Brief Report: Antisynthetase Syndrome−Associated Myocarditis

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ABSTRACT

Background: The antisynthetase (AS) syndrome is characterized by autoimmune myopathy, interstitial lung disease, cutaneous involvement, arthritis, fever, and antibody specificity. We describe 2 patients with AS syndrome who also developed myocarditis, depressed biventricular function, and congestive heart failure.

Methods and Results: Both patients were diagnosed with AS syndrome based on clinical manifestations, detection of serum AS antibodies, and myositis confirmation with the use of skeletal muscle magnetic resonance imaging and skeletal muscle biopsy. In addition, myocarditis resulting in heart failure was confirmed with the use of cardiac magnetic resonance imaging and from endomyocardial biopsy findings. After treatment for presumed AS syndrome−associated myocarditis, one patient recovered and the other patient died.

Conclusions: AS syndrome is a rare entity with morbidity and mortality typically attributed to myositis and lung involvement. This is the first report of AS syndrome−associated myocarditis leading to congestive heart failure in 2 patients. Given the potentially fatal consequences, myocarditis should be considered in patients with AS syndrome presenting with heart failure. (*J Cardiac Fail 2014;20:939−945*)

Key Words: Antisynthetase syndrome, myocarditis, heart failure.

Idiopathic inflammatory myopathies (IIMs) comprise a heterogeneous group of diseases including dermatomyositis (DM), polymyositis (PM), inclusion-body myositis, and immune-mediated necrotizing myopathies.[1−4] DM and PM are the most common IIMs and share several clinical features, including proximal muscle weakness, elevation of serum skeletal muscle enzymes, irritability on electromyography, and histopathologic evidence of chronic inflammatory cell infiltrates in the skeletal muscle.[1] In 25%−30% of cases, DM and PM are associated with antibodies against aminoacyl-tRNA synthetases, also known as antisynthetase (AS) antibodies.[4,5] Of these, the anti-histidyl (Jo-1) antibody is most common, with a prevalence of 15%−25% in patients with myositis.[6−9] The presence of AS antibodies along with a distinctive clinical phenotype characterized by inflammatory myopathy, nonerosive arthritis, interstitial lung disease (ILD), fever, and scaly, fissured, hyperkeratotic skin changes on the lateral and palmar surface of the hands and fingers (''mechanic's hands'') constitutes the AS syndrome.[6−10] In patients with AS syndrome, significant morbidity and mortality is attributed to ILD, and the presence of AS antibodies is the strongest predictor for the development of ILD.[10,11]

Cardiac involvement in DM and PM was first reported in 1899, has varying reported prevalence (6%−75%), and is associated with worse outcomes compared with cases without cardiac involvement.[12−16] Abnormalities of nearly every component of the cardiac structure have been reported, including the pericardium (pericarditis), myocardium (conduction system abnormalities, myocarditis), and endocardium (mitral valve prolapse).[13,14] Congestive heart failure occurs in 3%−25% of patients, leading to death in 10%−20% of patients with PM.[14,17] Several reports have described myocarditis associated with IIM, identified with the use of cardiac magnetic resonance imaging (MRI).[18−20] Cardiac involvement in AS syndrome is far less common, however, with only scant case reports, including a 63-year-old woman with severe congestive

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cardiomyopathy, a 26-year-old man with right heart failure, and a 47-year-old woman with severe aortic valve regurgitation.[21–23] To our knowledge, the 2 patients with AS syndrome described in the present report are the first to have histologically proven myocarditis leading to congestive heart failure.

Case Descriptions

Patient 1

A previously healthy 44-year-old African-American man developed 3 months of unexpected weight loss, progressive leg and forearm edema, and hand "roughness." His symptoms improved after 3 weeks of diuretic treatment; however, he declined a diagnostic work-up. He remained asymptomatic for 1 year but then developed progressive anasarca, orthopnea, paroxysmal nocturnal dyspnea, exertional dyspnea, muscle "tightness," and a 9-kg weight increase. The patient's familial history was rather unremarkable except for hypertension. He did not use alcohol, tobacco, illicit substances, or supplements. At presentation, he appeared fatigued and dyspneic after speaking a few sentences. Physical examination revealed signs consistent with acute decompensated congestive heart failure and marked bilateral proximal muscle weakness of the upper and lower extremities. In addition, he had "mechanic's hands."

