Case Report

Signal Recognition Particle (SRP) Positive Necrotizing Autoimmune Myopathy: A Case Report

Anand Soni[1*], Muktaram Chate[2], Sohel Khan[2], Sagar Jaiswal[2], Srabani Tripathy[2]

[1]Department of Neurology, Electromyography (EMG), Intravenous Immunoglobulin (IVIG), Aurangabad, Maharastra, India, [2]Department of Medicine, MGM Medical College and Hospital, Aurangabad, Maharashtra, India

Corresponding author:
Anand Soni, Department of Neurology, MGMIHS University, Aurangabad, Maharastra, India, E-mail: dranandsoni@gmail.com
Received: 01-Nov-2022, Manuscript No. amhsr-22-82300;
Editor assigned: 04-Nov-2022, Pre QC No. amhsr-22-82300(PQ);
Reviewed: 21-Nov-2022, QC No. amhsr-22-82300;
Revised: 30-Nov-2022, Manuscript No: amhsr-22-82300(R);
Published: 07-Dec-2022, DOI: 10.54608.annalsmedical.2022.72

Abstract

Necrotizing Autoimmune Myopathy (NAM) is a sub-type of inflammatory myopathy which is characterized by acute or subacute onset progressive weakness of the proximal muscle of the body. Recognition of this subtype is important as prognosis varies with subtype. As for other myopathies, elevated CPK-total is hallmark. On the basis of histopathology differentiation is made from others subtypes of inflammatory myopathy. Most common antibodies associated with Necrotizing Autoimmune Myopathy (NAM) are Anti-Signal Recognition Particles (anti-SRP) and anti-3 Hydroxy- 3-Methylglutaryl-Coenzyme A Reductase (anti-HMGCR) antibodies. Patients with anti-SRP antibodies often present clinically with rapidly progressive proximal muscle weakness leading to significant disability. We are here presenting a clinical case of a patient with autoimmune necrotizing myopathy with positive anti-SRP autoantibodies and typical clinical presentation, who responded to treatment on diagnosis.

Keywords: Necrotizing Autoimmune Myopathy (NAM); Signal Recognition Particles (SRP); Electromyography (EMG); Intravenous Immunoglobulin (IVIG)

Introduction

Necrotizing Autoimmune Myopathy (NAM) also called Immune-Mediated Necrotizing Myopathy (IMNM) is a rare disease grouped under idiopathic inflammatory myopathy showing signs of necrosis in muscles on histopathology. It is characterized by acute or subacute weakness in the proximal muscles such as forearms, thighs, hips, shoulders, neck and back muscles, difficulty in climbing stairs, difficulty in standing up from chair, difficulty in lifting arms over the head, falling tendency with difficulty in getting up and general feeling of tiredness [1,2]. Most commonly antibodies associated with Necrotizing Autoimmune Myopathy (NAM) are Anti-Signal Recognition Particle (anti-SRP) and anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (anti-HMGCR) antibodies [3]. Anti-signal Recognition Particle (anti-SRP) autoantibodies are myositis specific and found in about 4% to 6% of patients of idiopathic inflammatory myopathy [4,5]. The Patients with anti-SRP antibodies often present clinically with rapidly progressive proximal muscle weakness leading to significant disability which on histopathology demonstrates a necrotizing myopathy without primary inflammation [6-8]. Marked and sustained clinical response has been observed to combination of intravenous methylprednisone pulse therapy followed by oral steroid therapy, intravenous immunoglobulin therapy [9], plasma exchange and repeated courses of Rituximab [10]. In this study we report a case of necrotizing autoimmune myopathy with positive anti-SRP autoantibodies presented at our tertiary care hospital and which responded to IVIG.

Case Presentation

A 32-year-old female patient presented in medicine OPD at our hospital in February 2022 complaining of progressive weakness and fatigue of proximal muscles in upper and lower limbs. Weakness was first noticed first in proximal upper limb (left>right) which gradually progressed to involve both lower limbs proximal muscles. Weakness which was characterized by difficulty in holding neck, standing up from sitting and squatting position, combing hair, changing cloths. Comorbidities like diabetes and hypertension were absent. History was short here hence inherited myopathies was not considered. Physical examination findings showed wasting of proximal muscle groups with atrophy of girdle and arm muscles (Figure 1). Skin rashes, oral ulcers, photosensitivity, hair fall or weight loss was absent. Manual muscle strength was graded as 2/5 in the proximal lower extremities as well as in the proximal upper extremities. Physical examinations of respiratory system, cardiovascular system and gastrointestinal system were unremarkable with pulse 80 beats/min, BP 110/80 mm of Hg and SpO_2 99% on room air. No organomegaly Peripheral lymph nodes were normal. No history of consumption of any myotoxic drugs or statins.

