Near-Fatal Statin-Associated Autoimmune Myositis

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Dear Editor,

An 82-year-old male arrived in the emergency room after been found lying on a floor for 36 hours. He had attempted to transfer from his bed and fell, without loss of consciousness.

He reported 4 months of gradual weakness affecting his proximal lower limbs and spine, causing kyphosis. He was previously fully mobile and independent. This weakness was preceded by 17 months of atorvastatin use (10 mg daily) for the primary prevention of ischemic heart disease. The statin was discontinued 4 months prior this fall due to elevated alanine aminotransferase and muscle weakness. He had atrial fibrillation and was taking aspirin.

A physical examination revealed bilateral medial quadriceps wasting and proximal lower limb weakness. His power in the upper limbs and ankles were preserved. The cranial nerves were normal, but he had neck extensor weakness with associated head drop. The findings of a cardiovascular examination were normal, but he had increased respiratory effort. He was cognitively intact.

Creatinine kinase (CK) was elevated at 4,000 UI/L (normal upper limit 150 UI/L), with normal renal function. Needle electromyogram of the biceps, first dorsal interosseous, and vastus medialis showed positive sharp waves and myotonic discharges with spontaneous fibrillations, consistent with myopathy. A quadriceps muscle biopsy showed necrotising myopathy, with necrotic fibers, rimmed p62-positive vacuoles, and the absence of inflammation. Autoantibody screening was positive for hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase, which is consistent with statin-associated autoimmune myositis. Screening for other autoimmune myopathies including dermatomyositis and polymyositis was negative.

The patient required intubation and ventilator support in intensive care for type 2 respiratory failure and percutaneous endoscopic gastrostomy feeding for severe oropharyngeal dysphagia demonstrated on video fluoroscopy. He was commenced on high-dose intravenous methylprednisolone before switching to 60 mg of oral prednisolone daily. He was extubated and weaned off tracheostomy after 2 months.

At 3 months after presentation he was transferred to a neurology center and received 2 g/kg intravenous immunoglobulin (IVIg) in divided doses over 4 days. After an initial improvement in lower leg strength, he was commenced on six cycles of cyclophosphamide at 2-week intervals, with a tapering steroid course. After the second cycle the patient was able to stand independently and was transferred to neurorehabilitation. After four cycles of cyclophosphamide he was able to swallow and could ambulate independently, and was discharged to his home.

The first cases of statin-associated autoimmune myositis (SAM) were reported in 2007.¹ As demonstrated here, SAM patients present with subacute symmetrical proximal limb weakness associated with elevated CK, autoantibodies to HMG-CoA reductase, muscle-cell necrosis, and minimal or no inflammatory infiltrates in muscle biopsies.² The presence of rimmed vacuoles has only been described in one other case of SAM,² but our patient had no other clinical or histological features consistent with inclusion body myositis. Other presenta-

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tions include mild joint pains, rash, and (in severe cases) respiratory failure.²⁻⁴ Two fatal cases of biopsy-confirmed SAM have been reported,^{3,4} both of which involved statin use before the development of necrotising myopathy and subsequent respiratory failure. Our case is the first in which high-dose steroids, IVIg, and cyclophosphamide in combination were effective for treating near-fatal SAM.

Guidelines are not currently available for the management of SAM, with treatment reliant on clinical experience. An algorithm for the diagnosis of SAM has been suggested.² If SAM is suspected, statins must be discontinued immediately. Once a diagnosis is established, immunosuppressants are initiated as first-line treatment, typically high-dose prednisolone (1 mg/kg).² Other immunosuppressants may be used in combination, such as methotrexate, azathioprine, or mycophenolate, to optimize the response.² If severe weakness persists after 8–12 weeks, IVIg or drugs such as rituximab may also be considered.²

The morbidity and mortality of SAM remain uncertain. The present case highlights the importance of clinicians being aware of this significant adverse effect of statins, which can

develop even after long-term use and discontinuation, so that appropriate investigations and treatment are initiated as soon as possible to prevent progression to a debilitating state.

Conflicts of Interest

The authors have no financial conflicts of interest.

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