

Oropharyngeal Dysphagia: Rare Presenting Symptom of Statin-induced HMG CoA Reductase Necrotizing Autoimmune Myopathy

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Received date: November 13, 2017; Accepted date: December 15, 2017; Published date: December 26, 2017

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Abstract:

Necrotizing Autoimmune Myopathy (NAM) associated with 3-hydroxy-3-methylglutarylcoenzyme A Reductase (HMGCR) antibodies has been described in statin-induced and statin-naive patients. Proximal muscle weakness is the presenting symptom in HMGCR NAM. Creatine Kinase (CK) levels can exceed 10x normal values. Statin-induced cases involve two thirds of HMGCR NAM patients and are more likely to respond to immunosuppressive therapy. Muscle biopsy confirms the diagnosis. We report a case with progressive oropharyngeal dysphagia as the presenting complaint with delayed response to treatment. To our knowledge, there has been only one previously reported case of statin-exposed HMGCR NAM with a similar presentation.

Keywords: Necrotizing autoimmune myopathy; Statin-induced; Oropharyngeal dysphagia; Aggressive immunosuppressive therapy

Introduction

Background: Necrotizing Autoimmune Myopathy (NAM) associated with 3-hydroxy-3-methylglutaryl-coenzyme A Reductase (HMGCR) antibodies is described in statin-induced and statin-naive patients [1]. Proximal muscle weakness is the presenting symptom in HMGCR NAM. Creatine Kinase (CK) levels can exceed 10x normal values [2]. Statin-induced cases involve two thirds of HMGCR NAM patients and are more likely to respond promptly to immunosuppressive therapy [3]. Muscle biopsy confirms the diagnosis.

Objective: We report a case of HMGCR NAM of progressive oropharyngeal dysphagia as the presenting complaint with delayed response to treatment following diagnosis.

Case Report

A 79 year old Peruvian gentleman presented with four weeks of progressive dysphagia to solids and liquids, a 25 lb weight loss and fatigue. He reported inability to swallow with pooling of saliva. He denied odynophagia, vomiting, dyspnea, fevers, skin changes, or arthralgias. There was no history of upper respiratory infections or recent vaccinations. Over subsequent weeks he noted pain with weakness in bilateral lower extremity proximal muscle groups. Effort was needed to rise from the sitting position. Once upright he could ambulate. He denied tobacco, alcohol, or drug use. He had diabetes treated with metformin (A1C 6.2), hypertension controlled with amlodipine and lisinopril, and hyperlipidemia treated with 40 mg/day of atorvastatin. Atorvastatin was discontinued two weeks prior to admission. Age appropriate cancer screening was normal. He was afebrile with normal vital signs. He was thin with temporal wasting and gargled speech. No neck masses were detected. Cardiopulmonary and abdominal exams were normal. Rashes and edema was absent. Neurological exam revealed intact cranial nerves, without tremors,

fasciculations or muscle wasting. He had no difficulty in raising his arms above his head but had difficulty in rising from a chair. Reflexes were symmetric with normal cerebellar and sensory testing. Labs included a CPK of 8185, aldolase of 346 (normal <8), AST/ALT of 176/395, preserved renal function and a hemoglobin of 10. TSH and B12 levels were normal. HIV, T-SPOT, Hepatitis B/C were negative. Vitamin D levels were low (16.5). A barium swallow confirmed cricopharyngeal paralysis. MRI brain and cervical spine was normal. Myopathy workup was pursued. Myositis panel antibodies including Jo-1, MI-2, SRP, U2-snRNP, U1-RNP, NXP-2, and TIF1 were negative. Anti-HMGCR antibodies were markedly elevated at >200 (normal <20). MRI of the femur showed diffuse inflammatory changes consistent with myositis (Figure 1).

