CASE REPORT

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A Case of Antisynthetase Syndrome in Postpartum Period

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ABSTRACT Antisynthetase syndrome (ASS) is a rare autoimmune disease that is clinically manifested with interstitial lung disease (ILD), inflammatory myopathies, inflammatory arthritis, skin hyperkeratosis, and Raynaud's phenomenon. The pathophysiology of ASS is not clearly understood but the presence of anti-aminoacyl-tRNA appears to be a marker of ASS. The most common and first identified of anti-aminoacyl-tRNA antibody is anti-Jo-1. Being a rare and hardly diagnosed entity, we present a 33-year-old woman referring to the hospital with fever, dry cough and dyspnea in the postpartum period. She had Raynoud's phenomena and her upper extremity power was decreased. High resolution computed tomography and pulmonary function test were performed, and these tests were consistent with ILD. Electromyographic revealed myopathy. Her anti-Jo-1 was positive. She was diagnosed with ASS and administered immunosuppressive medications.

Keywords: Antisynthetase syndrome; interstitial lung disease; Raynaud's phenomenon; anti-Jo-1

Antisynthetase syndrome (ASS) is a rare, chronic, autoimmune disease affecting multiple organs. ASS is considered in a subgroup of idiopathic inflammatory myopathies.[1]

The patients with ASS have characteristic clinical picture: interstitial lung disease (ILD), myositis, hyperkeratotic skin changes on the hand (mechanic's hand), non-erosive arthritis, fever and Raynaud's phenomena.[2-5] Although viral infections, genetic predisposition, and medication may play a role in the pathophysiology of ASS, the true mechanism is not yet understood.

Anti-Jo was the first anti-synthetase antibody discovered.[6] When the patient is suspected to have ASS; we must measure anti-Jo-1 antibodies, as the titres of anti-Jo-antibody are strongly related to the disease activity.[7-9]

Here we present the case of a patient with features of ILD and fever in postpartum period. She had subsequently developed Raynaud's phenomenon, myositis and measures of anti-Jo-1 antibodies were positive. These findings lead to the diagnosis of ASS.

CASE REPORT

The patient gave informed consent. A 33-year-old Syrian women was referred to our infectious diseases clinic with progressive dyspnea, cough and fever. She had no comorbidities. Her family history was unremarkable. She had two healthy children. She had dry cough, dyspnea in fifth month of her last gestation. Fetal heart sounds were lost in the eight month of gestation and she had delivered a fetal baby two weeks before showing up in the infection clinic. She complained worsening of cough, dyspnea and fever. She was suspected to have lower respiratory tract infections-pneumonia and she was admitted to the infectious diseases clinic of our hospital. She was given a broad spectrum antibiotic (meropenem). Also, she

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was suspected to have pulmonary emboli, thus thorax computed tomography (CT) angiography and ventilation-perfusion scintigraphy were performed. Low grade pulmonary emboli was observed.

Later, she was referred to our internal medicine clinic. On admission, the patient's condition was moderate. She was conscious and cooperative. Her blood pressure was 110/57 mmHg, 88/minimum heart rate and her body temperature was 37.8 C. Physical examination revealed sub-crepitant rales in bilateral pulmonary bases and Raynaud's phenomenon. There were no peripheral lymphadenopathy and venous distension. Her abdominal examination was normal. Her proximal upper extremity strength was 4/5, proximal lower extremity strength was 3/5, while distal muscle strength was normal.

The results of the initial blood tests were as follows: hemoglobin: 11.2 g/dL, white blood cells: 11,450/mm³, neutrophil: 9,080/mm³, platelets: 36,8000/mm³. Renal and thyroid function tests were normal. Aspartate aminotransferase: 215 mg/dL, alanine aminotransferase: 175 mg/dL, gamma glutamyl transferase: 7 mg/dL, alkaline phosphatase: 63 mg/dL, lactate dehydrogenase: 938 mg/dL, creatinine kinase (CK): 8,690 mg/dL, D-dimer: 29.

Echocardiographic examination of the heart revealed right ventricular cavity expansion and normal left ventricular function, pulmonary arterial pressure: 50 mmHg and minimal pericardial effusion. She was started subcutaneous enoxaparin because of suspected pulmonary thromboembolism.

Serologic tests including antinuclear antibody, anti-DsDNA, anti-cyclic citrullinated peptid, perinuclear antineutrophilic cytoplasmic antibody (p-ANCA), cytoplasmic-ANCA were also negative. Angiotensin-converting enzyme levels were normal, anti-Jo-1: positive, aldolaz: 63.

High resolution computed tomography (HRCT) of chest was performed, ground glass opacities and consolidation in paramediastinal area and posterior basal segment of both lower lobes were seen.

Pulmonary function test: forced expiratory volume in one second (FEV1): 3.13, FEV1/forced vital capacity (FVC): 83%, peak expiratory flow: 7.05l/s; these findings show us restrictive pulmonary pattern.

