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CASE REPORT

Statin-Associated Immune-Mediated Necrotizing Myopathy: A Case Report

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Abstract

Statins are a widely used class of drugs that have been found to be safe and effective in treating hypercholesterolemia. Statin-associated muscle symptoms (SAMS) are a clinical spectrum defined as muscle pain, discomfort, and/or weakness with or without elevated CK levels. This spectrum ranges from more common minimal myalgias to rare, severe statin-associated immune-mediated necrotizing myopathy (IMNM). Diagnosis of IMNM can be difficult, as there is a gradual onset of vague symptoms presenting years after statin initiation. It is known that early intervention with medical therapies including IVIG and IV steroids are vital to preserving and improving muscle function, so swift diagnosis is key for maximal patient recovery. IMNM is a rare complication of statin use but should be considered in all statin users presenting with proximal weakness affecting functioning regardless of statin onset time. Treating this diagnosis requires a multi-disciplinary approach to facilitate restoring function and quality of life. This case report discusses a rare case of statin-associated IMNM.

Keywords

Statin induced myopathy, Statin associated immune mediated necrotizing myopathy, Myopathy

Introduction

Statins are a widely used class of drugs that have been found to be safe and effective in treating hypercholesterolemia. Dyslipidemia is a modifiable risk factor for cardiovascular disease. Thus, cholesterol treatment is commonly used for primary and secondary prevention of cardiovascular disease [1,2]. Statins inhibit HMG-CoA reductase, inhibiting the rate limiting step in cholesterol production [2]. Statin induced myopathy includes a clinical spectrum ranging from myalgia, myositis, rhabdomyolysis and asymptomatic increase in creatine kinase levels [3,4]. While statins are generally well tolerated, approximately 2-20% of patients on statins will have self-limited toxic myopathies that resolve with statin discontinuation [2,3]. Statin-associated immune mediated necrotizing myopathy (SA-IMNM) is a rare event occurring at a rate of 0.4 per 10,000 patient years [5].

Statins work by lowering low density lipoprotein cholesterol as well as upregulating levels of HMG-CoA reductase in myocytes. While the exact pathophysiology of statin associated IMNM has yet to be elucidated, it is proposed that the antibodies targeted against HMG-CoA reductase damage the myocytes in which HMG-CoA reductase is upregulated [2]. It has been shown that atorvastatin is the statin to be most implicated in development of SA-IMNM compared to rosuvastatin and simvastatin [6].

Several risk factors are associated with the development of statin-associated muscle symptoms including IMNM. These include advanced age, female gender, hypothyroidism, impaired renal or hepatic function, immunodeficiency, diabetes mellitus, vitamin D deficiency, major trauma, substance and alcohol use disorders, and a high level of physical activity [7]. There are genetic factors that can predispose patients to SA-IMNM. Patients with the class II HLA allele DRB1*11:01

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are more likely to develop SA-IMNM, whereas patients with the class II HLA alleles DQA1 and DQB6 are less likely to develop this disease [7]. It has been suggested thatup to 20% of the population is positive for HLA-DR11, affecting its use to determine risk for developing IMNM [6].

Patients typically present with proximal muscle weakness, with markedly elevated CK levels as well as antibodies recognizing HMG-CoA reductase. Muscle biopsy, while not required for diagnosis, may show necrotizing myopathy with minimal inflammatory cell infiltrates [6,7]. Differential diagnosis should include polymyositis, dermatomyositis, inclusion body myositis, drug-induced myositis and paraneoplastic syndrome[7].

Case Description

This patient is a 58-year-old male with a past medical history including hypertension, hyperlipidemia, hypothyroidism, pre-diabetes, IBS, and OSA who presented to a rehabilitation hospitalfor statin induced myopathy. In August 2024, he had elevated liver function tests with minor stiffness in his lower extremities. In November 2024, his liver function tests worsened, and he was having increased stiffness and weakness, specifically in his bilateral proximal lower extremities. His weakness progressed and in January 2025, began affecting his bilateral proximal upper extremities. In January 2025, he was admitted to the hospital with suspected statin induced myopathy and concern for rhabdomyolysis given his markedly elevated CK levels. His statin was discontinued and Neurology recommended following up for outpatient EMG testing. Myositis antibodies were sent, and his HMG-CoA reductase antibodies resulted positive. One month later, he was evaluated by out-patient neurology. His symptoms were markedly worse-he had multiple falls at home and was unable to get up from the toilet without a 2 person assist.

This patient had been on atorvastatin since 2010, initially with a dose of 20 mg daily, increased to 40 mg in 2020, and increased again to 80 mg in 2021. He had had no recent increase in dose or change in additional medications prior to symptom onset.

