A Case of Acute Necrotizing Myopathy in a Patient with Systemic Lupus Erythematosus

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Patient: Female, 30-year-old
Final Diagnosis: Necrotizing myopathy
Symptoms: Muscle weakness
Medication: —
Clinical Procedure: —
Specialty: Rheumatology

Objective: Rare disease

Background: Systemic lupus erythematosus (SLE) is an autoimmune disorder affecting multiple organ systems with a wide spectrum of clinical presentation and associated with positive serologies. Musculoskeletal involvement in patients with SLE is relatively uncommon, occurring in approximately 4% to 16% of cases. Some patients can develop necrotizing myopathy without myositis. MRI in patients with SLE-associated necrotizing myopathy usually shows interstitial edema, while muscle biopsy often shows type 2 muscle fiber atrophy. We herein report an unusual case of acute necrotizing myopathy in a patient recently diagnosed with SLE. This case report focuses on the pertinent features related to the diagnosis of this patient while highlighting the management of acute necrotizing myopathy.

Case Report: A 30-year-old African American woman presented to the Emergency Department with skin rashes, myalgia, polyarthralgia, and muscle weakness resulting in the inability to walk, 2 weeks after being diagnosed with SLE. Laboratory analysis showed elevated creatine kinase and myoglobin. She was found to have both MRI and biopsy findings suggestive of necrotizing myopathy. She was treated with mycophenolate mofetil and steroids, with an improvement of muscle strength and decrease in creatine kinase over a 2-week period.

Conclusions: Immune-mediated necrotizing myopathies are a rare group of debilitating myopathies that can be associated with SLE. The diagnosis of necrotizing myopathy in patients with SLE requires a high index of suspicion and careful work-up to establish a diagnosis. Muscle biopsy often shows type 2 muscle fiber atrophy. Immunosuppressive therapy is the mainstay of treatment, and early initiation of immunotherapies is associated with an improvement in patient outcomes.

Keywords: Lupus Erythematosus, Systemic • Autoimmune Diseases

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Systemic lupus erythematosus (SLE) is an autoimmune disorder affecting multiple organ systems, with a wide spectrum of clinical presentations and positive serologies. SLE is more common in women of childbearing age, with a female: male ratio of up to 13: 1 and higher prevalence in African Americans, who also have worse outcomes [1]. Muscle involvement in SLE often involves the proximal muscle in both upper and lower limbs and may be the main reason patients seek medical attention [2]. Muscle involvement often presents as weakness, myalgia, and atrophy, but severe weakness is uncommon [2]. Muscle biopsy in patients with SLE can show a broad spectrum of findings, including inflammatory myopathy, vasculitis, perifascicular atrophy, and neurogenic atrophy [3]. This case report describes a young woman with a recent diagnosis of SLE complicated by severe muscle weakness and later diagnosed with necrotizing myopathy.

**Case Report**

A 30-year-old African American woman presented to the Emergency Department for evaluation of multiple concerns, including dark urine, skin rash, myalgia, polyarthralgia, and muscle weakness resulting in the inability to walk. She was diagnosed with SLE 2 weeks before presentation; at that time, she started on a tapering dose of methylprednisolone. She had not been taking any statins, potentially myotoxic medications (steroids, colchicine, amiodarone, hydroxychloroquine, antimalarial medications, and antiviral therapy), dietary supplements, herbal preparations, or over-the-counter medications. She also denied any trauma or alcohol use.

Two weeks prior to this admission, our patient was diagnosed with SLE using the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Our patient had an ANA titer of 1: 1280 on HEP-2 cells along with thrombocytopenia, joint involvement, lupus nephritis, low C3, low C4, and positive Anti-dsDNA antibody using crithidia luciliae substrate, resulting in a total score of 30. Using the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus, a patient with a total score of 10 or more can be classified as having SLE [4]. Antibody serologies were tested using serum indirect immunofluorescent assay.

On presentation, her vitals were within normal range. The physical examination revealed ulcers under her tongue and on the buccal surface of the lips, with scattered hyperpigmented macular rashes on her face and extremities, bilateral lower-extremity edema, and 2/5 motor strength in all extremities, with proximal muscle weakness.