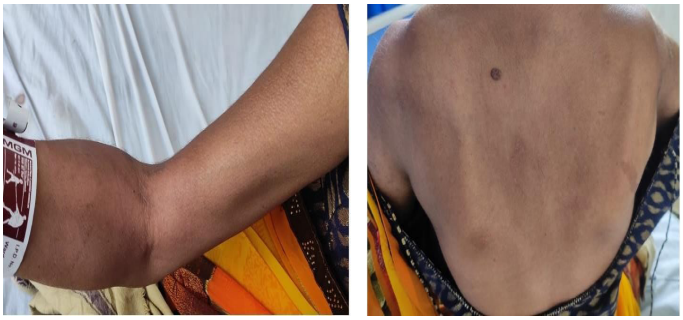

Figure 1. Gross muscle wasting.

How to Cite this Article: Soni A, et al. Signal Recognition Particle (SRP) Positive Necrotizing Autoimmune Myopathy: A Case Report. Ann Med Health Sci Res. 2022;12: 364-366.

Investigation

Hemogram revealed haemoglobin 12.30 g/dl, total leukocyte counts 12750/dl, thrombocytes 324 × 10^9/l. Non specific inflammatory biomarker like Erythrocyte Sedimentation Rate (ESR) 7 mm/h and C-reactive protein 0.7 mg/l were normal, renal function rest results showed urea 14 and creatinine 0.4. Liver enzymes SGOT 126 U/l, SGPT 126 U/l and ALP 68 U/l were increased. Cpk- total were markedly elevated >5000 U/l. Urine test results were normal. Hepatitis B and C, HIV, were all negative. Antinuclear Antibodies (ANA) on indirect immunofluorescence were positive ANA 1:320 (normal<1:160). Myositis specific antibodies against SRP antigen were positive. EMG showed myopathic changes.

Muscle biopsy of left quadriceps revealed necrotizing changes without any evidence of significant inflammatory process and scattered muscle fibre regeneration. Necrotic altered rhabdomyocytes dominated. Echocardiography was normal. Computed Tomography (CT) scan of the chest and abdomen for any possible malignancy was negative. Nerve Conduction Studies (NCS) was characterized by the presence of normal CMAP values over right axillary, bilateral radial, bilateral peroneal and bilateral tibial nerves whereas reduced values over bilateral suprascapular, bilateral musculocutaneous, left axillary, bilateral median and bilateral ulnar nerves. F wave latencies were normal over bilateral lower and upper limb nerves. Sensory nerve parameters found normal SNAP over bilateral lower and upper limb nerves.

Differential diagnosis of Limb-girdle muscular dystrophy was rule out as muscle biopsy in limb-girdle dystrophy shows “dystrophic” triad- anisometry, muscle fiber necrosis and interstitial Fibrosis and positive result of anti-SRP in present case

Treatment

Patient initially started on IV Methylprednisolone 1 gm/day for 5 days. Pulse therapy with intravenous immunoglobulin (0.4 gm/kg/day.) for five days was given. After five days patient was started on oral steroid [Tab Omnacortil] according to body weight and dose of steroid was tapered overtime. Daily Limb Physiotherapy was given. Steroid Sparing Agent Azathioprine 100 mg/day was added to this treatment regimen. Initially patient's response to the therapy was minimal. After four months CPK Total, Hemogram SGOT, SGPT normalized with concurrent improvement in muscle weakness and muscle bulk. Patient has received another pulse therapy with intravenous immunoglobulin (0.4 gm/kg/day) given for 5 days. Prednisolone dosage was tapered slowly with Azathioprine.

Microscopic findings

Section studied from the left quadricep muscle biopsy revealed mild myopathic changes including focal myofiber size variation with small round myofibrils. At places scanty lymphocytic infiltration surrounding the non-necrotic fibres is seen. Few degenerating myofibers and scanty fibrosis is noted (Figure 2).