Electromyographic examination revealed proximal muscular myopathy. Positron emission tomography (PET-CT) was normal.

In light of these findings: ILD, Raynaud's phenomenon, proximal muscular myopathy, anti-Jo-1 positive; she was suspected of ASS. She was started methylprednisolone 1 mg/kg via intravenous route. for 3 days, then 64 mg via peroral route. Her complaints were relieved. Her prednisolone dose was slowly decreased to 2x16 mg and azathioprine 3x50 mg was added.

She was referred to the Department of Rheumatology of the İstanbul Medical Faculty and has been followed-up since then.

DISCUSSION

Though ASS was first diagnosed in 1990, the diagnostic criteria of ASS were first introduced by Connors in 2010.[10] In 2011, Solomon proposed these alternative criteria: presence of an aminoacyl t-RNA synthetase autoantibody with two major or one major and two minor criteria (major criteria: ILD, PM or DM, minor criteria: arthritis, Raynaud's phenomenon, mechanic's hands).[7]

Aminoacyl t-RNA synthetase is accepted as one of the markers of ASS. Since viral infections, genetic predisposition and disease activity may cause fluctuations in the serum level of aminoacyl t-RNA syn- thetase, it is a sensitive test; which can be performed only at a limited number of laboratories. Anti-Jo-1 is produced against the antigen histidyl t-RNA. Anti-Jo-1 is one of the most common antisynthetase antibodies and may be tested by many laboratories.

ILD has been observed in 60% of patients with ASS. Symptoms of ILD are persistent cough, chest pain, diminished exercise tolerance and dyspnea. fibrosis.[1] The pulmonary function tests reveal restrictive pulmonary pattern and decrease in total lung capacity (TLC) depending on the severity of the disease and so there is impaired gas exchange (TLC≤60%, FVC≤60%, diffusing capacity≤50% of predicted).[7] Whereas obstructive pattern is rare.

ILD is investigated by pulmonary function tests and HRCT of lungs. On HRCT, three common pat-

terns are seen: nonspecific interstitial pneumonia, cryptogenic organizing pneumonia and combination of the two. On top of the above mentioned, reticular and ground-glass opacities, traction bronchiectasis and scattered areas of consolidation are also observed in HRTC.[8,10]

Myositis is often sub-clinical at the beginning of ASS. Muscle enzymes such as aldolase and creatine kinase are raised in myositis. Even CK serum levels can reach 5-10 times the upper limit of normal levels.[3]

Electromyography can show the presence of inflammatory myopathies. Magnetic resonance imaging and muscle biopsy are rarely needed for the diagnosis of ASS-related myositis. Raynaud's phenomenon has been seen in 17% of patients with ASS.

The major initial manifestations of ASS are ILD and myositis preceding other manifestations. The diagnosis of ASS and clinical manifestations may be seen in average of 13 mounts.[2,11]

Our patient was diagnosed with ASS in light of the symptoms and physical examination, HRCT findings, pulmonary function testing and serologic outcome. She was diagnosed with ASS in the postpartum period, yet her history indicated that she probably had it in pregnancy as well. A woman with ASS in pregnancy and also postpartum period is a very rare condition.[12] Her diagnosis with the disease had the utmost importance to optimize medications.

Immunosuppressive agents treat the pulmonary and muscle manifestations of ASS. Corticosteroids have long been first line of treatment in ASS. Prednisone is initially given 1 mg/kg/day. When muscle and ILD symptoms stabilize, providers slowly taper corticosteroids to spare patients from the long-term side effects. There is frequent lung disease recurrence with corticosteroid tapering. If recurrent lung disease, progressive-refractory lung disease and intolerable corticosteroids' side effects are observed, steroid-sparing drugs should be used. These drugs could be azathioprine, mycophenolate mofetil, tacrolimus, rituximab and cyclophosphamide though there is little consensus about which agent is preferred and duration of therapy.[4,5]

This case report showed that in the diagnosis of ASS, it is important to suspect patients presenting with unexplained ILD. The clinical manifestations may not be always present at the onset of disease. They may arise over time. ILD and myositis combinations are seen with higher frequency. The diagnosis is impor tant for therapeutic and prognostic implications. Fre quently, the diagnosis is delayed because the clinical presentations are nonspecific. ILD associated ASS is more severe and rapidly progressive and related to increased morbidity and mortality.

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Conflict of Interest

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Authorship Contributions

Idea/Concept: *Esma Altunoğlu;* ***Design:*** *Esma Altunoğlu;* ***Control/Supervision:*** *Esma Altunoğlu;* ***Data Collection and/or Processing:*** *Sena Hekimoğlu;* ***Analysis and/or Interpretation:*** *Doğan Can Çelik;* ***Literature Review:*** *Enes Özsoy;* ***Writing the Article:*** *Esma Altunoğlu;* ***Critical Review:*** *Doğan Can Çelik;* ***References and Fundings:*** *Enes Özsoy;* ***Materials:*** *Sena Hekimoğlu.*

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