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# Necrotizing Autoimmune Myopathy; an Emerging Entity in the Spectrum of Inflammatory Myopathies

## Abstract

**Background:** Necrotizing autoimmune myopathy is a relatively newly recognized rare form of idiopathic inflammatory myopathy. It presents clinically with symmetrical proximal muscle pain and weakness, associated with a markedly elevated Creatine kinase. These myopathies are usually immune mediated with a good response to immunotherapy.

**Case presentation:** We present a case of a 52 year old man of Asian descent, who presented with a 5 month history of symmetrical proximal muscle weakness. Patient underwent extensive workup and was diagnosed as having Necrotizing autoimmune myopathy with characteristic findings on muscle biopsy and positive HMGCR antibodies.

**Conclusion:** The disease process of Necrotizing autoimmune myopathy is still not completely understood. A delay in diagnosis may however lead to potential complications as the disease progresses rapidly.

**Keywords:** Myopathy; Rheumatology; Proximal interphalangeal; Biochemistry; Hematology; Immunosuppressant drugs

Case Report

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**Abbreviations:** NAM: Necrotizing Autoimmune Myopathy; PIP: Proximal Interphalangeal; MCP: Metacarpophalangeal; SLR: Straight Leg Raise; SRP: Signal Recognition Particle; HMGCoAR: Hydroxy Methyl Glutaryl Co A Reductase; CK: Creatine Kinase; IVIG: Intravenous Immunoglobulin; IL-1: Interleukin 1; IIM: Idiopathic Inflammatory Myositis

## Introduction

Idiopathic inflammatory myopathies are a group of chronic, autoimmune conditions affecting primarily the proximal muscles. These are identified by their clinical presentation consisting of muscular and extra muscular manifestations. Necrotising autoimmune myopathy presents in adults with progressive proximal muscle weakness without the appearance of a rash [1]. We discuss a case of an elderly male who presented with similar complaints and was diagnosed with Necrotising autoimmune myopathy.

## Case Presentation

A previously healthy 52 year old male patient presented in the rheumatology clinic with complaint of Limb pain and weakness in upper and lower limbs for last 6 months, worsening with time. Weakness was characterized by difficulty standing up from sitting position, combing hair and changing clothes. Pain was mild aching type in multiple joints including the Proximal Interphalangeal and Metacarpo phalange joints of both hands, both the shoulder joints and knee joints. Pain was associated with morning stiffness that lasted up to 30 to 40 minutes. However, there was no history of skin rashes, oral ulcers, genital ulcers, photosensitivity, hair fall or weight loss. On further questioning, there was no history of intake of any myotoxic drugs or Statins. Family history for any connective tissue disorder was negative. On general physical examination patient was vitally stable. There were no skin rashes or oral ulcers. All the sub vitals were negative. No signs of synovitis were identified. Examination of Abdomen, cardiovascular and respiratory system was unremarkable. On neurological examination, higher mental funtions and cranial nerves were intact. Motor examination revealed decreased bulk in the right proximal upper and lower limbs, tone was however normal in all four limbs. Power was 3/5 in the flexor compartment of right upper and lower limbs and 4/5 in flexor compartment of left upper and lower limbs. On sensory examination, vibration and position senses were intact with down going plantar. On Musculoskeletal examination there were no signs of inflammation in any joint (redness, warmth, and swelling). Mild tenderness was noted in the PIP and MCP joints of both hands along with tenderness in both knee and shoulder joints. The range of motion, active and passive, of all joints was normal with no limitations. No structural deformity was noted.

Gower's sign was positive. SLR (Straight leg raise) was >60 degrees with a negative Schober's test. On initial laboratory investigations, baseline hematology showed normal blood count. Biochemistry showed urea, creatinine, electrolytes and LFTS within normal range. ESR was found to be 65mm/hr. Serum CK levels were markedly elevated 4418 units/L (normal range 26-192). Chest X-Ray and Ultrasound abdomen were normal. Viral markers screening was negative for Hepatitis B, C and HIV. R.A factor and Anti CCP were also negative. SRP-IgG (Anti Signal recognition particle) tested negative while HMGCoAR-IgG antibodies were found to be positive. Electromyography was abnormal showing mild active degenerative upper and lower limb muscles with myopathic unit. Incisional biopsy from Quadriceps muscle was taken which showed the presence of scattered necrotic myofibres with no inflammatory infiltrates. In light of the

signs and symptoms of the patient and aforementioned laboratory findings, a diagnosis of Necrotising Autoimmune Myopathy was made.