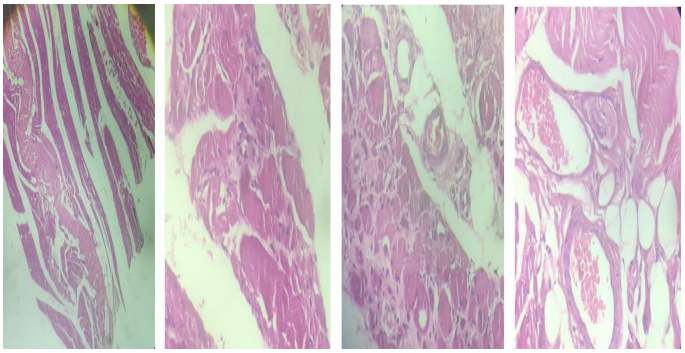

Figure 2. Microscopic findings.

Results and Discussion

Necrotizing Autoimmune Myopathies (NAM) was described for the first time in 2004. It is categorized based on the presence of different autoantibodies in the patient’s blood as cases with positive Anti-Signal Recognition Particle (anti-SRP) antibodies and cases with positive anti-3-hydroxy-3-methylglutaryl-coenzyme. A reductase (anti-HMGCR) antibodies. Signal Recognition Particle (SRP) is a cytoplasmic RNA protein consisting of 7S RNA and 6 proteins with molecular weights of 9, 14, 19, 54, 68 and 72 kD which regulates translocation of newly synthesized protein across the endoplasmic reticulum [11]. HMGCR (3-hydroxy-3-methylglutaryl-coenzyme A reductase) is a key enzyme in production of cholesterol. Diagnosis is based on detection of anti-SRP antibodies in patient’s serum and histological diagnosis of necrotizing myopathy. Other test results including markedly elevated serum creatine kinase, electromyography and muscle images support the diagnosis. Anti-SRP antibodies were first discovered in serum of patients with clinical polymyositis by RNA immunoprecipitation with presence of 7S RNA which can also be detected by immunoassay using a 54-kD subunit protein of SRP (SRP54) [12]. Anti-SRP antibodies are regarded as myositis-specific antibodies and used as serological markers of necrotizing myopathy.

Muscle weakness is the predominant clinical feature [13]. Patients may also have complaints of dysphagia, cardiac involvement, including rhythm or conduction abnormalities as well as cardiac insufficiency [14,15]. Other extra-muscular manifestations include mild interstitial lung disease [16]. In present case progressive weakness and fatigue of proximal muscles in upper and lower limbs were found. In similar study by Kalinova, et al. [17] patient manifested with proximal muscle weakness with atrophy of quadriceps and gluteus muscles, conduction abnormalities, elevated CK levels, and myopathic EMG findings. Muscle biopsy demonstrated prominent necrotic myofibres. In present case muscle biopsy revealed necrotizing changes with scattered muscle fibre regeneration. Antinuclear antibodies on indirect immunofluorescence were positive ANA 1:320. In similar study by Allenbach, et al. [18] in muscle biopsies necrotic muscle fibres were distributed with a diffuse pattern, lymphocytic infiltration was sparse or absent and muscle fibre regeneration was scattered. When clinical phenotypes of both anti-SRP and anti-HMGCR patients were compared anti-SRP myopathy showed

more severe and with intense muscle damage. In present case combined therapy with corticosteroids, Azathioprine and IVIG was found beneficial. In similar study by Milone, et al. and Suzuki, et al. early administration of therapy of corticosteroids with immunosuppressant was found beneficial [3,14]. Kassardjian, et al. stated that the early initiation of IVIG was seen to be advantageous [19]. Arlet, et al. [10] demonstrated marked and sustained clinical response to the combination of prednisone, plasma exchange and repeated courses of Rituximab in two patients with refractory anti-SRP myopathy.

Conclusion

In conclusion SRP positive autonomic necrotizing myopathy is one of the disabling myopathies causing an initial severe muscle weakness with often poor muscle recovery even after treatment.

Hence it is necessary to identify this subtype early by myositis profile and histopathology. Aggressive combined therapy including corticosteroids and immunotherapy (Plasma exchange vs. IVIG) early in case benefits patients as seen in our case. Clinical characteristics, autoantibody status and neurological outcome study in present case suggests that anti-SRP antibodies could define a distinct subset of inflammatory myopathies.