Laboratory studies detailed in Table 1 were significant for elevations of serum creatine kinase (CK), lactate dehydrogenase (LDH), aldolase, CK-MB, and cardiac troponin I. Anti−Jo-1 antibody was positive. Electrocardiography (ECG) revealed a normal QRS axis at 92, sinus tachycardia, first-degree atrioventricular block, and an age-indeterminate anteroseptal infarct pattern. Transthoracic echocardiography (TTE) showed severe enlargement of all 4 cardiac chambers, left ventricular end-diastolic diameter (LVEDD) of 6.2 cm, left ventricular ejection fraction (LVEF) of 20%−25%, marked right ventricular (RV) dysfunction, and moderate tricuspid regurgitation, without evidence of pericardial effusion. Chest computerized tomography (CT) revealed signs consistent with congestive heart failure, and coronary CT angiography showed no coronary artery disease. MRI of the legs showed diffuse increased T2-signal intensity in the proximal thighs, leg muscles, and subcutaneous tissue, consistent with myositis. Electromyography (EMG) revealed features of irritable myopathy and sensory-motor axonal polyneuropathy. A biopsy obtained from the right rectus femoris muscle showed chronic perivascular inflammation, myofiber atrophy degeneration, and regeneration worse in perifascicular regions, along with moderate type 2 fiber atrophy with minimal neurogenic atrophy, consistent with DM.

He underwent pulmonary artery catheterization, which revealed elevated right- and left-sided filling pressures [right atrial (RA) mean 20 mm Hg, right ventricular (RV) 37/18 mm Hg, pulmonary artery (PA) 39/25 mm Hg, PA mean 31 mm Hg, pulmonary capillary wedge pressure (PCWP) mean 20 mm Hg, PA oxygen saturation 60%]. Cardiac MRI and endomyocardial biopsy of the RV intraventricular septum were performed, with findings consistent with myocarditis in the setting of AS syndrome.

He was initiated on 3 days of pulse-dose corticosteroid therapy, which resulted in improved muscle strength and exercise tolerance during his hospital admission. He was treated with diuretic therapy and initiated on guideline-based heart failure management, including angiotensin-converting enzyme inhibitor (ACE-I) and aldosterone antagonist therapies; beta-blocker therapy was initiated before discharge. From an immunosuppression standpoint, he was changed to an oral prednisone and methotrexate regimen. After his discharge, the patient declined further care. Further contact was limited to 1 telephone call 6 months later, when he reported continued improvement in his exercise tolerance, with mild leg edema as his only symptom. He remained on corticosteroid therapy, but declined further medication adjustments.

Patient 2

A 51-year-old white woman with inflammatory arthritis and hypothyroidism presented to another hospital with 6 months of increasing fatigue, bilateral proximal muscle weakness, leg edema, dyspnea, and orthopnea. She was transferred to our hospital with severe biventricular heart failure. Her family history was notable for esophageal cancer in her mother and coronary artery disease in several first-degree relatives. The patient smoked tobacco for 20 pack-years but had quit several years earlier and rarely consumed alcoholic beverages. Laboratory studies summarized in Table 1 were notable for elevated CK, aldolase, CK-MB, and cardiac troponin I levels. Anti-nuclear (ANA), anti−thyroid peroxidase, and anti−Jo-1 antibodies were all positive. ECG showed a QRS axis of 75, sinus rhythm, occasional premature atrial complexes, and low voltages in all leads. TTE showed mild to moderate LV dysfunction, mild RV dysfunction, and a moderate-sized circumferential pericardial effusion, measuring 1.4 cm inferiorly and 1.0 cm anteriorly, without signs of tamponade. MRI of the bilateral hips and thigh muscles demonstrated diffuse moderately increased T2 signal. EMG showed mildly irritable myopathy with evidence of right median neuropathy and ulnar neuropathy. Right triceps muscle biopsy from another hospital revealed severe type II fiber atrophy, perifascicular atrophy, and chronic perivascular inflammation, histopathologically consistent with DM. Given the presence of anti−Jo-1 antibody, she was diagnosed with AS syndrome and treated with prednisone. In addition, her thyroid replacement therapy was increased, and she was started on guideline-based heart failure medications, including ACE-I and beta-blocker therapies.

Two months later, she presented with progressive heart failure but with improved muscle strength. Her ECG