

Anti-EJ Antisynthetase Syndrome Associated with Mycobacterium Tuberculosis Infection

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Received May 01, 2020; Revised June 01, 2020; Accepted June 08, 2020

Abstract Antisynthetase Syndrome is a rare type of idiopathic inflammatory myopathy. It is characterized by interstitial lung disease, non-erosive arthritis, Raynaud's phenomenon, and mechanic's hands. Diagnosis is confirmed with the detection of an antibody directed against amino-acyl transferase RNA. Opportunistic infections are common causes of mortality in patients with autoimmune diseases. Immunosuppressive treatment further contributes to the risk of infection. We report, for the first time in the literature, a 62-year-old woman diagnosed with Anti-EJ antisynthetase syndrome who died from disseminated mycobacterial tuberculosis infection. This case emphasizes the importance of early recognition and prompt treatment of opportunistic infections in order to decrease mortality.

Keywords: *antisynthetase syndrome, Anti-EJ antibody, idiopathic inflammatory myopathy, mycobacterium tuberculosis*

Cite This Article: Michael Trevisonno, Daniel E. Diaz, Steven S. Chin, FCAP Jenny Libien, and Yamen Homsí, "Anti-EJ Antisynthetase Syndrome Associated with Mycobacterium Tuberculosis Infection." *American Journal of Medical Case Reports*, vol. 8, no. 9 (2020): 306-310. doi: 10.12691/ajmcr-8-9-12.

1. Introduction

Idiopathic inflammatory myopathies (IIMs) are rare autoimmune diseases characterized by proximal muscle weakness in association with various clinical involvement of the joints, skin, lungs, and esophagus. [1] One subset, antisynthetase syndrome, requires an antibody directed against aminoacyl transfer RNA. Disseminated tuberculosis in autoimmune conditions is accredited to various immune irregularities as well as to treatment with immunosuppressive therapy. Herein, we report a 62-year-old woman who presents with fever and migratory myositis who was diagnosed with anti-EJ antibody associated antisynthetase syndrome. Fatal disseminated tuberculosis was identified as the cause of death at autopsy.

2. Case Presentation

A 62 year-old Afro-Caribbean woman presented to the emergency room (ER) with migratory muscle pain and swelling of her left upper arm, left upper chest, and bilateral thighs. One month prior, she presented to an outside ER with the complaint of acute right upper extremity muscle pain and swelling. At that time, she underwent a right biceps muscle biopsy, which showed necrotizing myopathy, with macrophages associated with necrotic fibers but without significant lymphocytic

infiltrates. MHC Class I antigens (HLA A, B, C) were upregulated by immunohistochemical staining of the biopsy (Figure 1). She was treated with pulse IV steroids for three days then prednisone at 60 mg/day until she presented to our ER.

Review of systems was positive for fever, shortness of breath, and generalized weakness. Past medical history included diabetes mellitus. She was not on any medication besides prednisone. She denied smoking, alcohol, and drug abuse. She had recently traveled to Trinidad three months ago.

In the ER, she was febrile at 101.5° F with a heart rate of 130. The patient was alert and oriented. Physical exam revealed swelling and tenderness of the left pectoral muscle area, left upper arm, and left thigh. Fine crackles were heard at the bases of the lungs. Skin exam was negative for rash. The rest of the exam was normal.

Initial laboratory data was significant for a white blood cell count of 6.3 k/ul with critical bandemia of 20 %, c-reactive protein of 351 mg/L, erythrocyte sedimentation rate of 60 mm/hour, lactic acid of 4 mmol/L, creatine kinase of 3852 u/L, and Procalcitonin of 30 ng/mL. Given the history of necrotizing myopathy, a myositis panel was sent to a national reference laboratory. Computed tomography of the chest showed a heterogeneous appearance of the left pectoralis muscle with surrounding fluid attenuation and scattered subcentimeter lymph nodes. Pulmonary findings included bilateral basilar thickening of the interlobular septa with surrounding and scattered ground-glass opacities.