References

1. Khan MH, Patel A, Pendharkar S. Anti-signal recognition particle necrotizing autoimmune myopathy: An atypical presentation. Cureus.2018;10: e3766.
2. Khan NAJ, Khalid S, Ullah S, Malik MU, Makhoul S. Necrotizing autoimmune myopathy: A rare variant of idiopathic inflammatory myopathies. J Investig Med High Impact Case Rep.2017; 5: 1-4.
3. Milone M. Diagnosis and management of immune-mediated myopathies. Mayo Clin Proc. 2017; 92: 826-837.
4. Brouwer R, Hengstman GJ, Vree Egberts W, H Ehrfeld, B Bozic, Ghirardello A, et al. Autoantibody profiles in the sera of European patients with myositis. Ann Rheum Dis. 2001;60: 116-123.
5. Kao AH, Lacomis D, Lucas M, Fertig N, Oddis CV. Anti-signal recognition particle autoantibody in patients with and patients without idiopathic inflammatory myopathy. Arthritis Rheum. 2004;50: 209-215.
6. Miller T, Al-Lozi MT, Lopate G, Pestronk A. Myopathy with antibodies to the signal recognition particle: Clinical and pathological features. J Neurol Neurosurg Psychiatry. 2002;73: 420-428.
7. Hengstman GJ, ter Laak HJ, Vree Egberts WT, IE Lundberg, HM Moutsopoulos, Vencovsky J, et al. Anti-signal recognition particle autoantibodies: marker of a necrotizing myopathy. Ann Rheum Dis. 2006;65: 1635-1638.
8. Dimitri D, Andre C, Roucoules J, Hosseini H, Humbel RL, Authier FJ, et al. Myopathy associated with anti-signal recognition peptide antibodies: Clinical heterogeneity contrasts with stereotyped histopathology. Muscle Nerve. 2007; 35: 389-395.
9. Valiyil R, Casciola-Rosen L, Hong G, Mammen A, Christopher-Stine L. Rituximab therapy for myopathy associated with anti-signal recognition particle antibodies: A case series. Arthritis Care & Res. 2010; 62: 1328-1334.
10. Arlet JB, Dimitri D, Pagnoux P, Boyer O, Maisonobe T, Authier FJ, et al. Marked efficacy of a therapeutic strategy associating prednisone and plasma exchange followed by rituximab in two patients with refractory myopathy associated with antibodies to the Signal Recognition Particle (SRP). Neuromuscul Disord.2006;16: 334-346.
11. Mimori T, Imura Y, Nakashima R, Yoshifuji H. Autoantibodies in idiopathic inflammatory myopathy: an update on clinical and pathophysiological significance. Curr Opin Rheumatol. 2007;19:523–9.
12. Benveniste O, Drouot L, Jouen F, Charuel JL, Bloch-Queyrat C, Behin A, et al. Correlation of anti-signal recognition particle autoantibody levels with creatine kinase activity in patients with necrotizing myopathy. Arthritis Rheum. 2011;63:1961–71.
13. Pinal-Fernandez I, Mammen AL. Spectrum of immune-mediated necrotizing myopathies and their treatments. Curr Opin Rheumatol. 2016; 28: 619-624.
14. Suzuki S, Hayashi YK, Kuwana M, Tsuburaya R, Suzuki N, Nishino I, et al. Myopathy associated with antibodies to signal recognition particle: Disease progression and neurological outcome. Arch Neurol.2012;69: 728-732.
15. Watanabe Y, Uruha A, Suzuki S, Nakahara J, Hamanaka K, Takayama K,et al. Clinical features and prognosis in anti-SRP and anti-HMGCR necrotizing myopathy. J Neurol Neurosurg Psychiatry. 2016;87: 1038-1044.
16. Pinal-Fernandez I, Casal-Domingez M, Carrino JA, Lahouti AH, Basharat P, Albayda J, et al. Thigh muscle MRI in immune-mediated necrotizing myopathy: Extensive oedema, early muscle damage and role of anti-SRP autoantibodies as a marker of severity. Ann Rheum Dis. 2017;76: 681-687.
17. Kalinova D, Kopchev A, Kolarov Z, Rashkov R. Immune-mediated necrotizing myopathy with anti-srp autoantibodies and typical clinical presentation. Clin Med Rev Case Rep 2020, 7:314. ,
18. Allenbach Y, Mammen A, Benveniste O, Stenzel W. 224th ENMC International Workshop: Clinico-sero-pathological classification of immune-mediated necrotizing myopathies. Neuromuscular Disorders. 2018; 28: 87-99.
19. Kassardjian CD, Lennon VA, Alfugham NB, Mahler M, Milone M. Clinical features and treatment outcomes of necrotizing autoimmune myopathy. JAMA Neurol. 2015;72:996-1003.