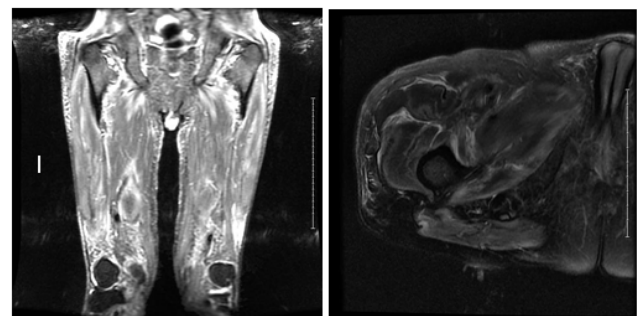


Figure 1: Diffuse myositis involving bilateral lower extremities. There is diffuse interstitial intramuscular edema involving the muscles of bilateral legs. No significant muscular atrophy noted.

Biopsy revealed muscle fiber necrosis, phagocytosis, macrophages and regeneration with minimal inflammatory features consistent with necrotizing myopathy (Figures 2A-2D). Over the course of hospitalization, a feeding gastrostomy tube was needed and he was unable to ambulate. Pulse dose steroids followed by oral prednisone

was ineffective. With progressive weakness and persistent dysphagia, a trial of weekly rituximab was instituted without clinical improvement. When monthly IVIG was initiated, slow clinical progress was noted. Over the next six months he no longer required tube feeding or a wheelchair for mobility. His CK level declined. At his last follow-up, approximately one year after initial presentation, the patient was eating normally and ambulating with the assistance of a walker. He continues to receive IVIG and rehabilitation.

Discussion

Statin induced myopathy is estimated to occur in 3/100,000 patients on statins [2]. Stopping the drug typically leads to improvement of myopathy [1,2]. Statin induced HMGCR NAM characterized by proximal muscle weakness, elevated CK levels and evidence of muscle fiber necrosis without inflammation is associated with antibodies against HMGCR [1]. Oropharyngeal dysphagia replacing the classic presentation of proximal muscle weakness in statin-induced HMGCR NAM is uncommon [4]. Necrosis of the muscle persists despite statin discontinuation, suggesting statins may trigger an autoimmune process independent of the medication [1,2]. In such cases, immunosuppressive therapy is generally required [3]. Recommended initial treatment is high dose corticosteroids. In refractory cases, systemic multimodality immunosuppressive medications are used [3,5]. Although there are no clinical trials for treatment of statin-induced myopathy, success has been reported with use of intravenous gammaglobulins, often in addition to other immunosuppressants such as rituximab, methotrexate, azathioprine, and mycophenolate [3,5]. Improvement in muscle strength, reduction in CK levels, and decrease in Anti-HMGCR antibodies are considered markers of response to therapy [1,2]. Early recognition of statin induced NAM will allow for initiation of prompt immunosuppressive therapy with the opportunity for improved outcomes.

References

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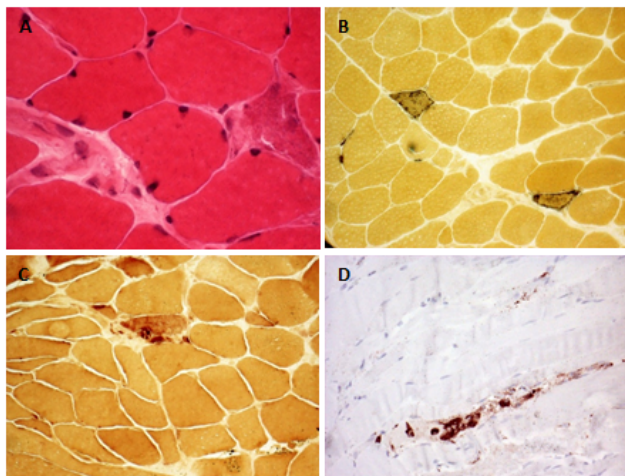


Figure 2: (A) Frozen section of muscle, with phagocytosis on left, and a basophilic, regenerating figure on right. Hematoxylin and eosin (H&E) stain (25X magnification); (B) Frozen section, alkaline phosphatase stain, with two dark stained degenerating/regenerating fibers. Alkaline phosphatase histochemistry. (10X magnification); (C) Frozen section, with phagocytosis of a fiber. Esterase histochemistry (10X magnification); (D) Paraffin section, immunohistochemistry using an antibody to the macrophage marker CD68, phagocytosis of a muscle fiber, in longitudinal section. Diaminobenzidine stain, with light hematoxylin counterstain (10X magnification).