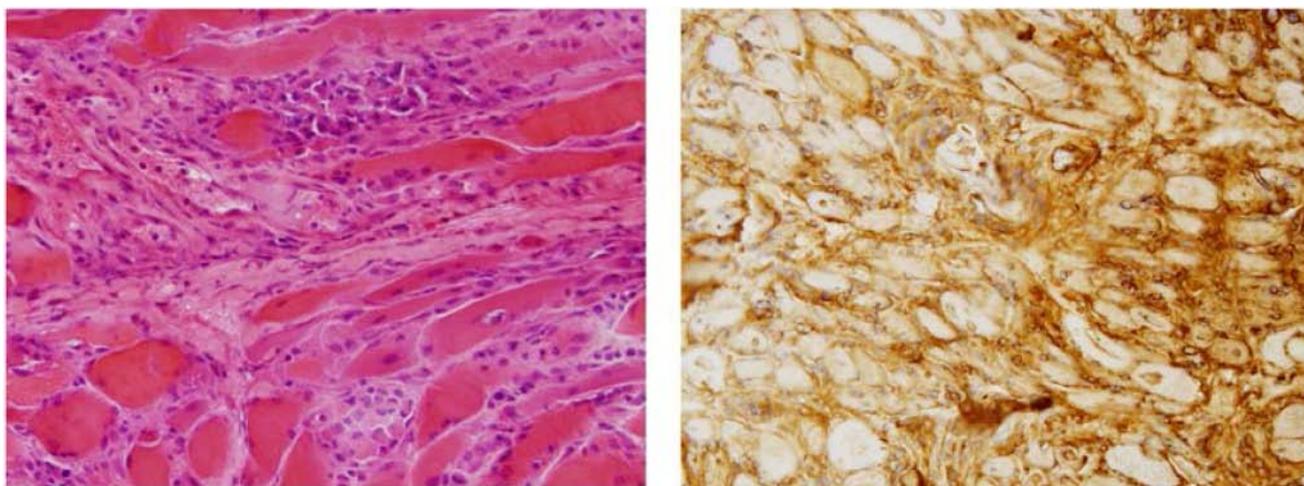


Figure 1. (Left - H&E, 20x; Right - IHC of MHC Class I, 20x) Left: Muscle showing atrophy and chronic inflammation in the endomysium. Right: Muscle showing diffuse upregulation of MHC class I molecules

The patient was initially treated empirically with broad-spectrum antibiotics and admitted to the intensive care unit. Her condition rapidly declined as she went into septic shock, had acute renal and hepatic failure, and disseminated intravascular coagulation. On hospital day ten, the patient went into cardiac arrest and died.

Post-mortem examination concluded disseminated mycobacterium tuberculosis complex infection, confirmed by PCR of paraffin-embedded tissue as the cause of death. There were numerous acid fast bacilli in areas of acute necrotizing inflammation in soft tissue, primarily in adipose and lymph nodes of the chest wall (Figure 2). The

outside muscle biopsy did not show soft tissue granulomatous inflammation on initial levels; however, on deeper levels performed after the patient's death, soft tissue revealed granulomatous inflammation (Figure 3). The right quadriceps muscle showed perifascicular atrophy and necrosis, a distinctive feature of antisynthetase syndrome (Figure 4). Microscopic examination of the lungs showed fibrosing and cellular interstitial lung disease with thickened pleura consistent with non-specific interstitial pneumonia (NSIP) (Figure 5). No granulomatous inflammation was identified on representative sectioning of the lungs.

