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A Rare Case of Necrotizing Myopathy and Fibrinous and Organizing Pneumonia with Anti-EJ Antisynthetase Syndrome and Sjögren's Syndrome (SSA) Antibodies

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABDEF 1 Muhammad Kashif
BEF 2 Divya Arya
CDE 3 Masooma Niazi
ABCDEF 1 Misbahuddin Khaja

1 Division of Pulmonary and Critical Care Medicine, Bronx Lebanon Hospital Center, Affiliated with Icahn School of Medicine at Mount Sinai, Bronx, NY, U.S.A.
2 Department of Medicine, Bronx Lebanon Hospital Center, Affiliated with Icahn School of Medicine at Mount Sinai, Bronx, NY, U.S.A.
3 Division of Pathology, Bronx Lebanon Hospital Center, Affiliated with Icahn School of Medicine at Mount Sinai, Bronx, NY, U.S.A.

Corresponding Author: Misbahuddin Khaja, e-mail: drkhaja@yahoo.com
Conflict of interest: None declared

Patient: Male, 34
Final Diagnosis: Necrotizing myopathy • fibrinous • organizing pneumonia
Symptoms: Short of breath • weakness in limbs
Medication: —
Clinical Procedure: —
Specialty: Rheumatology

Objective: Rare co-existance of disease or pathology

Background: Idiopathic inflammatory myopathies are autoimmune disorders that can involve the skin, joints, muscles, and lungs. The most common of these disorders are dermatomyositis, polymyositis, overlap syndrome, and inclusion body myositis. Necrotizing autoimmune myopathy is an idiopathic inflammatory myopathy that is rarely associated with Sjögren's syndrome. The most common lung findings associated with anti-EJ antisynthetase syndrome are nonspecific interstitial pneumonia and usual interstitial pneumonia; this condition is rarely associated with fibrinous and organizing pneumonia.

Case Report: Here, we present a rare case of necrotizing myopathy and fibrinous and organizing pneumonia in a 34-year-old African American man with Sjögren's syndrome and anti-EJ antibodies. The patient's presenting symptoms were cough and proximal muscle weakness of the extremities. He had elevated serum creatine kinase level, aldolase level, and erythrocyte sedimentation rate. Myositis panel was positive for anti-EJ antibodies. Chest radiography was consistent with bilateral interstitial infiltrates. CT chest showed patchy bilateral infiltrates. Quadriceps muscle biopsy revealed widespread necrotic fibers and lung biopsy showed fibrinous and organizing pneumonia. The patient responded well to immunoglobulin therapy, mycophenolate, and prednisone, which resulted in complete resolution of bilateral infiltrates and improved muscle pain and weakness.

Conclusions: Myopathies are characterized by myalgia and muscle weakness due to muscle fiber dysfunction and are associated with autoimmune diseases. Histopathological features may differ in idiopathic inflammatory myopathies. It is important to recognize the rare association of anti-EJ autoantibodies with necrotizing myopathy and interstitial lung disease, which responds well to methylprednisolone and intravenous immunoglobulin.

MeSH Keywords: Lung Diseases, Interstitial • Myositis • Sjogren's Syndrome

Abbreviations: CT – computed tomography

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/903540

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Background

Myopathies are muscular disorders caused by abnormal muscle cell structure and metabolism, resulting in weakness and dysfunction [1]. Myopathies can be either inherited or acquired. The temporal course, pattern of muscle weakness, and family history can help distinguish between the 2 types. Inherited myopathies can be further subclassified as muscular dystrophies, congenital myopathies, mitochondrial myopathies, and metabolic myopathies [2]. Acquired myopathies can be subclassified as inflammatory myopathies, infectious myopathies, toxic myopathies, and myopathies associated with systemic conditions (e.g., critical illness myopathy, amyloid myopathy, and myopathies associated with endocrine disorders or electrolyte imbalance) [3]. The following systemic inflammatory diseases can also cause acquired myopathy: systemic lupus erythematous, rheumatoid arthritis, scleroderma, mixed connective tissue disease, sarcoidosis, and Sjögren's syndrome [4].

Antisynthetase syndrome is a rare condition associated with inflammatory myopathy, inflammatory polyarthritis, and interstitial lung diseases. Sjögren's syndrome is also associated with respiratory complications such as xerotrachea, non-Hodgkin lymphomas, pleural thickening, pleural effusions, thromboembolism, pulmonary hypertension, and interstitial lung diseases. Here, we report a rare case of necrotizing myopathy and fibrinous and organizing pneumonia in a patient with anti-EJ antisynthetase syndrome and Sjögren's syndrome.

