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Case report

Severe respiratory failure as a presenting feature of an interstitial lung disease associated with anti-synthetase syndrome (ASS)☆

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ABSTRACT

Anti-synthetase syndrome (ASS) is defined as a heterogeneous connective tissue disorder characterized by the association of an interstitial lung disease (ILD) with or without inflammatory myositis with the presence of anti-aminoacyl-tRNA-synthetase antibodies. ILD is one of the major extra-muscular manifestations of polymyositis and dermatomyositis. We report a case of a patient with dyspnea, cough, and intermittent fever as well as ILD associated ASS in the absence of muscular involvement. This patient was admitted to the emergency department with severe respiratory failure requiring non-invasive ventilation. Our patient's case demonstrates that the diagnosis of ASS may not be obvious. However, its diagnosis leads to appropriate and potentially life-saving treatment.

1. Introduction

Interstitial lung disease (ILD) encompasses a diverse group of pulmonary disorders also known as diffuse parenchymal lung diseases. These diseases are typically classified together because of unifying clinical, physiological, pathological, and radiographic manifestations.

Since its description in 1956 by Golden and Bronk and an initial effort at classification by Liebow and Carrington in 1969, a precise classification system for ILD has evolved as new clinical, histopathologic, and radiographic information develops [1,2].

There are a number of etiologies associated with ILD. It is found in over 60% of patients with anti-synthetase syndrome

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(ASS) and is a major cause of morbidity. Lung involvement may occur in the absence of muscular involvement [3,4]. ASS is characterized as inflammatory myositis associated with fever, arthritis, Raynaud's phenomenon, mechanic's hands and ILD with the presence of anti-RNA synthetase antibodies (ARS) [5]. Most patients present with some, but not all, clinical manifestations.

ILD associated with ARS is the most prevalent ASS manifestation; it is the principal cause of morbidity and mortality in ASS [5,6]. According to the American Thoracic Society (ATS), criteria for ASS diagnosis are a positive serologic testing for an anti-RNA synthetase autoantibody plus one or more of the following conditions: evidence of myositis, evidence of ILD by ATS criteria, evidence of arthritis by clinical examination, radiographic findings, and patient self-report of unexplained persistent fever, Raynaud phenomenon, and the presence or absence of mechanic's hands [2].

Anti-ARS antibodies in polymyositis (PM) patients are strongly correlated with the presence of ILD [3]. Associated symptoms of Sjogren's syndrome or systemic sclerosis (SSc) have also been reported in various cohorts [4]. Various anti-ARS specificities have been described, with anti-histidyl (Jo1)-tRNA-synthetase antibodies being the most common (20% of polymyositis (PM) and dermatomyositis (DM) patients). Other antibodies including antialanyl (PL12), anti-threonyl (PL7), anti-isoleucyl (OJ) and anti-glycyl (EJ)-tRNA-synthetase are less commonly found; each antibody being found in 0.5% of PM and DM patients. Although anti-ARS antibodies may be associated with other anti-extractable nuclear antigen antibodies, including anti-Ro/SSA and anti-La/SSB antibodies, they are mutually exclusive in most cases [4–6]. 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. ILD is a common early manifestation in patients with anti-Jo-1-positive PM/DM. Moreover, respiratory signs are the presenting problem in up to 61% of patients with PM/DM [3]. ILD is one of the major extra-muscular manifestations of PM/DM, occurring at a frequency ranging 5–64% of patients [5].

We report a rare case of a patient presenting with severe respiratory failure and ASS with isolated lung involvement initially treated with non-invasive ventilation.

2. Case report

A 48 year-old woman presented with an 8-year history of recurrent episodes of acute bronchitis that had been treated as exacerbations/flare-ups of asthma. Each episode lasted for approximately one week and occurred every 6 months. The patient was treated with inhaled bronchodilators plus corticosteroids twice a day during these exacerbations. Prior to admission to our facility, the patient suffered a flare-up. She later provided the following history: no history of skin diseases, no prior malignancies, pregnancy, alcohol use, smoking, or exposure to toxins. She denied dysphagia and extensor muscle weakness.

