Early inflammatory myopathy in EJ antibody positive Antisynthetase Syndrome

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Abstract

A 51 yo man presented with weakness and constitutional symptoms, found on labs to have EJ-antibody antisynthetase syndrome. Myopathy is usually a late manifestation of Antisynthetase syndrome and is steroid-responsive, however in our case it occurred earlier. It is important to consider Antisynthetase syndrome in patients presenting with inflammatory myopathy.

Early inflammatory myopathy in EJ antibody positive Antisynthetase Syndrome

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Key Clinical Message : It is important to consider antisynthetase syndrome in the differential diagnosis of any patient presenting with weakness and a constellation of complaints or diagnoses spanning multiple organ systems, as this will change clinical management.

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Abstract: A 51 yo man presented with weakness and constitutional symptoms, found on labs to have EJ-antibody antisynthetase syndrome. Myopathy is usually a late manifestation of Antisynthetase syndrome and is steroid-responsive, however in our case it occurred earlier. It is important to consider Antisynthetase syndrome in patients presenting with inflammatory myopathy.

Introduction

Antisynthetase syndrome is a constellation of "mechanic's hands," interstitial lung disease (70%), myositis, arthritis (50%), rash (30%), sicca syndrome, Raynaud's phenomenon and constitutional symptoms.[1-3] Antibodies are produced to aminoacyl tRNA synthetases that catalyze attachment of amino acids to tRNA and recruit inflammatory cells to sites of muscle and lung injury.[1] In EJ-antibody antisynthetase syndrome, the antigen is glycyl tRNA synthetase (GARS).[2]

Eight anti-aminoacyl-tRNA synthetases (ARS) have been described; anti-EJ comprise 2-5%.[3] Myositis is a late manifestation at 17 months.[2] EMG, muscle MRI and biopsy show steroid-responsive myopathy.[3] Long term immunosuppression is required 80% of the time.[4]

Case Report

We present a man with 2 years of leg weakness, starting with trouble rising from bed and red papular rash. He was inpatient for 3 weeks with improvement on prednisone. After discharge, he required a wheelchair and had intermittent aches, fever and periorbital edema. His past medical history included connective tissue disorder, eczema, costochondritis, arthritis, and sleep apnea.

Examination showed periorbital edema, diminished breath sounds, and papular rash on his extremities. Neurologically, the only finding was 5-/5 strength of bilateral hip flexors. EMG revealed a length dependent, axonal neuropathy. Muscle biopsy showed CD3 positive cells and atrophic angulated fibers, suggestive of neurogenic atrophy. Sural nerve biopsy showed loss of myelinated fibers, regenerative clusters and thinly myelinated axons. CT Chest showed bibasilar ground glass opacities.

Abnormal labs were ESR 51, CRP 35.4, CK 1874 (peak 5973), elevated aldolase and Sjogren's anti-SSA. A myositis panel revealed positive EJ autoantibodies. The patient was diagnosed with EJ-antibody antisynthetase syndrome. He was treated with Cyclosporine, improved significantly and was lost to follow up.

Discussion

Antisynthetase syndrome is a multi-organ syndrome causing myositis, which manifests as symmetric (85%) proximal (60%) weakness, acute pain (34%-50%), progressing to muscle atrophy and fibrosis in 66%.[3] Weakness of cricopharyngeus and hypopharynx can lead to dysphagia 15-40% of the time.[1] Spirometry can reveal weakness in the diaphragm or the intercostal muscles.[1]

ARS antibodies are detected in 25-35% of patients with idiopathic inflammatory myopathy. Myopathy is detected by electrodiagnostic or laboratory evidence in the non-Jo-1 groups.[1,5]Steroid-responsive myopathy is usually a late manifestation of the disease course (17 months), however here it occurred on presentation.[1,5]

Labs reveal elevated muscle enzymes, positive ANA, antisynthetase antibodies, and elevated acute-phase reactants.[1]Electromyography shows myopathy, but up to 15% of tests are normal.[1] Muscle MRI shows edema not limited to compartment or myotome.[6]

Muscle biopsy shows perimysial macrophages and lymphocytes, degenerating muscle fibers and regenerating muscle fibers, muscle fiber necrosis and perifascicular atrophy similar to dermatomyositis, but without vascular changes.[1] EJ-antibodies produce a cytoplasmic pattern on immunofluorescence.[1]

Corticosteroids produce an incomplete response.[4] Long term immunosuppressant medications, such as Rituximab, Cyclophosphamide, IVIG, or Methotrexate are required 80% of the time.[4]75% of patients respond to Rituximab at 375 mg/M^{2}every 10 to 12 weeks.[1]

It is important to consider antisynthetase syndrome in the differential diagnosis of weakness and signs of mult-organ disease, often diagnosed as multiple diseases. Successfully diagnosing antisynthetase syndrome results in better patient outcomes.

Appendix 1: Authors

Dr. Robin Warner collected all clinical information and wrote the paper.

Appendix 2: MCQ

A patient presents with trouble walking up stairs and rising from the bed or toilet with some muscular pain. She has a history of interstitial lung disease and psoriasis. On examination, in addition to proximal leg weakness, you observe cracked skin on the fingers and Raynaud's phenomenon. EMG reveals low amplitude, short duration motor units. What labs would you consider for assisting with diagnosis?

CK

Myositis panel

Serum immunofluorescence

Ganglioside antibodies

The correct answer is B. This patient is presenting with a constellation of interstitial lung disease, rash, inflammatory myopathy, mechanic's hands and raynaud's phenomenon, which is typical for Antisynthetase syndrome, although differential diagnosis will be broader. A Myositis panel is the blood test that may confirm Antisynthetase syndrome by revealing one of the eight antibodies known to cause this. Depending on institution, the panel may also include testing for other myopathies. A CK will be elevated, but not diagnostic, as it is not specific. Serum immunofluorescence may be helpful in work up, but is also non-diagnostic. Ganglioside antibodies are probably not useful because the EMG revealed this is a myopathy and not a neuropathy.

A patient comes to you for a second opinion after his primary physician diagnosed him with dematomyositis. He thinks he has ALS because he is short of breath, progressively weak and has fatigue. He is upset that treatment with oral prednisone has not helped much and he has significant side effects and wants to start Riluzole instead. On reviewing his diagnostic testing, you notice that his muscle biopsy did not have perivascular inflammation typical for dermatomyositis and there are no inclusion bodies. Myositis panel reveals Anti-Jo1 antibodies. The next step in treatment is:

Start Riluzole

Physical therapy

Referral to psychiatry for anxiety

Trial of Rituximab

The correct answer is D. This patient was diagnosed with dermatomyositis, which explains the inflammatory myopathy, rashes and possibly constitutional symptoms, however does not account for the dyspnea and lack of biopsy evidence typical for dermatomyositis (perivascular infiltration). The presence of Anti-Jo antibodies is diagnostic, so consideration for ALS is not necessary at this time. We first should further address and treat the inflammatory myopathy. Physical therapy is beneficial in conjunction with medical treatment, but not on its own. The patient's anxiety is probably situational due to illness and magnified by corticosteroid use, so psychiatry referral is not necessary at this time.

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