Laboratory analysis revealed hemoglobin 11.7, platelet 116, sodium 132, BUN 32, creatinine 1.71, AST 791, ALT 264, GGT 171, alkaline phosphatase 73, ESR 67, CRP 1, CK 20,875, LDH 1468, and urine myoglobin 2880. Urinalysis was consistent with 2+ proteinuria and hematuria. Chart review showed ANA 1: 1280, C3 complement 40, C4 complement 7, SS-A > 8, SS-B > 8, and smooth muscle antibody 22(positive). Further laboratory analysis revealed aldolase 75.8, RNP antibody > 8, double-strand DNA 131, anti-SMA 22, SCL-70 negative, ACE 85, P-ANCA 1: 320, and myoglobin quantitative serum 2880 (normal is <66). Myositis panels including SRP antibodies and anti-Jo 1 antibodies were negative. The viral hepatitis panel was non-reactive and EBV IgM was negative. TSH was within normal limits.

Differentials included SLE-induced myositis, SLE-induced myopathy, SLE-neuropathy, macrophage activation syndrome, antiphospholipid antibody syndrome, signal recognition particle myopathy, drug-induced myopathy, thyroid-related myopathy, sarcoidosis, and dermatomyositis.

Abdominal ultrasound showed mild hepatic steatosis. Renal biopsy showed acute tubular injury with increased proximal tubular cytoplasmic myoglobin stained, suggestive of class III focal lupus nephritis. MRI of the thighs showed interstitial edema throughout both thighs, suggestive of myositis (Figure 1).

Quadriceps muscle biopsy using hematoxylin and eosin showed an active myopathic process characterized by frequent regenerating, and necrotic muscle fibers with very sparse associated chronic lymphocytic inflammation suggestive of necrotizing myopathy and type 2 muscle atrophy. There was no morphologic evidence of vasculitis identified. Perifascicular atrophy seen in dermatomyositis was not observed. Modified Gomori trichrome preparation showed a subset of pale-staining necrotic muscle fibers, as well as a few muscle fibers with mildly increased intermyofibrillar mitochondria-type staining and no abnormal inclusions, rimmed vacuoles, or well-developed ragged red fibers. Nicotinamide adenine dinucleotide dehydrogenase-tetrazolium reductase (NADH-TR) and succinate dehydrogenase (SDH) preparation showed necrotic muscle fibers and no well-developed target muscle fibers, ragged blue fibers, loss of staining or other abnormality of staining. No selective cytochrome oxidase (COX) negative muscle fibers were seen on the combined SDH-COX preparation. Alkaline phosphatase preparation showed scattered degenerating and necrotic muscle fibers with moderate to strong staining intensity. Esterase stain highlights leukocytes within frequent necrotic muscle fibers. Immunohistochemical stains for myosin heavy chain fast-twitch and slow-twitch isofrom showed good differentiation of type I and type II muscle fibers with type II muscle fiber-specific atrophy. Activities for myophosphorylase, myoadenylate deaminase, cytochrome C oxidase, and succinate dehydrogenase were present and were of appropriate staining intensity. Congo red stain was negative for amyloid deposition.

**Figure 1**
and intracellular congophilic inclusions. Immunohistochemical staining for major histocompatibility complex (MHC) class 1 and C5b-9 showed a moderate to strong diffuse increase in membranous muscle fibers staining for MHC 1 and moderate to strong diffuse cytoplasmic staining for C5b-9.

During hospitalization, she was started on methylprednisolone 250 mg IV daily and mycophenolate mofetil 500 mg twice daily. She also received IVIG for 5 days. Methylprednisolone taper was started with transition to oral prednisone and was increased to 1500 mg daily.

ESR, CRP, creatine kinase, liver enzymes, and kidney functions all improved over a 2-week period. The patient was discharged on day 18 of hospitalization and was continued on prednisone, which was tapered over a 4-month period. She is currently receiving mycophenolate mofetil, and hydroxychloroquine was later added.