She was admitted to the emergency department presenting with complaints of breathlessness, weakness, fever, and productive cough. During the 48 h before admission, her respiratory condition had rapidly and progressively deteriorated. Vital signs included a blood pressure of 105/55 mmHg, heart rate of 122 beats/min, and breathing rate of 32 breaths/min with a core temperature of 38.5 ° cardiac frequency: physical examination revealed bilateral basilar fine crackles with a normal abdominal examination, including the absence of hepatomegaly. There was no lymphadenopathy and no dermatological manifestations were seen.

At admission the patient exhibited acute respiratory failure, and had a paO_2 of 59 with oxygen 6 L/m', $paCO_2$ of 29, pH of 7.50, HCO_3 of 24 mEq/L, and a paO_2/FiO_2 ratio of 168. Laboratory examinations revealed neutrophilic leukocytosis (white blood cells 19.23 × 10.e3/UL, neutrophils 15.85 × 10.e3/μL), elevated CPK (creatine phosphokinase) of 367 U/L (60–174 U/L), elevated LDH (lactate dehydrogenase) of 581 U/L (280–450 U/L), elevated AST (aspartate aminotransferase) of 39 U/L (6–34 U/L), normal alanine transaminase (ALT) level of 31 (6–34 U/L), C-reactive protein of 18.4 mg/dL (0–.50 mg/dL), and normal ferritin level of 13.4 ng/mL (12.0–150.0) ng/mL. Urine antigen tests for *Streptococcus pneumoniae* and *Legionella pneumophila* were negative. A thoracic radiograph demonstrated multiple pulmonary infiltrates consistent with interstitial lung disease (Fig. 1a).

The patient was treated with non-invasive ventilation (NIV) delivered by an oronasal mask and bi-level positive airway pressure (BiPAP). Respiratory parameters were set at an IPAP of 14 cmH_2O, EPAP of 9 cmH_2O, and FiO_2 of 30% to achieve a tidal volume of 6–8 ml/kg and maintain an oxygen saturation above 92%. After 1 h of NIV, an arterial blood gas analysis demonstrated a paO_2 of 71, $paCO_2$ of 36, pH of 7.45, and HCO_3^- of 23.4 mEq/L with paO_2/FiO_2 of 236. The patient continued NIV for 5 days; during which time inspiratory and expiratory pressures were gradually reduced. On the sixth day of hospitalization, she continued oxygen therapy with a Venturi mask (FiO_2 35%).

Antibiotic therapy was prescribed (piperacillin/tazobactam 4.5 g/8 h and clarithromycin 500 mg/12 h) in addition to a high dose of intravenous corticosteroids (methylprednisolone 160 mg/day). An high-resolution computed tomography (CT) scan showed bilateral reticular opacities, traction bronchiectasis, peribronchovascular scattering, and architectural distortion (Fig. 1b). Following clinical improvement by day 10 of hospitalization, the patient was transferred from the emergency department to the pulmonology unit to complete clinical investigations. Her preliminary diagnosis was severe respiratory failure due to idiopathic pulmonary interstitial lung disease.

Pulmonary lung function demonstrated a mild restrictive ventilator syndrome with a forced vital capacity (FVC) of 73.6%, forced expiratory volume of 1 s (FEV_1), lung capacity of 76.9%, total lung capacity (TLC) of 78.1%, residual volume (RV) of 89.8%, and diffusing lung carbon monoxide (DLCO) of 60.9%. A six-minute walk test (6MWT) covered a distance of 330 m with a minimum $satO_2$ of 87%. During this period the patient's respiratory condition improved (paO_2 71, $paCO_2$ 42, pH 7.389, and HCO_3 24 mEq/L on room air), and oxygen supplementation was stopped. Corticosteroid therapy was reduced to prednisone 50 mg/day on the seventh day of hospitalization.