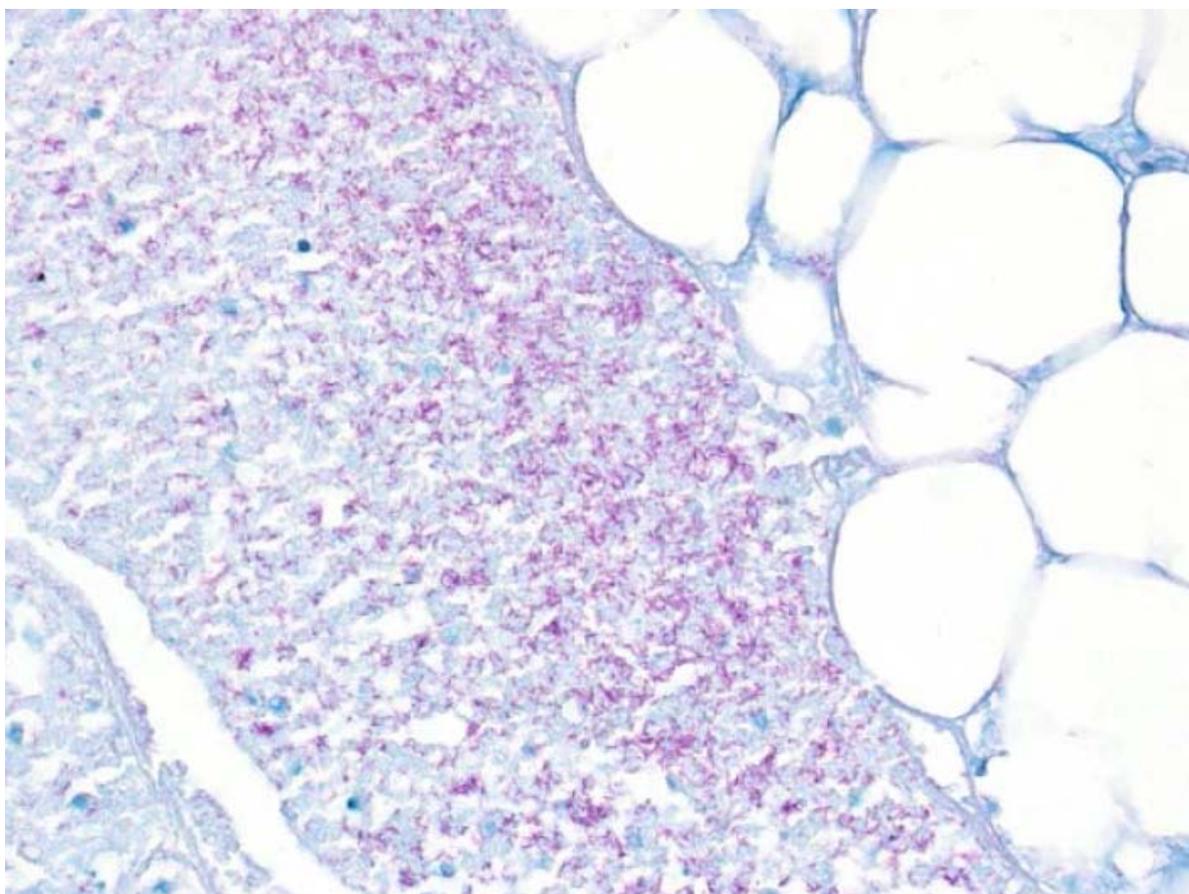


Figure 2. (AFB stain, 40x) Numerous positive acid fast bacilli in a background of inflamed necrotic subcutaneous tissue