Discussion

Immune-mediated necrotizing myopathy is a rare group of debilitating myopathies characterized by symmetrical proximal muscle weakness that has a subacute onset and myofiber necrosis without significant inflammation [2,5,6]. SLE is a chronic systemic autoimmune disease that can involve the musculoskeletal system, with approximately 4%-6% of patients with SLE demonstrating muscle involvement [2]. Muscle involvement in SLE usually presents with myalgia, weakness, and atrophy, usually in a proximal distribution, and both the upper limbs and the lower limbs can be involved [3]. Patients can present with necrotizing autoimmune myopathy with muscle weakness and rhabdomyolysis. A study found that approximately 21% of patients with necrotizing myopathy had SLE [7].

Two weeks prior to this admission our patient was diagnosed with SLE using the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Our patient had an ANA titer of 1: 1280 on HEp-2 cells along with thrombocytopenia, joint involvement, lupus nephritis, low C3, low C4 and positive Anti-dsDNA antibody using crithidia luciliae substrate, resulting in a total score of 30. Using the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus, a patient with a total score of 10 or more can be classified as having SLE [4]. Antibody serologies were tested using serum indirect immunofluorescent assay.

Our patient initially presented with generalized muscle weakness with predominant proximal muscle involvement, with both upper and lower extremities being affected. In some patients, muscle weakness is the initial presentation. Elevated creatinine kinase and aldolase are found in patients with myopathy. Drug-induced myopathy was less likely given that our patient was not on any medications besides methylprednisolone. Steroid-induced myopathy usually occurs in patients

Figure 1. MRI of the thighs shows abnormal signals in the subcutaneous fat of both thighs, with a reticular pattern. There is a feathery hyperintense signal within the muscles of the anterior and posterior compartment of the right and left thigh, suggesting interstitial edema.
on long-term glucocorticoid therapy [8]. Myopathies caused by medications were less likely in our patient given that they were without vacuolar changes and mitochondrial dysfunction, although muscle necrosis was present on muscle biopsy [8].

We should always be aware that malignancies can be associated with necrotizing myopathy, and cancer screening is recommended [9]. Muscle involvement seen on MRI in patients with SLE is characterized by interstitial edema, as found in our patient [10-12]. Biopsy can confirm the diagnosis of necrotizing myopathy. Type 2 muscle atrophy is thought to be a major cause of symptoms and is the predominant finding in patients with SLE necrotizing myopathy [13,14]. Muscle biopsy in our patient showed type 2 muscle fiber atrophy without myositis, which confirmed necrotizing myopathy. One study showed that 86.6% of patients with SLE who had muscle biopsy were found to have type 2 muscle fiber atrophy, with no significant clinical, serological, or histological difference between the groups of patients [15]. An important differential diagnosis to keep in mind is macrophage activation syndrome (MAS), which can occur in patients with SLE and other autoimmune disorders. MAS was less likely in our patient given the absence of fever, which is extremely important in the diagnosis to keep in mind is macrophage activation syndrome (MAS), which can occur in patients with SLE and other autoimmune disorders. MAS was less likely in our patient given the absence of fever, which is extremely important in the diagnosis and is further supported by the absence of hepatosplenomegaly and lymphadenopathy [16,17].

The treatment of immune-mediated necrotizing myopathies should be started early, with medications options including corticosteroids, methotrexate, azathioprine, mycophenolate, tacrolimus, cyclosporine, IVIG, or cyclophosphamide [9]. Combination therapy can be used, and our patient was started on glucocorticoid and mycophenolate mofetil. Over a 2-week period, we noticed an improvement in muscle strength from 2/5 in all extremities to 4/5 in all extremities and downtrend CK from 20 875 to 997 over a 2-week period.

Conclusions

Necrotizing myopathy can be associated with SLE, but due to the rarity, a high index of suspicion and careful work-up is needed to arrive at this diagnosis. Patients usually present with muscle weakness and myalgia with a proximal distribution. Muscle biopsy often shows type 2 muscle fiber atrophy with minimal inflammation and no evidence of myopathy. Immunosuppressive therapy has been shown to improve muscle weakness.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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