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A Case of Immune-Mediated Necrotizing Myopathy in a 75-Year-Old with Anti-HMG-CoA Reductase Antibodies

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ABSTRACT

Statins are the first-line therapy in the management of hyperlipidemia. Unfortunately, patients often stop the drug within the first year due to intolerable myalgias. Despite the removal of the drug, some patients experience myotoxicity, and their myalgia persists. In this case, a 75-year-old female presented with myalgias and an elevated creatine phosphokinase (CPK) level despite discontinuing statin therapy. Antibodies to 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA) were found in this patient; she was diagnosed with a rare form of statin-associated autoimmune myopathy, and she was successfully treated with leflunomide, methotrexate, and physical therapy.

KEYWORDS

Stain induced myositis, statin, HMG-CoA antibody, creatine phosphokinase

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INTRODUCTION

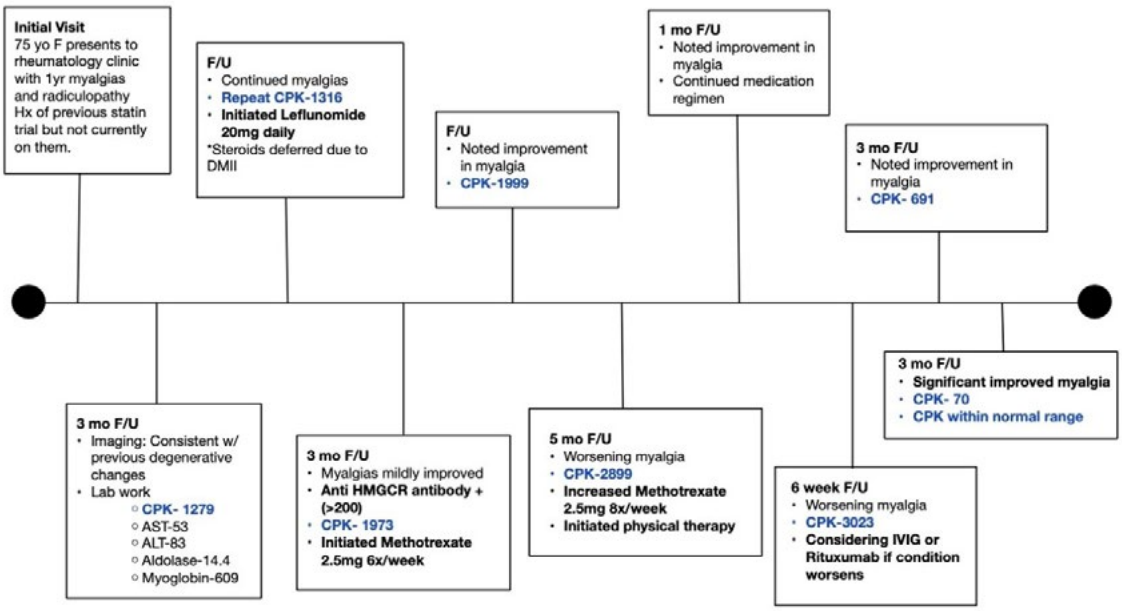
Cardiovascular disease (CVD) remains the greatest source of disease burden world-wide. With the number of cases doubling from 1990 to 2019, the global trend is steadily rising.[1] Hyperlipidemia is one of the well-known causes contributing to CVD. Patients with hyperlipidemia are approximately twice as likely to develop CVD compared to those with a normal-range lipid panel.[2] Statins (HMG-CoA inhibitors) are currently the first-choice drug therapy in the management of dyslipidemias and are therefore the foundation of preventative measures against atherosclerosis CVD.[3] Unfortunately, it has been estimated that 25-50% of individuals that begin statin therapy stop the drug within the first year, with 60% of patients naming muscle pain as the primary reason for intolerance.[4]

Statin-associated muscle symptoms (SAMS) is a broad definition covering a wide clinical spectrum of statin-induced muscle insults that resolve upon removal of the offending agent. Despite the removal of the drug, some patients continue to experience myotoxicity. This was later discovered to be of auto-immune origin and termed statin-associated autoimmune myopathy (SAAM), an immune-mediated necrotizing myopathy (IMNM).[4] A connection was found between the presence of an autoantibody to 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA Reductase), hyperCKemia, and prolonged symptomology, usually requiring profound immunosuppression.[4-6]

In this case, a 75-year-old female presented with myalgias and an elevated CPK level. Antibodies to HMG-CoA were found, and the patient was successfully treated with leflunomide, methotrexate, and physical therapy (Figure 1). The patient's myalgias were significantly improved, and her CPK levels returned to normal. This case highlights the importance of having a high clinical suspicion of this rare autoantibody myopathy as the use of statins becomes more common in cardiovascular disease.

CASE STUDY

Our patient is a 75-year-old female that presented to the rheumatology clinic as a new patient. The patient



Parameters	Reference Values
Aldolase	1-7.5 U/L
ALT	10-40 ng/mL
AST	12-38 ng/mL
Creatine phosphokinase (CPK)	>200 mcg/L
Myoglobin	25-72 ng/mL

FIGURE 1 AND TABLE 1. Timeline of patient presentation.

presented with the chief complaint of myalgias and upper and lower extremity radiculopathy for one year. The patient had type 2 diabetes mellitus (DM), hypothyroidism, degenerative bone disease in her back, hypertension, hyperlipidemia, and osteoarthritis. The patient expressed that she was not currently on statin therapy as she could not tolerate the associated myalgias, but that she had taken them in the past. The patient's physical exam was normal except for left knee crepitus and pain in her left arm, back neck, hips, and knees. The patient did not have any weakness.

