, and no signs of synovitis. All her extremities exhibited normal muscle tone, with a power of 5/5. Neurological examination demonstrated normal cranial nerves and normal reflexes. Cardiovascular and abdominal examinations were unremarkable.

Laboratory analysis results were white blood cell count 12,700/ μ L, hemoglobin 12.9 g/dL, platelets 337,000/ μ L, and normal creatinine kinase 265 IU/L (26–308 IU/L). Erythrocyte sedimentation rate was mildly elevated at 26 mm/H, immunological workup revealed a weak but positive anti-nuclear antibody (ANA) titer of 1:80, and the patient was also positive for anti-JO-1 (168 U/mL). Other results included normal levels of rheumatoid factor (9.19

IU/L), complement, perinuclear anti-neutrophil cytoplasmic antibodies (ANCA), cytoplasmic ANCA, anti-cyclic citrullinated peptide antibody (0.7 U/mL), and scleroderma-70 antibody.

Chest X-ray revealed bilateral predominantly mid and lower-lung interstitial opacities (Figure 1). High-resolution chest computed tomography (CT) confirmed bilateral, scattered, patchy, ground-glass opacities and consolidations with basilar and peribronchovascular predominance. A few areas of suspected perilobular opacification were noted (Figure 2). Pulmonary function testing was consistent with parenchymal restriction, with a vital capacity of 1.14 L which was 45% of the predicted level, and a normal forced expiratory volume in the first



Figure 3. Repeat HRCT: There is interval improvement of the interstitial lung disease, predominantly in the form of resolution of the consolidation. Although the ground-glass opacities remain unchanged, no fibrosis or new abnormalities is present.

second: forced vital capacity ratio (FEV1/FVC) of 87%.

The patient was diagnosed with AS based on clinical, radiological, and immunological findings, and she was started on oral prednisolone 50 mg once a day, oral hydroxychloroquine 200 mg twice a day, and oral azathioprine 50 mg twice a day. She showed a remarkable improvement and high resolution CT performed after 3 months of treatment showed interval improvement of the bilateral patchy peripheral and predominantly lower lung airspace opacities, mainly in the form of resolution of the consolidation. The ground-glass opacities remained relatively unchanged. No new opacities were seen, and no fibrosis had developed (Figure 3).

DISCUSSION

AS is a multisystem autoimmune disease, characterized by the presence of anti-aminoacyl-tRNA antibodies. Anti-JO-1 is the next most common antibody in AS patients, and is present in approximately 80% of cases (Friedman et al., 1996). PL-7, PL-12, OJ,EJ, KS, and WA antibodies are less commonly seen (Arnett et al., 1996; Yoshifuji et al., 2006). The syndrome is more common in female patients (Dugar et al., 2011), and can entail numerous clinical findings such as polymyositis-dermatomyositis (PM-DM), ILD, Reynaud's phenomenon, fever, and mechanic's hands.

ILD is reported in most AS patients, and the prevalence of lung involvement is approximately 75–90% (Tillie-Leblond et al., 2008; Yousem et al., 2010). Furthermore, lung involvement is the most important determinant of prognosis, and can be the sole clinical presentation (Tillie-Leblond et al., 2008). Patients may present with

acute, subacute, or chronic dyspnea on exertion, coughing, and rarely, hemoptysis (Aslam, 2013; Chatterjee, et al., 2013). Chest X-rays can be normal in 20% of patients with ILD due to antisynthetase. Therefore, high-resolution chest CT is always needed for these patients, to investigate potential ILD. The most common ILD subtype associated with AS is NSIP with diffuse patchy ground-glass opacities and subpleural predominance (Shinjo and Levy-Neto, 2010). Features of advanced fibrotic changes consistent with UIP, and diffuse alveolar damage have also been described (Haydour, Wells et al. 2012). The current case exhibited predominantly peripheral, peribronchovascular, and subpleural consolidations consistent with organizing pneumonia, which have been described less frequently than NSIP (Priyangika et al., 2016).

Myositis is reported in 90% of AS patients (Chatterjee et al., 2013). PM and DM subtypes have been reported in 64% and 24% of AS patients, respectively. However, myositis can be clinically absent at initial presentation, as demonstrated in one series of ILD patients with anti-JO-1 antibodies in which myositis was present in only 31% at initial presentation (Tillie-Leblond et al., 2008). The subject of the current study did not exhibit any clinical or biochemical evidence of myositis. Nevertheless, a diagnosis of AS was supported by the positive anti-JO-1 serology, fever, and the organizing pneumonia pattern on high resolution CT pending other connective tissue disease CTD features, which may appear within 6 months or more of initial presentation as noted in the literature (Zamora et al., 2016).

The current patient did not have any arthritis, Reynaud's phenomenon, or mechanic's hands, features seen in only 29%, 23%, and 20% of AS patients, respectively (Zamora et al., 2016).

It is important to note that ILD may precede the diagnosis of other CTD manifestations. Therefore, testing for anti-JO-1 is advised in all patients with ILD without clear etiology, because pulmonary involvement may be the sole presenting manifestation (Aslam and 2013;1–6.). Early detection of anti-JO-1 antibodies is an indicator of late-onset myopathy, and provides prognostic information because anti-JO-1-positive patients usually respond to treatment yet they have a high recurrence rate (Yoshifuji et al., 2006; Katzap et al., 2011). Male gender and low initial diffusing capacity of the lungs for carbon monoxide have been considered poor prognostic factors for disease progression and increased mortality (Zamora, Hoskote et al. 2016). In another study, UIP pattern was associated with poor outcome (Marie et al., 2013).

Corticosteroids are the mainstay of treatment in AS patients. We treated the current case with prednisone at 1 mg/kg for 4 weeks with a slow taper over 6 months. She exhibited significant clinical improvement with stable radiological appearance on follow-up visits. Other drugs such as azathioprine, methotrexate, cyclophosphamide, cyclosporin, tacrolimus, and rituximab can be used as steroid-sparing agents and to achieve adequate disease control (Tillie-Leblond et al., 2008).

CONCLUSION

Organizing pneumonia can be the presenting manifestation of AS, which is a rare multisystem autoimmune disease. A diagnosis of AS should be considered in any patient with ILD with or without inflammatory myopathy at presentation. Clinicians are advised to utilize a low threshold when testing for anti-JO-1 antibodies in patients with ILD without clear etiology. Oral steroids and immunosuppressive agents are the mainstay of treatment.

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