Avens Publishing Group
J Orthopedics Rheumatol
January 2025 Vol.:11, Issue:1

Open Access Case Report

Journal of
Orthopedics & Rheumatology

Pediatric Anti-HMGCR Myopathy – A Case Report

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Submission: 20 December 2024
Accepted: 10 January 2025
Published: 15 January 2025

Abstract

Anti - HMGCR (3- hydroxy – 3- Methyl glutaryl – Coenzyme A reductase) autoantibody positive Immune – mediated necrotizing myopathy was 1st recognized in an adult patient with a history of statin exposure. The clinico pathologic spectrum of the disease is constantly updated, including in statin unexposed patients, childhood- onset Cases in pediatric and adult patient with a LGMD phenotype. HMGCR myopathy should be considered as a differential diagnosis in children with idiopathic limb girdle muscular dystrophy with silent neuromuscular family history. In 2017 at least four reports described further cases of pediatric anti- HMGCR associated necrotizing myopathies [1].

Introduction

Idiopathic inflammatory myopathy (IIM) is a group of auto immune diseases causing muscle inflammation without other organ involvement. Initially IIM was categorized into Dermatomyositis and Polymyositis. In past one decade, antisynthetase syndrome and Immune mediated necrotizing myopathy (IMNM) have been determined as a new subgroup of IIM by clinical, pathological and Serological parameters. IMNM can be further divided into 3 subtypes based on the seroantibodies involved, these are – Anti-HMGCR Myopathy, Anti-SRP (Signal recognition particle), and seronegative myopathy. In 2010 Anti-HMGCR antibody myositis was first identified as an autoantibody in pts with necrotizing myopathy [4]. It was also first described in older adults with a history of statin exposure. Over time, statins have been used in children and adolescents. although most studies have been conducted on patients with pediatric familial hypercholesterolemia. In accordance with recent studies, HMG-CoA reductase inhibitors in children have led to reduction in LDL-C values by approximately 21- 41 % [8]. With increasing use of statin drugs as lipid lowering agent resulted in unmasking of distinct form of autoimmune myopathy associated with its use. Anti- HMGCR antibodies are highly specific and are not found in patients with other related diseases. Intake of Statins need to be stopped as a part of initial treatment [2]. Anti-HMGCR myopathy has been described in pediatric patients. The existence of a clinical presentation mimicking limb girdle muscular dystrophy and a delay in diagnosis have been reported in a few Adults and pediatric patients too [3].

Case Presentation

A 12-year-old girl presents with H/O gradual progressive weakness of proximal muscles of 4 months duration which had significantly increased since last 20 days. There was involvement of both upper and lower limbs. Patient had difficulty in standing, walking, climbing up the stairs. She was not able to lift arms over the shoulder since last one month. Neck muscle weakness was present. Presently patient had waddling gait.

There was no H/O - fever, rash, photosensitivity, cough, joint swelling, oral ulcers, dysphagia, skin lesion / Dermatitis, DM, HT Hypothyroidism.

Family history was noncontributory.

On examination – patient was conscious, oriented

Power-

Rt Upper limb – proximal 3/5, distal 4+ /5

Left upper limb – proximal 3/5, distal 4+ /5

Rt lower limb – proximal 3+ /5, distal 4+ /5

Left lower limb – proximal 3+ /5, distal 4+ /5

Investigations

Hb – 12.2gm%, TLC – 10,400/cumm , Plt – 3 lakh/ cumm , ESR – 37mm1st hr ,TSH – WNL , KFT –WNL ,Urine R/M – WNL , LFT – ALT 62 U/L, AST 55U/L , Low AST/ALT ratio , CPK > 17000 U/L.

Nerve conduction velocity – normal

EMG (Electromyography) -- Severe diffuse myopathy, s/o active inflammatory myopathy.

Provisional Diagnosis - Inflammatory Myositis (likely)

Limb Girdle muscular dystrophy

Myositis extended profile (LIA) –Negative

Muscle Biopsy – Showed myofiber degeneration and necrosis, perivascular chronic inflammation along with lymphocytic invasion of healthy myofibres suggestive of inflammatory myositis.

Anti – HMGCR antibody testing {chemiluminescenceimmunoassay} using INNOVA diagnostic kits (werfen)– POSITIVE.

FINAL DIAGNOSIS- Anti – HMGCR myopathy

Discussion

Necrotising autoimmune myopathy {NAM} is a subgroup of the idiopathic inflammatory myopathies that is defined by clinical and histopathological features. Patients with anti HMGCR myositis presented with either profound or insidious onset muscle weakness as

ISSN: 2334-2846

was seen in our case [5]. In our case the CPK was significantly raised and a similar study carried out to detect the prevalence of raised CPK was the hallmark of immune mediated myopathies [6]. Cutaneous involvement in the form of skin rash can be seen in 40 – 60% of cases however it was not seen in our case [6].

A higher level of alanine transaminases level with low (AST /ALT Ratio) is seen in the anti HMGCR myositis as was seen in our case also [7].

Conclusion

Anti HMGCR myositis has been described in pediatric pts. Most cases presenting with profound muscle weakness of proximal muscles and raised CPK levels [5]. Patient may or may not present with skin rash [6]. Patient usually have elevated ALT, with low AST/ALT ratio [7]. Muscle biopsy, EMG (electromyography), myositis antibody profile and testing for anti HMGCR antibodies are helpful for early diagnosis and in differentiating this from limb girdle muscular dystrophy [6].

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