

Anti-HMGCR autoantibody positive necrotizing autoimmune myopathy with dermatomyositis-like eruption

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A 47 year-old man presented with a 4-week history of myalgia, dysarthria, dysphagia and generalized weakness, after having been receiving atorvastatin for one year. On examination, he had a heliotrope rash, and non-pruritic, erythematous macular rashes that were present around the neck, upper chest, and the extensor surfaces of the interphalangeal and metacarpophalangeal joints. No nail findings such as telangiectasia or ragged cuticles were seen. Neurological examination revealed flaccid dysarthria associated with palatal weakness, and mild weakness in the orbicularis oculi and orbicularis oris muscles. Motor strength was graded as follows using the Medical Research Council (MRC) scale: neck flexors 3, neck extensors 4, shoulder abductors 4, elbow flexors 4, elbow extensors 5, wrist extensors 3, wrist flexors 4, finger extensors 3, first dorsal interossei 2, hip flexors 4, knee extensors 4, knee flexors 4, ankle dorsiflexors 3, and plantar flexors 4. Creatine kinase (CK) was elevated, with a peak level of 37,527 U/L (normal: 30-220 U/L). Needle electromyography showed short-duration and small-amplitude motor unit potentials, fibrillation potentials and positive-wave discharges in the proximal and distal limb muscles. Serum testing for the autoantibodies Jo-1, PM-SCL, SRP and NXP2 was negative. A right rectus femoris muscle biopsy revealed muscle fiber size variability, mild fiber necrosis, and mild mononuclear infiltration without perifascicular atrophy. C5b9 staining for membrane attack complex was unremarkable and major histocompatibility complex class I (MHC-1) staining revealed a diffuse sarcolemmal overexpression (Figure). A request for a biopsy of a distal limb muscle with more significant weakness was declined by the patient. Serum anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (anti-HMGCR) antibody exceeded 200 units (normal ≤ 20 units) on ELISA (via RDL Reference Laboratory) and was also positive

by immunoprecipitation by our own laboratory, confirming the diagnosis of statin-associated necrotizing autoimmune myopathy (NAM). Treatment was initiated with intravenous methylprednisolone 1 g per day for 5 days, followed by intravenous immunoglobulin (IVIG) 0.4 g/kg/day for 5 days and oral prednisone at 80 mg per day. However, muscle weakness persisted and CK remained significantly elevated in the range of 19,000 to 34,000 U/L. Subsequent treatment with plasmapheresis for 5 sessions led to a reduction of CK level to 6,481 U/L. The patient's muscle strength returned to normal in all muscles except for the neck flexors, shoulder abductors, wrist extensors, and ankle dorsiflexors which were graded as MRC 4. Maintenance plasmapheresis 2 days a month was continued. Mycophenolate mofetil was initiated at 1000 mg twice a day, and prednisone dosage was tapered down to 20mg per day over the next 4 months. At month 5, the heliotrope and other skin rashes had resolved with a near complete recovery of limb strength and a CK level of 1427 U/L.

NAM can be a rare complication of statin usage that is associated with anti-HMGCR antibodies, and is characterized by histopathological features of muscle fiber necrosis with minimal to no inflammation.¹⁻³ Typically patients present with various degrees of symmetrical proximal limb weakness, and prominent CK elevation that often exceeds 6000 U/L.¹ Treatment usually consists of corticosteroids, steroid sparing agents or IVIG. Most patients require combination therapy and do not respond to corticosteroids alone.^{1,4} The history of statin use, prominent CK elevation, muscle fiber necrosis with minimal inflammation and high-titer anti-HMGCR antibodies confirmed the diagnosis of anti-HMGCR associated NAM in our patient.

Our patient also showed a heliotrope rash and Gottron's sign, cutaneous manifestations that are considered pathognomonic for dermatomyositis. Typical histopathological features of dermatomyositis such as perifascicular atrophy and prominent inflammation were not observed. Although anti-HMGCR antibody was not detected in 33 adult cases of dermatomyositis, it has been found in rare cases (0.8%) of juvenile dermatomyositis.^{2,5} Our case report raises the possibility of anti-HMGCR myopathy presenting with dermatomyositis-like features in adult patients. Recently, Lavian et al described a patient who developed anti-HMGCR antibody positive NAM with similar dermatomyositis-like features.⁶ As with our patient, theirs demonstrated heliotrope rash and Gottron's signs, significant elevation of CK (3,000 to 20,000 U/L), and lack of inflammation or perifascicular atrophy on muscle biopsy. Their patient responded well to high-dose prednisone, methotrexate, and monthly IVIG. The common features shared by these two patients show the overlapping characteristics of anti-HMGCR antibody positive NAM with dermatomyositis, and the value of detecting serologic markers such as anti-HMGCR antibody.

Our patient also had a few additional unique features. Severe distal limb weakness was the predominant manifestation while only mild proximal weakness was observed. Significant distal limb muscle weakness is rarely encountered in statin-associated NAM, but was described in all 3 cases of juvenile dermatomyositis with positive anti-HMGCR antibodies.⁵ Finally, limited cases of NAM responding to plasmapheresis have been described, one of which included 2 patients with anti-HMGCR myopathy.⁷ The use of plasmapheresis in our patient who had minimal response to corticosteroids and IVIG, led

to significant clinical and laboratory improvements, suggesting its role as a potential therapeutic option in patients with NAM.

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Figure Legend

Figure. Muscle biopsy. A. Rare necrotic fibers on H & E staining (X 400). B. Diffuse sarcolemmal overexpression of MHC-I (X200).

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List of abbreviations used

CK: creatine kinase

MHC-1: major histocompatibility complex class I

HMGCR: 3-hydroxy-3-methylglutaryl-coenzyme A reductase

NAM: necrotizing autoimmune myopathy

IVIG: intravenous immunoglobulin

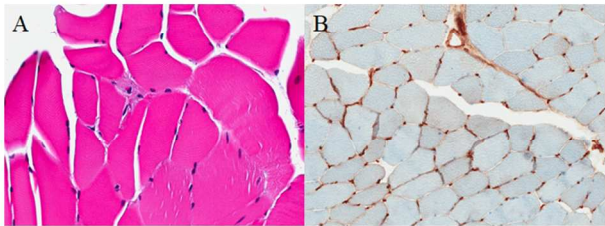
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Figure

254x190mm (300 x 300 DPI)

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