# Necklace body myopathy: A rare entity

Sir,

There are numerous causes of muscle diseases that present as early respiratory failure (ERF). Some of these conditions have ERF as a typical manifestation, whereas in others, they are uncommonly seen.[1-3] Diseases that typically have ERF are adult-onset Pompe disease, myotonic dystrophy type 1, Limb-girdle muscular dystrophy [LGMD] 2I, cystic fibrosis (C-F), myofibrillar myopathies, TPM3 (α-tropomyosin-3) myopathy, and oculopharyngeal muscular dystrophy.[3] Hereditary myopathy with early respiratory failure (HMERF; OMIM: 603689) is one such entity in which respiratory insufficiency is an important entity and needs to be recognized. Cytoplasmic bodies (CBs) are abnormal protein aggregates usually visualized as red-colored objects on modified Gomori trichrome stain and can be observed in a large group of myopathic conditions. In muscle biopsy of HMERF, CBs are often located in the subsarcolemmal region with a necklace-like alignment. Here, we report a case of HMERF with proximal muscle weakness whose respiratory symptoms were overlooked during the initial visit to the neurology clinic and the patient was misdiagnosed as having LGMD.

An 18-year old boy presented with progressive weakness of both lower limbs since childhood. Currently, he was not able to stand up without support. On examination, Gower's sign was positive and power was reduced in the proximal muscles of lower limbs more than the upper limbs. However, the distal muscles were spared. Detailed power testing showed the upper limb power to be Medical Research Council (MRC) grade 4+/5 proximally and 5/5 distally. In the lower limbs, the power was MRC 4-/5 proximally and 5/5 distally. There was evidence of neck or facial weakness, and the single breath count was 22. His CK-NAC (N-acetyl-cystein-(**NAC**)- activated creatine kinase) was 114.9 U/L (normal range: 26–308 U/L). Electromyogram was consistent with a myopathic pattern. Deltoid muscle biopsy revealed myopathic features with the presence of necklace cytoplasmic bodies (CBs) in >2 muscle fibers exclusively localized in the subsarcolemmal area, covering more than 50% of the circumference of each muscle fiber in three nonserial sections (each section was at least 250 μm apart and included at least 300 muscle fibers), which was confirmed to be degenerated Z-band material on electron microscopy [Figure 1]. On the subsequent visit, the patient on probing gave a history of shortness of breath and recurrent respiratory infections. At 6 months of follow-up, he is still ambulatory without support and needs assistance while getting up from the sitting position.

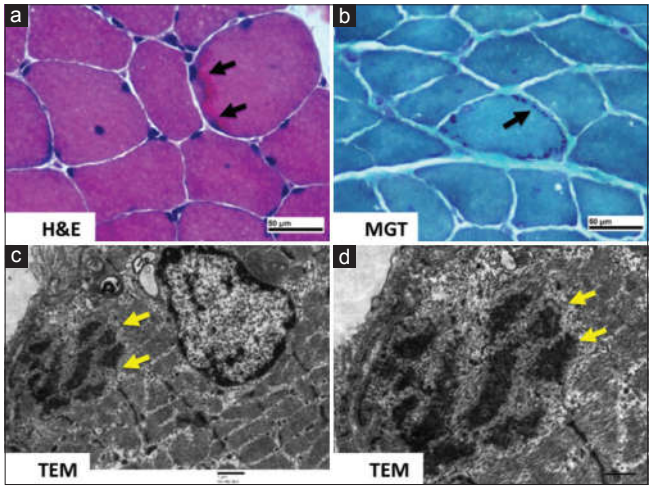


**Figure 1:** (a) Hematoxylin and eosin image of the transverse section of muscle showing eosinophilic globular sub-sarcolemmal necklace like inclusions occupying >1/3rd of the circumference of muscle fiber. (b) Modified Gomori Trichrome stain: The globules are reddish and are better highlighted. (c and d) Electron microscopic image of the transversely cut muscle fibre confirms the electron dense material to be material restricted to the Z-band

HMERF is an adult-onset disease (with the age of occurrence being 30–50 years) and presents as distal lower limb weakness. Our case is unique in that the patient presented with proximal limb weakness mimicking an LGMD.[4] HMERF is caused by exon 343 mutation in the A-Band region in the titin (*TTN*) gene, which codes for the biggest protein known so far.[5] The entity is characterized by abnormalities in the myofibril alignment and presence of cytoplasmic bodies, and is therefore, classified pathologically as myofibrillar myopathy.[1] Current literature states that necklace CBs have a high specificity of 99% and a sensitivity of 82% for the diagnosis of HMERF, as shown by the largest study on this entity published so far.[1] It has been demonstrated that HMERF have selective involvement of semitendinosus and peroneus longus muscles on MRI. Sometimes, they can have atypical presentations and can be confused with LGMDs.[2]

The necklace CB is a useful light microscopic diagnostic marker for HMERF. In atypical clinical presentations, the typical muscle biopsy features are diagnostic of HMERF and are especially helpful in the settings where gene mutation facilities are not always available.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.