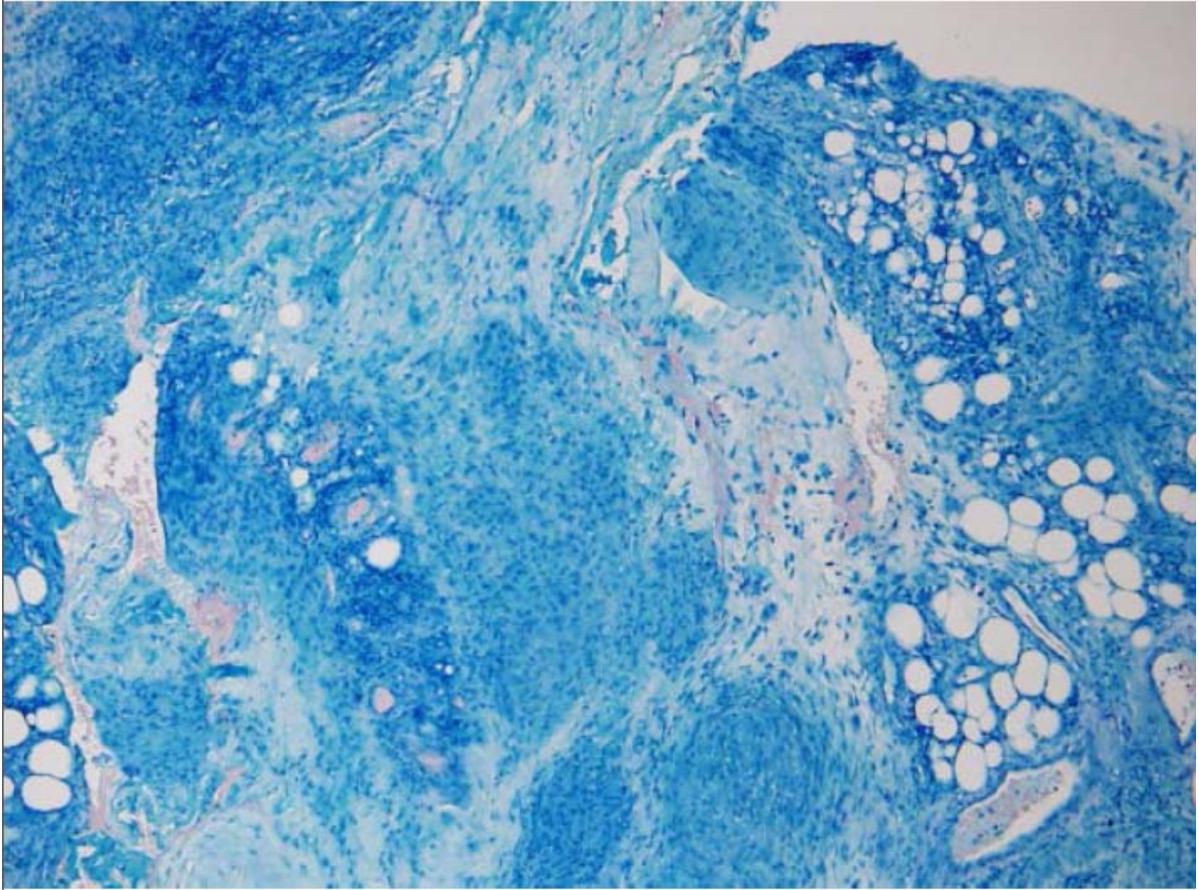


Figure 3. (AFB stain, 40x) AFB stain of the deeper levels of the initial muscle biopsy showing soft tissue with granulomatous inflammation.