As myopathies can be inherited and acquired, having differential for most common acquired myopathies will lead to early diagnosis and helps in patient management in timely manner. Anti-EJ Abs and SSA antibodies with uncommon histopathological and radiographic ILD patterns are described in this case report.

Case Report

A 34-year-old African American man was admitted to the hospital with proximal weakness of the extremities during the previous 2 months. The progressively worsening weakness was associated with pain. He also reported dry cough and dyspnea on exertion for 2 weeks. He had no fever, rash, sick contacts, recent travel, diplopia, dysphagia, dysarthria, numbness, or headaches. He denied any constitutional or gastrointestinal symptoms and had no significant comorbidities. He was not taking any prescription medications and had no surgeries. He had smoked half a pack of cigarettes per day for 2 years but quit several months previously. He denied use of illicit drugs and alcohol abuse. The patient was born and raised in West Africa and had been in the United States for 1 year. He had no family history of any muscular diseases.

Physical examination revealed a young man of average build with temperature of 98.6°F (37°C), heart rate of 120 beats/min, respiratory rate of 18 breaths/min, blood pressure of 104/70 mmHg, and oxygen saturation of 98% on ambient air. Neurological examination showed moderate symmetrical proximal weakness of the upper and lower limbs but no distal weakness. Sensations and tendon reflexes were normal. Respiratory examination was significant for fine bibasilar crackles. There were no nail changes and no abnormal findings on cardiac, abdominal, or skin examination.

Laboratory results were significant for elevated serum creatine kinase level of 14 155 U/L, aldolase level of 135 U/L, and erythrocyte sedimentation rate of 80 mm/h. Diagnostic tests for infections were negative. The patient was negative for antinuclear antibodies, double-stranded DNA, rheumatoid factor, and anti-CCP antibodies but was positive for anti-SSA antibodies. Results of the myositis panel were negative for PL-7, PL-12, MI-2, KU, OJ, SRP, and JO-1 antibodies but positive for anti-EJ antibodies. Chest radiography was consistent with bilateral interstitial infiltrates (Figure 1A). Results of electromyography and nerve conduction studies were suggestive of inflammatory myopathy involving the proximal muscles. Left quadriceps muscle biopsy (Figure 2A, 2B) revealed widespread fiber necrosis and regeneration but no mononuclear inflammatory cell infiltrate. There was no large or small grouped atrophy, perifascicular atrophy, or vasculitis. CD68 staining showed scattered necrotic muscle fibers invaded by phagocytes. At the ultrastructural level, no pipe-stem capillaries or endothelial microtubular inclusions were observed.

The patient was given 80 mg prednisone daily, but his clinical status continued to deteriorate, with worsening rhabdomyolysis. Echocardiography showed normal left ventricular function. Chest computed tomography (CT) showed worsening patchy infiltrates bilaterally (Figure 3A). Fiber optic bronchoscopy with bronchoalveolar lavage and transbronchial biopsy ruled out superimposed infections and diffuse alveolar hemorrhage. Histopathology of the lung biopsy revealed acute fibrinous and organizing pneumonia (Figure 4). Intravenous immunoglobulin therapy (2 g/kg body weight) and intravenous methylprednisolone were initiated. In the following weeks the patient's strength improved, and creatine kinase levels decreased to 450 IU/L. He was discharged on a tapering dose of prednisone along with oral mycophenolate. At the 1-month follow-up visit, chest radiograph (Figure 1B) and chest CT (Figure 3B) showed complete resolution of bilateral infiltrates. The patient's weakness and muscular pain improved considerably, and he was able to function normally. His creatinine kinase levels were in the normal range at 1-month follow-up. The patient attends monthly follow-up at our pulmonary and rheumatology clinic. He is on a tapering dose of prednisone.