He was admitted to Neurology inpatient and treatment was initiated. He received 4 days of IVIG (0.5 g/kg × 4 days), 3 days of solumedrol (1 g daily), followed by daily 40mg prednisone. His CK had peaked at 24,230 on 1/21. While inpatient, his CK down trended from 13,187 on admission to 4,928 on discharge. He was evaluated by endocrinology while inpatient regarding his hypothyroidism, and his levothyroxine dose was increased to 137 mcg daily. His symptoms only minimally improved following completion of IVIG and IV Solumedrol.

Due to a significant change in function from his baseline, he was admitted for inpatient rehabilitation. He was initially independent, living alone and was using a single point cane prior to his admission due to progressive weakness and had been sleeping in a lift recliner. He was working as a mail carrier. On arrival to the acute rehab facility, a PT/OT evaluation was completed. The patient was requiring max assistance of 2 person for transfer and minimal assistance for ambulation 10 ft × 2.

While in inpatient rehabilitation, his CK levels remained in the 4-5,000 range. 2 weeks into his rehabilitation stay, his CK up trended to 7,045. Neurology was consulted, and he went to an office visit 3 days later. At that appointment, it was decided the patient would be directly admitted to the hospital neurology service for further IVIG treatment due to lack of improvement in symptoms and elevated CK levels. He returned to inpatient rehabilitation after 3 days in the acute hospital with normalizing CK levels. While inpatient, neurology increased his daily prednisone to 60 mg daily and planned to continue IVIG (2 grams/kilogram divided over four days followed by 1 grams/kilogram divided over two days every two weeks thereafter) to be set up for at-home infusions after discharge from rehab. On discharge from the rehabilitation hospital, his strength improved with manual muscle testing, and he felt subjectively much stronger than when he was first admitted. He was ambulating confidently with a rolling walker, and requiring assistance with all mobility, ambulating, activities of daily living. He was discharged home with home therapy. Given his decline in CK levels and improvement with therapies, he is likely to continue to regain strength without need for adjunct medical therapies.

Treatment

Initial treatment for patients with concern for SA-IMNM is to discontinue statin treatment. Unlike patients with less severe statin-associated symptoms, patients with IMNM shouldnot undergo rechallenge with statins. In the Nazir review, five patients underwent rechallenge with statins after statin-associated autoimmune myopathy and in all cases, the rechallenge was unsuccessful with worsening of symptoms [2]. When examining alternative cholesterol management medications, a small case series showed that PCSK9 inhibitors (alirocumab and evolocumab) were well tolerated in six out of six patients who had to discontinue statins due to IMNM without symptom recurrence. Two patients were switched to ezetimibe, where one patient had recurrence of SA-IMNM symptoms [8].

Corticosteroids, oral prednisone or pulsed intravenous immunoglobulin therapy are options for first-line therapy, with glucocorticoids seen as insufficient when used alone. Steroids in conjunction with another agent, such as intravenous immunoglobulin or methotrexate should be trialed in patients depending on severity and

response to treatment. With refractory disease, plasma exchange, cyclophosphamide, mycophenolate mofetil, cyclosporine, azathioprine, or rituximab can be utilized [4,9].

For those with severe deficits, rehabilitation can be helpful to restore and preserve function as severe proximal muscle weakness can result in reduced mobility, difficulty with activities of daily living thus preventing a safe return home [10]. Exercise, especially promotion of range of motion and stretching help keep the joints mobile and avoid contractures. Assistive devices such as elevated seat cushions or lever-controlled booster seats can help patients with proximal weakness that may have difficulty getting up from a chair. Other assistive devices may include long handled reachers, hair, tooth and back brushes, shower chairs, and handheld shower extensions. Walkers, canes, and scooters may be helpful assistive devices for patients with moderate to severe weakness or issues with balancing due to core weakness [10].

Energy conservation is an important rehabilitation strategy to prevent further muscle damage. Patients should be educated on importance and open communication between them and their providers to avoid muscle damage. Utilizing appropriate assistive devices and aids, as wellas taking rest periods and maintaining strength, range of motion and proper posture are all important methods to promote energy conservation in these patients [10].

Conclusion

Diagnosis of statin-induced autoimmune necrotizing myopathy can be difficult, especially considering the gradual onset of vague symptoms potentially presenting years after statin initiation. It is known that early intervention with medical therapies including IVIG and IV steroids are vital to preserving and improving muscle function, so swift diagnosis is key for maximal patient recovery. SA-IMNM is a rare complication of statin use but should be considered in all statin users presenting with proximal weakness affecting functioning regardless of statin onset time. Treating this diagnosis requires a multi-disciplinary approach to facilitate restoring function and quality of life.

Author Disclosures

None of the aforementioned authors have any competing interests or financial ties that pertain to the information presented in the manuscript. No funding was received for this study.

Written informed consent was obtained by the patient prior to submission.

We used the CARE checklist when writing this report.

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