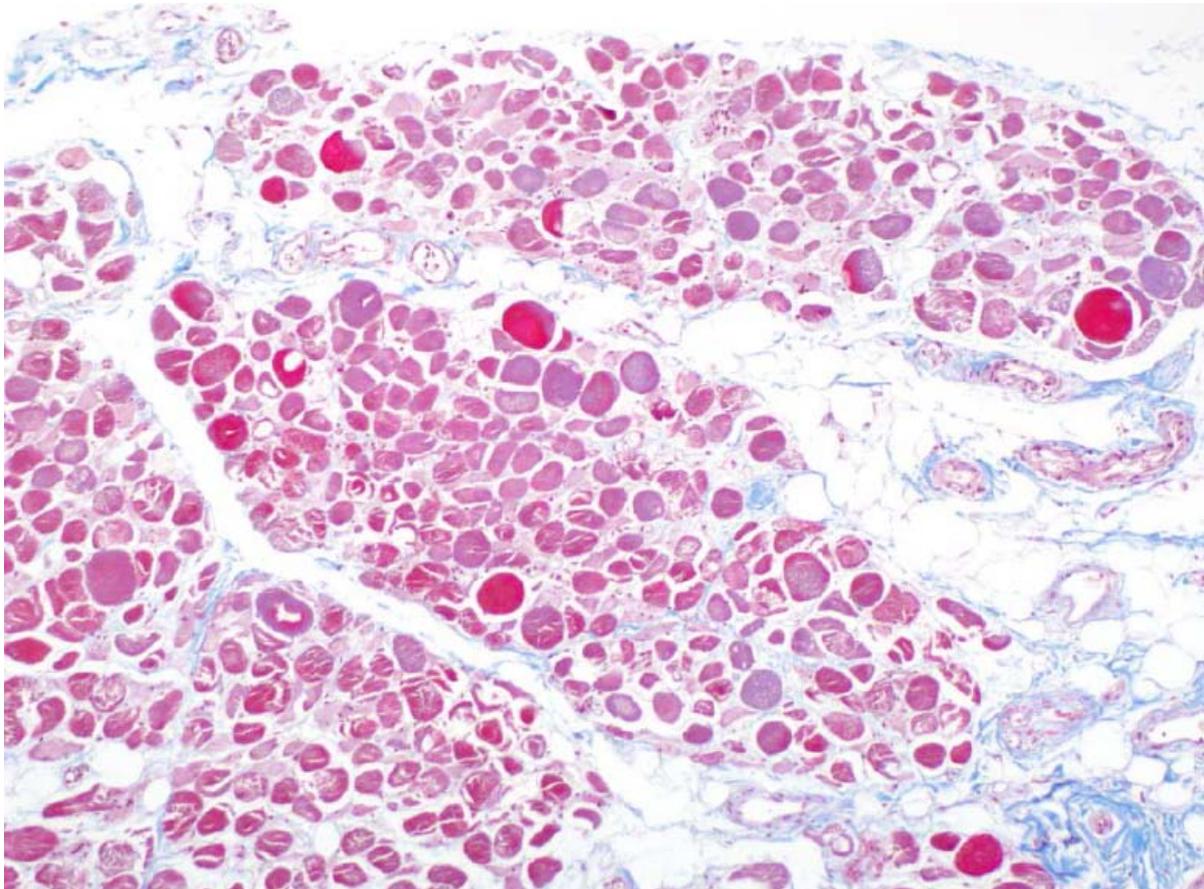


Figure 4. (H&E, 10x) Perifascicular involvement of postmortem quadriceps muscle.

