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SRP-positive necrotising myopathy: takes more than just the muscles

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SUMMARY

Necrotising myopathy is an autoimmune disease that commonly affects muscles. Here we examine a case of a middle-aged women presenting with a chief report of shortness of breath, who subsequently developed muscle weakness. Her clinical course was complicated by respiratory failure and pulmonary hypertension likely due to the underlying pathology of signal recognition particle-positive necrotising myopathy. After further evaluation, her shortness of breath was thought to be secondary to muscle pathology rather than cardiopulmonary pathology. She was transferred to our institution for workup by rheumatology. At the time of admission, 6 months after initial presentation, her weakness progressed, so that she was unable to lift her arms and legs against gravity. Furthermore, neurological examination revealed mild facial and nuchal weakness, severe proximal weakness, more moderate distal weakness and global areflexia.

BACKGROUND

Necrotising myopathy is a rare autoimmune disease that is thought to primarily affect muscles and commonly presents as weakness; it has been reported that there are associated effects on the heart and lungs. This case describes a middle-aged woman presenting with a chief report of shortness of breath, who was subsequently found to have muscle weakness and respiratory failure due to signal recognition particle (SRP)-positive myopathy. In this case, we evaluate her clinical course, review the literature regarding SRP-positive myopathy and strengthen the case that due to the ubiquitous nature of the SRP autoantibodies; patient presentations can extend beyond proximal muscle weakness.

CASE PRESENTATION

A previously independently functioning 52-year-old obese African American woman initially presented to her primary care office with a chief report of unresolving shortness of breath, which seemed to be incited after she tripped over a broom at work. Previous medical history was significant for hyperlipidaemia treated with simvastatin 40 mg for primary prevention from 2013 to 2020, morbid obesity, congestive heart failure and coronary artery disease.

Patient's primary care doctor sent the patient for a CT angiogram that was significant for pulmonary hypertension and hepatic inflammation. In the following weeks, she was admitted for progressive muscle weakness.

Patient was found to have a creatine kinase (CK) elevation that peaked at 25 295 U/L. MRI of the lumbar spine revealed diffuse oedema of the pelvic muscles. Left quadriceps muscle biopsy was interpreted with 'rare' necrotic fibres, 'occasional' cytochrome c oxidase-intermediate (COX)-negative fibres, without deposits of complement macrophage antigens (MAC), and major histocompatibility (MHC) class I staining. SRP and -hydroxy-3-methyl-glutaryl-coenzymereductase (HMGCR) antibodies were negative. Antinuclear antibodies (ANA), nuclear ribonucleoprotein (RNP), Sjögren's syndrome antibody (SSA), double-stranded DNA and myeloperoxidase antibodies were positive. Her home simvastatin was held, she was treated with prednisone and intravenous immunoglobulin. Her CK gradually decreased to the 2000–4000 U/L.

She continued to experience shortness of breath and was found to have a non-ST elevation myocardial infarction treated with medical management and stent placement for left anterior descending lesion. Further evaluation with an electromyography showed a diffuse, proximal-predominant, irritable myopathy and distal axonal polyneuropathy.

Laboratory workup was consistent with elevated erythrocyte sedimentation rate (ESR) and positive ANA with a homogeneous pattern, which is typically seen in lupus, RNP as well as SSA antibodies as noted at the outside hospital. SRP 54 was now positive. CT C/A/P did not identify any malignancy. Muscle biopsy was significant for highly active and chronic necrotising myopathy with inflammation, mild mitochondrial dysfunction, preferential type 2 atrophy, increased type 2C fibres, occasional rounded atrophic fibres and mild denervation atrophy, indicative of highly active and possibly chronic necrotising myopathy.

TREATMENT

Patient was treated with prednisone, IVIG and mycophenolate mofetil.

OUTCOME AND FOLLOW-UP

Patient initially failed to improve. Her course was complicated by worsening heart failure, respiratory failure requiring intubation with transition to tracheostomy and dysphagia requiring nasogastric tube for nutrition. She continued to slowly decline and was evaluated for placement at a long-term care facility. After a course at a long-term acute care, the patient returned home with continued needs for assistance with activities of daily living.

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DISCUSSION

Immune-mediated necrotising myopathy (IMNM) is characterised by minimal infiltration on muscle biopsy and is one of the most severe and progressive myopathies.[1 2] In our case, the patient was SRP 54 positive, a subunit of the SRP protein complex, presenting with shortness of breath, followed by weakness, then dysphagia. It is commonly thought that the type of autoantibody will predict the course of the myopathy and the associated extra muscular manifestations. SRP is a ribonuclear protein that regulates translocation of protein across the endoplasmic reticulum. It is not specific to muscle tissue but is ubiquitously found in all protein processing cells.[2] Myopathies associated with SRP antibodies were thought to have a similar clinical presentation; however, the literature suggests the presentation of SRP associated myopathy can vary greatly. Anti-SRP-related myopathy is now considered a subset of IMNM, also known as necrotising autoimmune myopathy. Symptoms of anti-SRP myopathy are range from weakness, dysphagia and cardiovascular involvement, with some studies showing lower association with interstitial lung disease (ILD).[3] While limb weakness is the most common manifestation of myositis, there are reports of the SRP protein antibodies leading to different presenting symptoms involving the lungs and heart.[2 4]Involvement of the haematologic system with neutropenia and other alterations in proliferation were also identified.[2 5] The ubiquitous nature of the SRP protein leads to multiple different manifestations when attacked by the immune system, from pulmonary, cardiac and haematologic.[6 7] Myocardial involvement in anti-SRP myopathy can be severe and is considered a poor prognostic factor. Extramuscular manifestations such as ILD, Raynaud's and arthralgia have been reported, though these features are typically mild. Some authors have suggested that radiographic suggestion of ILD in these patients may in fact arise from respiratory insufficiency due to musculoskeletal weakness.[8]

Other autoimmune conditions may have been at play in our patient and her dramatic hospital course. It has been shown that patients positive for ANA in a homogeneous pattern, consistent with SLE, is potentially associated with an overlap syndrome of SLE and necrotising myopathy. While this may have been present in our patient, the likelihood is low as there was no history of SLE in our patient. Furthermore, the overlap between SLE and necrotising myopathy has only been described in one case report to date.[9] With this knowledge, clinicians should be aware of the complications of dysphagia, respiratory and cardiac failure and initiate prompt treatment to avoid further complications in the patient's clinical course.

In fact, involvement of muscles with a symptom of weakness may not be as prominent as other symptoms such as shortness of breath or dysphagia. This is logical given the ubiquity of SRP and the ability of the antibody to cause dysfunction in different tissues.[2]

Patient's perspective

As this was during the COVID pandemic, it was extremely difficult for me to adjust to the situation and the loss of the ability to care for myself. I often felt alone and was very scared. As I was in the hospital for over 6 months, I feel that I missed out a lot with my family. We lost my son to a gunshot wound before my sickness and I was also grieving that loss.

Learning points

- Necrotising myopathy is a rare but fatal aetiology in patient's presenting with weakness and shortness of breath.
- Patients can have variable presentations and may initially present with symptoms other than skeletal muscle weakness.
- Treatment of the condition should not be delayed while workup is undertaken as it can result in pulmonary hypertension and serious pulmonary and cardiac manifestations.
- It is imperative to know a patient's functional baseline to set expectations for the clinical course of a myopathy pathology

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