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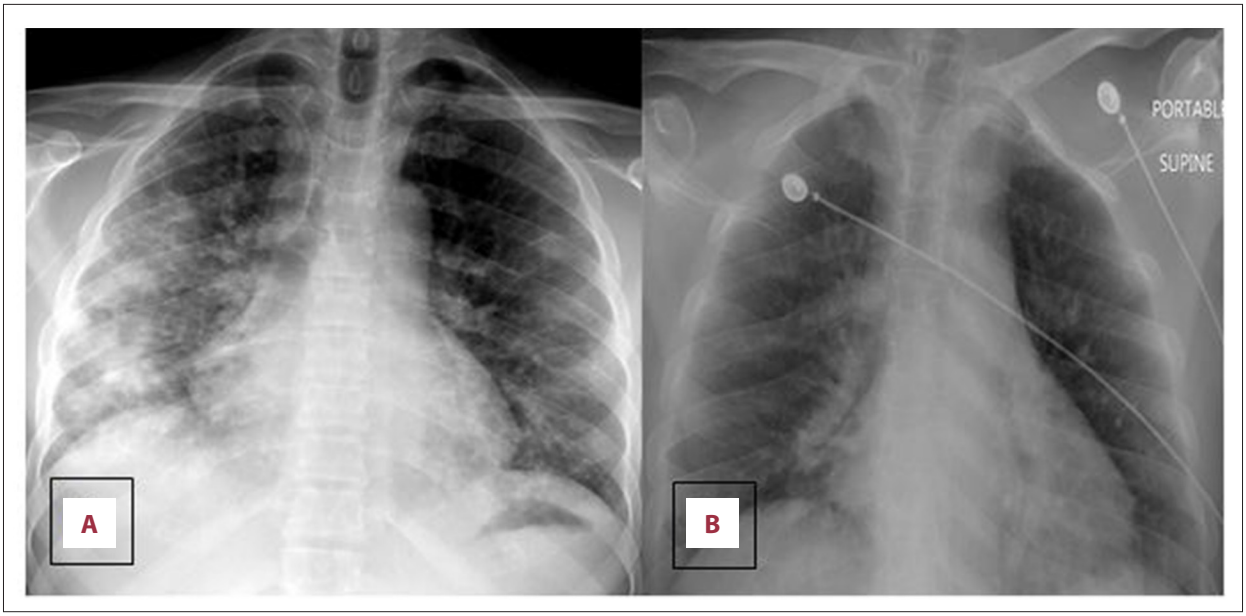

Figure 1. (**A**) Chest radiograph shows patchy areas of consolidation in the left lower lobe. (**B**) Chest radiograph shows complete resolution of the pulmonary infiltrates at the 1-month follow-up visit.

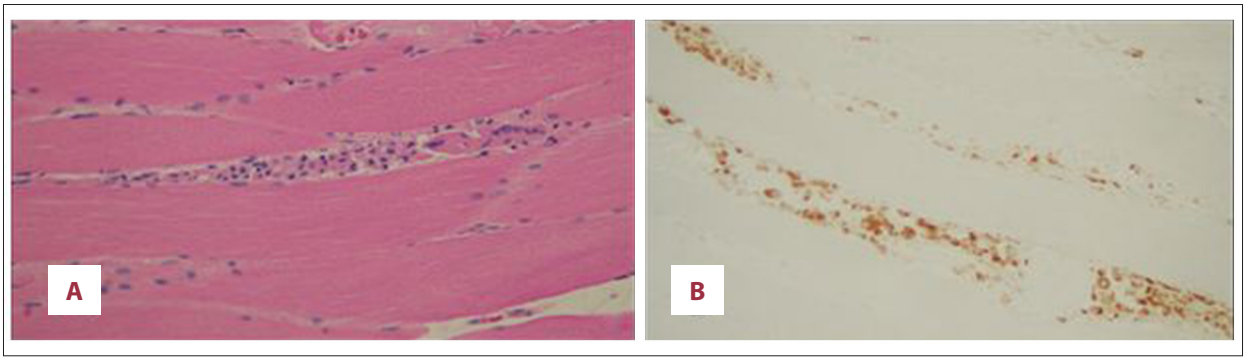

Figure 2. (**A**) Left quadriceps muscle biopsy revealed widespread necrotic fibers and regeneration but no mononuclear inflammatory cell infiltrate. (**B**) CD68 stain revealed scattered necrotic muscle fibers invaded by phagocytes.

