International Journal of Medical and Pharmaceutical Research
Website: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NLM ID: 9918523075206676
Volume: 4 Issue:3 (May-June 2023); Page No: 599-601

Case Report

IJMPR

Newly Diagnosed Patient with Anti-Hmgcoa Antibody-Associated Necrotizing Autoimmune Myopathy (Immune-Mediated Necrotizing Myopathy IMNM)

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ABSTRACT

Anti- HMGR antibody positive immune mediated necrotizing myopathy is a rare disease was first recognized and characterised in patients with a history of stating exposure and immune -mediated necrotizing myopathy. We reported a rare case of patient presenting with features of proximal myopathy which has a wide differential diagnoses of which a diagnosis of anti- HMGCR-antibody associated myopathy should not be neglected. Effective treatment can Improve the prognosis if diagnosed in time, We provide a summary of clinical findings, pathological features, muscle imaging and immunogenetic risk factors of the disease. We also discuss treatment strategies and approaches to monitoring the therapeutic response. lastly, we briefly summaries the current understanding of the pathophysiology of the disease and postulate a mode for autoimmunity initiation and propagation in the disease.

Key Words: *Anti-HMGCR myopathy , necrotizing myopathy, proximal myopathy, autoimmunity, statin-induced myopthy*

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INTRODUCTION

The spectrum of idiopathic inflammatory myopathies (IIMs) includes dermatomyositis (DM), overlap myositis, inclusion body myositis (IBM) and immune-mediated necrotizing myopathy (IMNM)[1]. IMNM induced by statin was initially described in patients on statin therapy who developed persistent myopathy in spite od statin discontinuation and were responsive only to immunosuppression [1]. The anti-HMGCR-antibody associated myopathy revealed the characteristics of myopathy including very high serum levels of creatine kinase ,widespread damage visible through MRI [2,3,4] and presence of the sacrolemmal and capillary membrane attack complex depositionon muscle biopsy [3,5,6-8] and the necessity of intense immunosuppressive therapy [3,7-12]. The clinical manifestations of IMNM are defined as the presence of proximal myopathy and high CK levels by published reports [13 -14-15] and European Neuromuscular Centre International workshop.

Case Report

61-years -old – male presented to medical decision unitwith complaints of difficulty walking and weakness of lower limbs started 3 weeks before presentation, these symptoms has worsened gradually, initially he was able to walk using walking aids, then he needed assistance to get out of bed. On the day of admission he found it difficult to get up of toleit seat and fell over. He also reported numbness on both feet which has been present for years. He denied back pain , shortness of breath, upper limb or facial weakness, no dysphagia or speech disturbance, no loss ofsphincter control .no skin rashes ,muscle pain or joint pain.

Regarding past medical history, he is known to have diabetes and hyperlipidaemia ,he is on oral Hypoglycaemic medications and 40 mg atorvastatin which was commenced one year ago.

On examination, he was comfortable not distressed, vital signs were stable, Cardio respiratory and abdominal examination were unremarkable, no muscle wasting or skin rashes. No focal neurological signs on cranial nerves and upper limb examination. However, there is symmetrical weakness of hip extension, flexion, abduction and adduction . The power in both, knees and ankles were normal as well as sensations.

Routine blood tests were normal. MRI of spine was carried out which ruled outspinal cord pathology. Next day neurology team reviewed the patients and asked for further blood tests, NCT and EMG.

Investigations results and progression during hospital stay:

- Creatine kinase was high more than 9,0000
  NCS :Normal.
- EMG : myopathic changes
- MRI of the thighs : multifocalo demaand enhancement of bilateral thigh muscle .

Serology : HMGCo Aantibodies were positive 76 AU (normal < 20)

A diagnosis of IMNM was confirmed and patient was treated with steroids ,intravenous immunoglobulin and statin discontinued, He has improved , CK has decreased and discharged home and to be followed up by rheumatology and was due for second cycle of IVIG in 4 weeks.

DISCUSSION

Anti-HMGCR Ab was discovered in 2010 among IMNM patients, where it recognized a 100-kDa protein corresponding to HMGCR antigen, a key enzyme in cholesterol biosynthesis targeted by statins.[3,4] Anti-HMGCR aAbs may be pathogenic as their titers correlate with disease activity (muscle strength and CK levels),[5] and in vitro aAbs induce muscle atrophy and impair muscle regeneration.[2] These aAbs are highly specific for autoimmune myopathy as they were not found in most statin-exposed individuals, including those with self-limited statin-associated myopathy.[6] The prevalence of anti-HMGCR was reported as highest in association with IMNM and only rarely in other IIM and connective tissue diseases (Figure 5).[6–8] Pathophysiology of anti-HMGCR IMNM is not yet entirely understood, but genetic susceptibility has been described with HLA-DRB1*11:01.[9] It is believed that this human leukocyte antigen (HLA) may present a strongly immunogenic HMGCR-derived peptide resulting from HMGCR overexpression with statin exposure.[9]