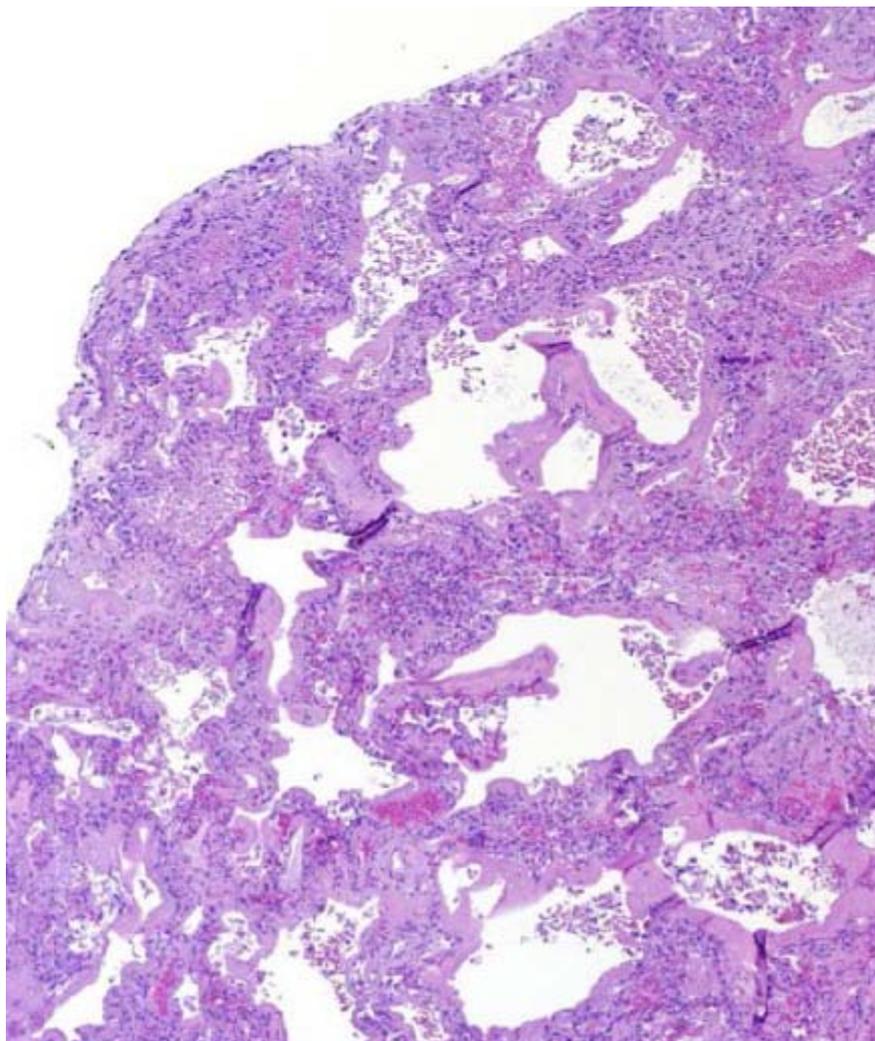


Figure 5. (H&E, 4x) Lung showing patterns consistent with non-specific interstitial pneumonia

The results of the myositis panel performed by immunoprecipitation assay were received postmortem and were positive for anti-glycyl (EJ) antibody. This result, in conjunction with the muscle biopsy showing necrotizing myopathy with upregulation of MHC Class I, the autopsy findings of NSIP, and perifascicular necrotizing myopathy, supports the diagnosis of antisynthetase syndrome.

3. Discussion

Antisynthetase syndrome is a subset of IIMs with unique clinical features that can include interstitial lung disease (ILD), non-erosive arthritis, Raynaud's phenomenon, mechanic hands, and the presence of antisynthetase antibodies. [1] Interstitial lung disease has a higher prevalence in antisynthetase syndrome compared to dermatomyositis and polymyositis. [2] Antibodies are directed against aminoacyl transfer RNA (tRNA) synthetases. Eight antibodies have been discovered, including anti-Jo-1 (most common), anti-EJ, anti-PL7, anti-PL12, anti-OJ, anti-KS, anti-ZO, and anti-Ha. [2] Nearly all are associated with ILD, but myositis is closely associated with Anti-Jo-1, Anti-PL-7, and Anti-EJ. [3] Patients with non-Jo-1 antibodies are shown to have lower survival rates. [4] In one study of 12 patients with anti-EJ antisynthetase syndrome who underwent surgical lung

biopsy, 9 had NSIP pattern and 3 had unclassifiable interstitial pneumonia. [5] The most characteristic histological feature of skeletal muscle involvement is myofiber necrosis in the perifascicular region. [6]

Individuals with systemic connective tissue diseases are at increased risk for developing infection, either from immune abnormalities, from the disease itself, or from immunosuppressive treatment. Bacterial infections are most common, but viral and fungal infections also contributed to increased morbidity and mortality. [7] A study of eighteen patients with PM/DM showed a high frequency of opportunistic infections, with more than 50% being fungal. [8] The incidence rate of *M. tuberculosis* infection in IIMs is greater than the incidence in the general population. [9] Extrapulmonary patterns of TB have also been described to be more common in IIMs; in a retrospective case series of thirty patients who had tuberculosis and systemic rheumatic disease, 2/3 of the patients had extrapulmonary tuberculosis while only 1/3 had pulmonary tuberculosis. [10] It is possible that the immunosuppression in our patient led to re-activation and dissemination of TB. Our patient also recently traveled to Trinidad, which is a high risk area for mycobacterial infection. The weakness, swelling, and pain in her affected muscle groups were likely due to a combination of antisynthetase syndrome and mycobacterial infection. This case illustrates the first association in the medical

literature between anti-EJ anti-synthetase syndrome and disseminated mycobacterium tuberculosis infection. Early diagnosis and treatment of opportunistic infection in rheumatic disease is crucial to increase survival.

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