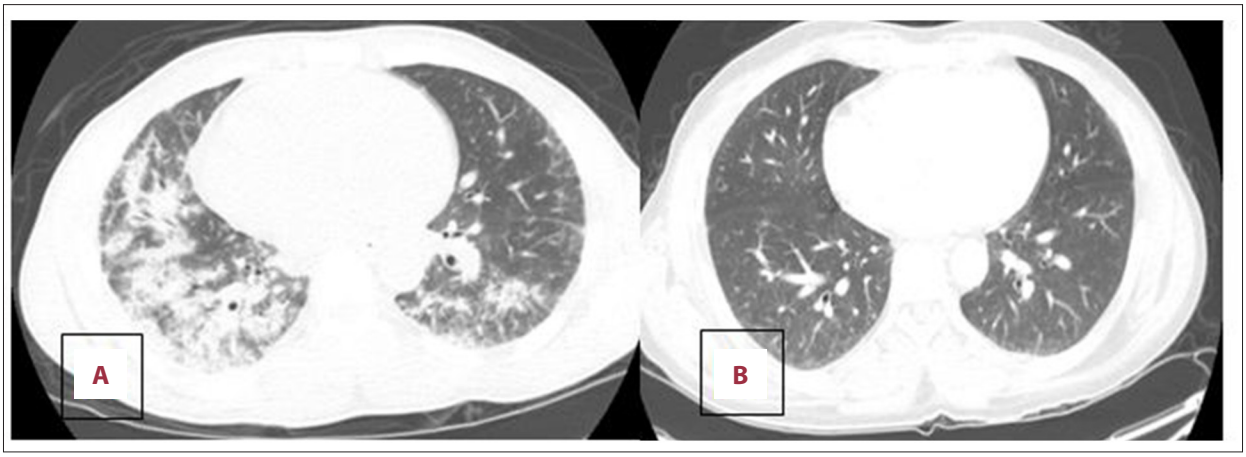

Figure 3. (**A**) Chest CT axial view shows patchy areas of consolidation, predominantly in lower lobes. (**B**) Chest CT axial view shows complete resolution of consolidation at the 1-month follow-up visit.

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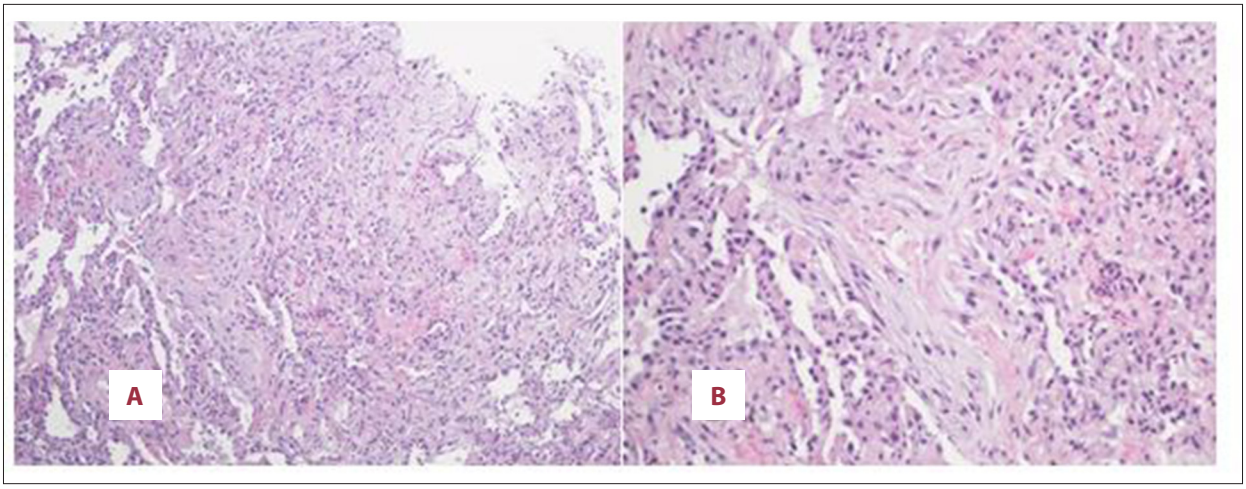

Figure 4. (**A**) Lung biopsy revealed acute organizing pneumonia with fibroblastic proliferation filling airspaces and a mild lymphocytic infiltrate. (**B**) Lung biopsy reveled fibroblastic proliferation within an alveolar space and mildly thickened alveolar septa.

This case highlights the rare association of anti-EJ antisynthetase syndrome and anti-SSA antibodies with necrotizing myopathy and fibrinous and organizing pneumonia. The patient responded well to immunoglobulin therapy along with mycophenolate and prednisone.

Discussion

Inflammatory myopathies include dermatomyositis, polymyositis, inclusion body myositis, overlap syndrome, and other autoimmune diseases [5]. Idiopathic inflammatory myopathies consist of autoimmune disorders that affect muscle, skin, joints, lung, and other organs. Subtypes include necrotizing myopathy, eosinophilic myositis, and granulomatous myositis [6]. The mechanisms of tissue injury in these myopathies are not well understood [7]. In addition, although these conditions share clinical features such as elevated creatinine phosphokinase levels and proximal muscle weakness, muscle biopsy findings differ among these myopathies [8]. For example, the muscle biopsy findings of dermatomyositis are perimysial and perivascular inflammation, perifascicular atrophy, and the presence of CD4 T cells, B cells, and plasmacytoid dendritic cells. Muscle biopsy findings of polymyositis include endomysial inflammation with CD8 T cells, macrophages, and myeloid dendritic cells. In contrast, necrotizing myopathy is characterized by necrotic muscle fibers without inflammatory infiltrates, whereas inclusion body myositis shows rimmed vacuoles and endomysial inflammation with CD8 T cells, macrophages, and myeloid dendritic cells [9].