Anti-HMGCR IMNM usually occurs between 40 and 60 years old, but pediatric cases were reported, and there is a female predominance.[2,4,5] Association with statin exposure is noted in half to two-thirds of patients, and mean duration before CK elevation is 39 months (15–84 months).[10] These patients present with a subacute onset of severe proximal muscle weakness, highly elevated CK (9,000 IU/L)[4,5] and myopathic EMG findings. In a cohort of atorvastatin-associated anti-HMGCR IMNM, CK elevation could precede muscle weakness by months, or even years, suggesting that persistent CK elevation despite statin discontinuation and/or onset of muscle weakness should prompt for anti-HMGCR aAb testing.[10] There is usually no significant extramuscular involvement.[2,4,5] Muscle biopsy helps to differentiate from other myopathies and shows randomly distributed necrotic, regenerating and atrophic muscle fibers, and no or mild inflammatory infiltrates.[2,5] C5b-9 deposits around fibers and/or capillaries are also observed, and MHC-I over expression is usually negative, or slight and focal if present.[11] Malignancy association with anti-HMGCR IMNM has been inconsistent.[2,12]

CONCLUSION

In the present case, a diagnosis of statin-associated anti-HMGCR IMNM was made based on sub acute and severe muscle weakness, high CK levels, statin exposure and anti-HMGCR aAb positivity.[11]In conclusion, the possibility of anti-HMGCR IMNM should be considered in patients with severe proximal muscle weakness and highly elevated CK levels, particularly with a history of statin exposure. This indicates the importance of muscle biopsy and specific autoantibody testing for accurate diagnosis, as well as significant therapeutic implications.

Ethics approval and consent to participate: ‘‘Not applicable’’, my manuscript does not report on or involve use of animal or human data or tissue

List of abbreviations:
HHMGoA(hydroxymethylglutaryl-coenzyme A reductase),CK (creatine kinase), EMG (electromyography),NCS(nerve condition study)

Conflict of interest: No
Funding Statement : personal
Authors’ contributions :

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REFERENCES

1. Benveniste O, Stenzel W, Allenbach Y(2016). Advances in serological diagnostics of inflammatory myopathies. CurrOpinNeurol ; 29(5): 662–673.
2. Allenbach Y, Benveniste O(2018). Peculiar clinicopathological features of immune-mediated necrotizing myopathies. CurrOpinRheumatol ; 30(6): 655–663.

3. Christopher-Stine L, Casciola-Rosen LA, Hong G, et al(2010). A novel autoantibody recognizing 200-kd and 100-kd proteins is associated with an immune-mediated necrotizing myopathy. Arthritis Rheum; 62(9): 2757–2766.
4. Mammen AL, Chung T, Christopher-Stine L, et al(2011). Autoantibodies against 3-hydroxy-3-methylglutaryl-coenzyme A reductase in patients with statin-associated autoimmune myopathy. Arthritis Rheum; 63(3): 713–721.
5. Allenbach Y, Drouot L, Rigolet A, et al(2014). Anti-HMGCR autoantibodies in European patients with autoimmune necrotizing myopathies: inconstant exposure to statin. Medicine (Baltimore); 93(3): 150–157.
6. Mammen AL, Pak K, Williams EK, et al(2012). Rarity of anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase antibodies in statin users, including those with self-limited musculoskeletal side effects. Arthritis Care Res (Hoboken); 64(2): 269–272.
7. Musset L, Allenbach Y, Benveniste O, et al(2016). Anti-HMGCR antibodies as a biomarker for immune-mediated necrotizing myopathies: a history of statins and experience from a large international multi-center study. Autoimmun Rev; 15(10): 983–993.
8. Hudson M, Luck Y, Stephenson M, et al(2016). Anti-HMGCR antibodies in systemic sclerosis. Medicine (Baltimore); 95(44): e5280.
9. Mammen AL, Gaudet D, Brisson D, et al(2012). Increased frequency of DRB1*11:01 in anti-hydroxymethylglutaryl-coenzyme A reductase-associated autoimmune myopathy. Arthritis Care Res (Hoboken); 64(8): 1233–1237.
10. Troyanov Y, Landon-Cardinal O, Fritzler MJ, et al(2017). Atorvastatin-induced necrotizing autoimmune myositis: an emerging dominant entity in patients with autoimmune myositis presenting with a pure polymyositis phenotype. Medicine (Baltimore); 96(3): e5694.
11. Allenbach Y, Mammen AL, Benveniste O, et al(2018). 224th ENMC international workshop: clinico-sero-pathological classification of immune-mediated necrotizing myopathies Zandvoort, The Netherlands, 14-16 October. NeuromusculDisord 2018; 28(1): 87–99.
12. Allenbach Y, Keraen J, Bouvier AM, et al(2016). High risk of cancer in autoimmune necrotizing myopathies: usefulness of myositis specific antibody. Brain; 139(Pt8): 2131–2135.
13. Lavian M, Mozaffar T, Goyal N(2017). Clinical dermatomyositis associated with anti-HMG-CoA reductase antibody positive immune mediated necrotizing myopathy: a case report (P2.125). *Neurology*; 88(16 Supplement): P2125.
14. Merlant M, Fite C, Kottler D, et al(2019). [Dermatomyositis-like syndrome revealing statin-induced necrotizing autoimmune myopathy with anti-HMGCR antibodies]. *Ann DermatolVenereol*; 146(8-9): 550–556.
15. Parikh P, Tavee J, Soltanzadeh P, et al(2018). Anti-3-hydroxy-3-methylglutaryl-coenzyme a reductase autoantibody-positive necrotizing autoimmune myopathy with dermatomyositis-like eruption. *Muscle Nerve*; 57(6): E135–E136.