The patient was initially started on Tab. Prednisolone 1 mg/kg/day. However, the patient's the weakness was refractory to steroid monotherapy, with CK level of 3553 U/L at 2 months of beginning the treatment. Immunosuppressive therapy was escalated to Tab. Azathioprine 0.80 mg/kg/day, 6 months after which he had a steady functional recovery and improved muscle strength. Calcium and vitamin D supplements were given as prophylaxis against steroid induced osteoporosis along with cap. Omeprazole to avoid gastric irritation. Regular blood CP and LFTs were advised to monitor azathioprine toxicity. Repeat CK was 2100 (6 months after commencing azathioprine). Steroids were tapered off gradually in a period of four weeks. The patient had improved clinically, remarkably. His last CK was found to be 150 U/L, and is presently on Azathioprine 0.5mg/kg twice daily with regular monthly follow ups.

## Discussion

The autoimmune side of NAM is evident by its association with auto antibodies directed against signal recognition particle and 3-Hydroxy-3-methyl glutaryl- co enzyme a reductase in majority of patients [2]. SRP antibodies affect women more than men. Majority of young patients suffering from NAM are seen to have SRP antibodies. HMGCR is pharmacologic target of the drugs Statin. Auto antibodies against HMGCR are found in patients exposed to Statin medication. However, these antibodies may also be found in patients without Statin exposure [3]. Improvement occurs in majority of patients upon stoppage of the offending agent. In a few cases, it persists even after discontinuation of the drug. Such cases require immunosuppression therapy [4]. Other than use of Statin medication, NAM can also occur on a background of neoplasms and connective tissue diseases [5]. Regarding clinical presentation, a study revealed that the predominant feature is lower extremity weakness. Distal weakness, dysphagia and dyspnea are also common. The study demonstrated out of 63 adult patients, diagnosed cases of NAM, 22 were receiving a Statin medication specifically atorvastatin and simvastatin. 6 were suffering from cancer that included gastrointestinal adenocarcinomas (2 colonic 1 esophageal) and single cases of lung adenocarcinoma, ovarian adenocarcinoma, and thymoma. 3 had a connective tissue disease, out of them 2 had scleroderma and 1 had Sjogren syndrome. Rest of them did not have any obvious causative factor [6].

A recently published case report shows that immune mediated necrotizing myopathies can present initially with symptoms of neck swelling and dysphagia. Prior to this report, no case has been published with initial head and neck involvement in patients suffering from NAM [7].

As discussed above, dyspnea and respiratory muscle weakness is also a common feature, it may lead to respiratory failure in some patients requiring intubation [5]. The diagnosis of NAM requires clinical, electrophysiological and pathologic evidence. The median CK value is several folds higher than normal. Presence of SRP (IgG) or HMGCR (IgG) is essential. Electrophysiology should show characteristic findings of myopathy recorded by EMG. The gold standard for the diagnosis remains muscle biopsy that reveals necrotic myofibres with little or no inflammatory infiltrate [6]. Previously mentioned retrospective study that was conducted on 63 patients proved that HMGCoAR IgG can be detected in patients who have never received statin therapy, as happened in our patient [6].

Treatment of NAM includes corticosteroids, oral steroid sparing immunosuppressant (methotrexate, azathioprine, mycophenolate mofetil) and IVIG [5]. Prednisone monotherapy is usually insufficient for the control of disease as evident in our patient as well. There is a high risk of relapse during immunosuppressant taper or discontinuation. Many patients may require multiple immunosuppressive agents [6]. Aggressive treatment is reserved for refractory cases which include intravenous methylprednisolone, IVIG, rituximab, cyclophosphamide and cyclosporine. IVIG may be used as an alternative to immunosuppressive agents for people who may develop toxicity against it or are unable to tolerate them [1]. Another emerging drug in the treatment of idiopathic inflammatory myopathy is Anakinra, a recombinant humanized IL-1 receptor antagonist, as there is over expression of IL-1 in muscle tissue of inflammatory myopathies. A clinical trial revealed that out of 15 patients with refractory myositis who were treated with Anakinra, 7 of them showed a positive clinical response over a period of 12 months. The efficacy of this drug in the treatment of IIM is still under consideration and needs large scale randomized trials [8].

## Conclusion

NAM is a severe immune mediated myopathy that has a variety of clinical presentations. Early diagnosis and prompt immunosuppressive therapy remains the gold standard for optimal prognosis and better clinical outcomes. The patients however need to be followed up for a longer period of time.

## Consent

Written informed consent was obtained from the patient for the publication of this case report.

## Competing Interests

The authors declare that they have no competing interests.

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