It was decided to obtain imaging studies of the patient's cervical and lumbar spine, routine labs, and CPK levels, and to have the patient return in three months.

The imaging studies were consistent with her previous diagnosis of degenerative disease. The patient's aldolase was 14.4 U/L, myoglobin was 609 ng/mL, aspartate transaminase (AST) was 53, alanine transaminase (ALT) was 83, and CPK was 1279 mcg/L (Table 1). On follow-up, the patient continued to have myalgias and CPK had risen to 1316 mcg/L. Treatment with leflunomide 20mg daily was initiated, and steroids were withheld due to the patient's type 2 DM. The patient was instructed to follow-up in three months and repeat labs. CPK and an HMG-CoA antibody test were to be checked in a month.

The patient's HMG-CoA antibody was found to be positive with a level of more than 200. Her CPK increased to 1973 mcg/L. At her follow-up, the patient expressed that the myalgias appeared to be improving from the leflunomide treatment. Methotrexate 2.5 mg six tablets weekly were initiated at this time on top of the leflunomide, and a three-month follow up with follow-up labs and CPK levels was ordered.

At follow-up, the patient noted improvement in her myalgias after starting methotrexate. CPK levels increased slightly to 1999 mcg/L. Five months passed before the patient presented to the clinic again for a follow-up, and she noted that her myalgias were worsening. Her CPK level was found to be 2899 mcg/L at this visit, warranting an increase in her methotrexate treatment to eight pills once weekly in addition to starting physical therapy.

One month later, the patient followed up and noted that she had a remarkable improvement in her myalgias since starting physical therapy and taking the increased dose of methotrexate and leflunomide. A six-week follow-up was scheduled at this time.

Six weeks later, the patient again presented with worsening myalgias from her last visit. CPK levels were 3023 mcg/L. At this time, it was decided that her serologic profile would be updated with more aggressive therapy such as intravenous immune globulin (IVIG) or rituximab if the results warranted. It was eventually found that these extra measures were not necessary, and the patient continued taking her disease modifying antirheumatic drug (DMARD) therapy and attending physical therapy.

At a three-month follow-up, her CPK level was down to 691 mcg/L, and she noted much improvement in her myalgias. Three months after this, her myalgias improved significantly with a normal CPK level of 70 mcg/L. The patient continued to have normal CPK levels and reduced myalgias at subsequent visits.

DISCUSSION

Immune-mediated necrotizing myopathy (IMNM) is a rare autoimmune complication of taking statins that occurs in about 14 out of 100,000 people.[7] Currently, anti-HMGCR antibodies are used as the diagnostic marker of statin-induced IMNM along with hyperCKemia. Necrotizing myopathy mediated by anti-HMGCR antibodies can cause relentless myopathy for those suffering from it. Patients may also suffer from proximal muscle weakness and truncal weakness. Although some may have stopped the offending statin before their symptom onset, it is important to keep this diagnosis in mind, as early treatment helps reach remission for these patients. With a combination of immune-modulating therapies, patients can reach a level of remission of symptoms and normalization of creatine kinase (CK) levels.

The mainstream treatment of this remains a combination of immunosuppressive agents, most commonly systemic corticosteroids, methotrexate, IVIG, and potentially the addition of rituximab.[4] The recommended therapy includes a combination of immunosuppressive agents, most commonly systemic corticosteroids, methotrexate, IVIG, and potentially the addition of rituximab. A minimum of two years is recommended to achieve remission and reduce the risk of relapse.[4] With early treatment initiation and an efficacious drug regimen, complete remission is now possible.

In this case, a 75-year-old female presented with myalgias and an elevated CPK level. Antibodies to HMG-CoA were found, making this case unique as it occurs in 14 out of 100,000 people.[7] The patient was successfully treated with leflunomide, methotrexate, and physical therapy (Figure 1). The patient's myalgias significantly improved, and her CPK levels returned to normal. This case highlights the importance of keeping a diagnosis in mind for rare immune-mediated myopathies. It also demonstrates the importance of early diagnosis, so that the patient may be treated as early as possible. Additionally, it is imperative to look at a patient's past medication trials for diagnoses. This patient was not currently on a statin when diagnosed but had previously trialed and failed therapy. Successful treatment in this case alleviated the patient's pain, and the patient was relieved to know they had a formal diagnosis.

AUTHOR AFFILIATIONS

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REFERENCES

1. Roth GA, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol. 2020;76(25):2982-3021.

2. Karr S. Epidemiology and management of hyperlipidemia. Am J Manag Care. 2017;23(9 Suppl):S139-S148.
3. Vinci P, et al. Statin-associated myopathy: emphasis on mechanisms and targeted therapy. Int J Mol Sci. 2021;22(21):11687.
4. Barron, R. Statin-associated autoimmune myopathy: review of the literature. JPharm Pract. 2022;08971900211040291.
5. Shovman O, et al. Anti-HMGCR antibodies demonstrate high diagnostic value in the diagnosis of immune-mediated necrotizing myopathy following statin exposure. Immunol Res. 2017; 65(1):276-281.
6. Meyer A, et al. Statin-induced anti-HMGCR myopathy: successful therapeutic strategies for corticosteroid-free remission in 55 patients. Arthritis Res Ther. 2020;22(1):1-10.
7. Svensson J, et al. Incidence and prevalence of idiopathic inflammatory myopathies in Sweden: a nationwide population-based study. Rheumatology. 2017;56(5):802-810.