Myositis is uncommon in Sjögren's syndrome, with an overall prevalence of 3% [10], and is associated with extra-glandular symptoms, including peripheral neuropathy, interstitial kidney disease, arthralgia, arthritis, skin changes, hepatomegaly, and primary biliary cirrhosis.

Necrotizing autoimmune myopathy can occur with Sjögren's syndrome and other connective tissue diseases (e.g., scleroderma, mixed connective tissue disease, and overlap syndrome) [4], as well as viral infections (e.g., hepatitis C), acquired immune deficiency syndrome, malignancies, and certain medications (e.g., statins) [11]. The most common clinical features of autoimmune myopathies are symmetrical proximal muscle weakness, difficulty rising from a chair, climbing stairs, hair washing, oropharyngeal weakness, dysphagia, diaphragmatic weakness, and myalgia, and cramps [12].

Antibodies directed against glycyl-tRNA synthetase (anti-EJ) are found primarily in patients with inflammatory myopathies. In addition, the anti-EJ type of antisynthetase syndrome primarily affects white women and has a high recurrence rate. Results of a retrospective cohort study showed that half of all patients with anti-EJ antibodies were diagnosed with classic dermatomyositis and clinically amyopathic dermatomyositis [13].

The most common diagnostic tests for inflammatory myopathy are muscle enzymes (e.g., creatine kinase), electromyography, muscle biopsy, and detection of autoantibodies. The presence of antinuclear antibodies suggests underlying connective tissue disease. Hamaguchi et al. and Hane et al. reported muscle weakness and interstitial lung disease as common symptoms in patients with anti-EJ antibodies, and both studies showed an association with Sjögren's syndrome [14,15]. In addition, nonspecific interstitial pneumonia, usual interstitial pneumonia, and fibrinous and organizing pneumonia have previously been reported in patients with anti-EJ antisynthetase syndrome [16,17].

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First-line treatments for idiopathic inflammatory myopathies are corticosteroids, and second-line treatments include steroid-sparing immunosuppressive drugs such as methotrexate, cyclosporine, cyclophosphamide, mycophenolate mofetil, and azathioprine [18]. For patients who do not respond to combinations of first-line and second-line therapies, intravenous immunoglobulin has been shown to be safe and efficacious, resulting in clinical improvement, altered expression of immune regulatory genes, and decreased levels of chemokines, cytokines, fibrosis, and complement consumption [19].

Our patient did not have heliotrope rash or Gottron's papules. Electromyography showed polyphasic potentials and early recruitment of motor units. Pulmonary function tests demonstrated reduced forced vital capacity (60%) and carbon monoxide diffusion capacity (DLCO/VA 25%). The lung biopsy results showed a histological interstitial lung pattern indicating fibrinous and organizing pneumonia, which is a newly defined pulmonary syndrome only rarely associated with anti-EJ antibodies. The presence of 2 autoantibodies (anti-EJ and anti-SSA antibodies) is unusual in a patient with necrotizing myopathy and interstitial lung disease.

Our case is unique in that muscle biopsy was done early to narrow down the differentials of acquired myopathy, as muscle biopsy findings in polymyositis, dermatomyositis, inclusion body myositis, and necrotizing myopathy are different. Myositis panel helps in finding the rare association of necrotizing myopathy, fibrinous, and organizing pneumonia with anti-EJ Antisynthetase syndrome. Acute fibrinous and organizing pneumonia has a rapid onset and progression. It shows no improvement in response to glucocorticoid hormone treatment and has a poor prognosis. Delayed diagnosis may contribute to poor response to treatment. Its association with anti-EJ antisynthetase syndrome should be recognized early [20].

Initially, our patient was started on prednisone but had no response. With initiation of intravenous immunoglobulin and intravenous methylprednisolone, he had tremendous improvement in strength and the level of creatinine kinase improved as well. Intravenous immunoglobulin is a reasonable second-line therapy for patients with refractory disease, but in our case early initiation showed dramatic improvement of outcome [21].

Conclusions

Myopathies are characterized by myalgia and muscle weakness due to muscle fiber dysfunction and are frequently associated with autoimmune diseases. Idiopathic inflammatory myopathies share many characteristics but have different histopathological features, clinical presentations, and treatment responses. It is important to recognize the rare association of anti-EJ autoantibodies with necrotizing myopathy and interstitial lung disease, which responds well to methylprednisolone and intravenous immunoglobulin.

Author's disclosure

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the manuscript. No financial support was used for this case series.

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