A Rare Case of Statin-Associated Autoimmune Myopathy

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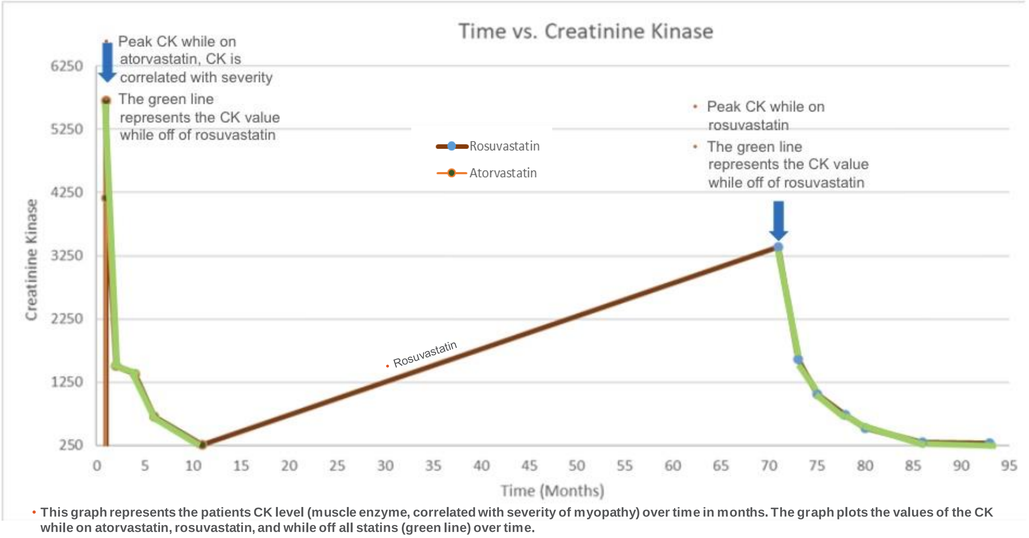
Introduction

- Management of heart disease with lipid lowering agents play a vital role in medicine. Statins are one group of medications that are widely utilized in the medical field to decrease the risk of cardiovascular disease. Statins work by inhibiting the hepatic enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR).
- While statin medications have shown to be effective in reducing vascular and heart disease, they include common complications like hepatitis, elevation in liver enzymes, and myopathy [1]. The incidence of statin-induced muscle symptoms is roughly between 0.01%-0.1% [2].
- Statin-induced autoimmune myopathy is a rare phenomenon that typically presents as unexplained proximal muscle weakness with a concomitant increase in serum creatine kinase level. Antibodies to HMGCR are very specific and rarely are they found in patients taking statin medication [2]. The presence of HMGCR antibodies suggest an autoimmune component to the statin-induced-myopathy and so the treatment warrants immunosuppression.
- Discontinuation of the offending agent (statin) most typically can lead to a quick improvement of the muscle symptoms and normalization of the serum creatine phosphokinase (CPK) level. Early diagnosis, discontinuation of statins and in combination with immunosuppressive drugs are considered the cornerstones of treatment [3]. Without treatment, the myopathy can persist and lead to significant morbidity and dysfunction.

Case Presentation

- A 74-year-old male with a past medical history of glaucoma, tension-type headaches, and coronary artery disease presented to our facility for evaluation of progressively worsening bilateral extremity weakness.
- His lower extremity muscle weakness first began 5 years ago after he underwent a multivessel coronary artery bypass graft (CABG). After the CABG, he started atorvastatin 80 mg and started to notice a gradual increase of weakness to complete tasks. He lacked any history of congenital muscular defects, traumatic injury, orthopedic or neurosurgical procedures. His personal and family history were negative for muscular disorders or autoimmune conditions.
- Physical exam showed weakened strength and symmetrical atrophy over bilateral lower and upper extremities. Gower's sign was negative. His deep tendon reflexes and sensation to light touch and pain were intact in all extremities. The patient lacked any dermatological skin findings that would suggest an inflammatory muscle disorder.
- Serum workup for inflammatory markers were normal. His serum creatinine kinase level averaged around 99 prior to his statin initiation. After he first started atorvastatin, his CPK became markedly increased, peaking at 5700 U/L.
- The dose of atorvastatin was decreased and although his CPK had improved, it remained elevated at around 4,162 U/L. His liver enzymes were not concerning for hepatotoxicity. Once he was weaned off the atorvastatin, his weakness symptoms slightly improved but persisted. After weaning off the statin, his CPK levels improved steadily over the next several months. Almost 6 months after the discontinuation of atorvastatin, he was placed on a trial of rosuvastatin, but this also led to a gradual increase in his CPK that peaked at a level of 3393 U/L.
- His autoimmune and myositis-specific antibody panel, complement levels, hepatitis and HIV were all negative. Electromyographic (EMG) was normal so he underwent a muscle biopsy of the left thigh. Muscle biopsy results were nonspecific. Serology testing showed anti-HMGCR antibodies at a level of 200 CU (reference range 0-19 units: Negative).
- Given the correlation of his statin use and symptoms, elevated muscle enzymes and the seropositivity of anti-HMGCR antibodies, a diagnosis of statin-associated autoimmune myopathy was made. He started evolocumab injections as an alternative to statin medications for secondary prevention of cardiovascular disease. He also started methotrexate with low-dose prednisone for immunosuppression. The patient exhibited recovery within the first few months of these two medications and illustrated improvement over time.



- This graph represents the patients CK level (muscle enzyme, correlated with severity of myopathy) over time in months. The graph plots the values of the CK while on atorvastatin, rosuvastatin, and while off all statins (green line) over time.

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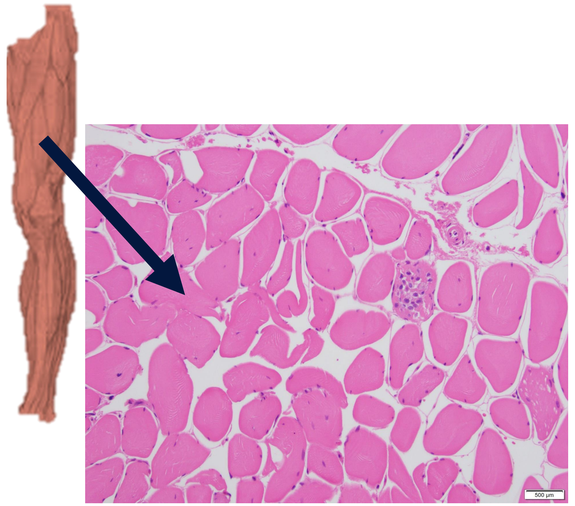

Muscle Biopsy of Left Anterior Thigh: There are also myofibers of various sizes and shapes which is also a nonspecific myopathic feature. There are increased internal nuclei which is a nonspecific myopathic feature.

Conclusion

- One must have a high clinical suspicion on the cases of generalized extremity muscle weakness in patients with no other risk factors and with usage of statins. The myotoxic and hepatotoxic correlation between statin use are widely recognized among medical professionals. However, there are instances whereby progressive muscle weakness persists despite discontinuation of the statin and the correlation is oftentimes not easily apparent. In cases where statin autoimmune-mediated myopathy is considered as a possible differential diagnosis, it is vital to attain a careful history, physical examination, and laboratory work up.
- In circumstances where the etiology of muscle weakness remains unidentified, one must also consider employing tests such as muscle biopsy, electromyography studies, and autoimmune serology workup. Prompt identification and initiation of treatment is imperative in decreasing morbidity for patients with statin autoimmune-mediated myopathy.

References

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