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NONAKA MYOPATHY

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INTRODUCTION

GNE myopathy/ hereditary inclusion body myopathy (HIBM)/ Nonaka myopathy, is a rare autosomal recessive muscle disease characterized by progressive skeletal muscle atrophy. It has an estimated prevalence of 1 to 9:1,000,000.
GNE myopathy is caused by mutations in the GNE gene which encodes for UDP-N-acetylglucosamine (GlcNAc) 2-epimerase/ N-acetylmannosamine (ManNAc) kinase, the bifunctional and rate-limiting enzyme in biosynthesis of sialic acid and a regulator of cell surface sialylation. GNE myopathy was initially reported by Nonaka et al. in Japan and Argov and Yarom in Israel. The differential diagnosis of GNE myopathy should be considered in young adults presenting with bilateral foot drop.

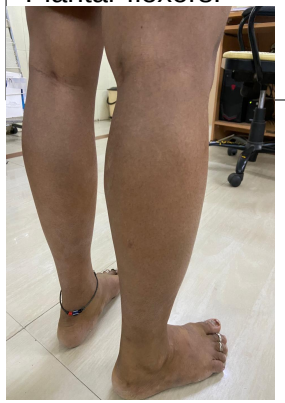
AIMS / OBJECTIVES

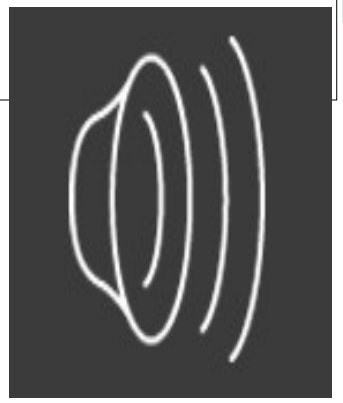
This case report aims to highlight late onset distal myopathies which can be mistaken for neuropathy if not examined systematically.

Gene[4] (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification[5]
GNE (-) (ENST00000642385.2)	Exon 11	c.1892C>T (p.Ala631Val)	Homozygous	Nonaka myopathy (OMIM#605820)	Autosomal recessive	Pathogenic ((PS3,PS4,PP3))

MATERIALS / METHODS

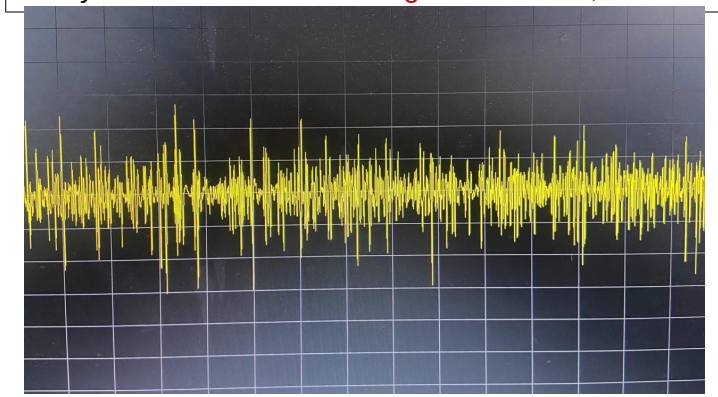
43-year lady, 7th in birth order, born out of 3rd degree consanguineous marriage, achieved developmental milestones according to age, Farmer by occupation who stopped working from past 6 years presented with Chronic progressive asymmetrical (left followed by right, left more than right, distal more than proximal) paraparesis from 10 years. No complaints of weakness in upper limbs. No cranial nerve or sensory or cerebellar or bladder symptoms. No history of trauma. History of myalgias, no cramps. No diurnal variation of symptoms. No other significant history. No similar complaints in the family. On examination calf hypertrophy present. Power-distal more than proximal weakness. Bilateral foot drop. Left more than right. Hip extension weaker than flexion, adduction weaker than abduction. Reflexes are normal. Plantar flexors.

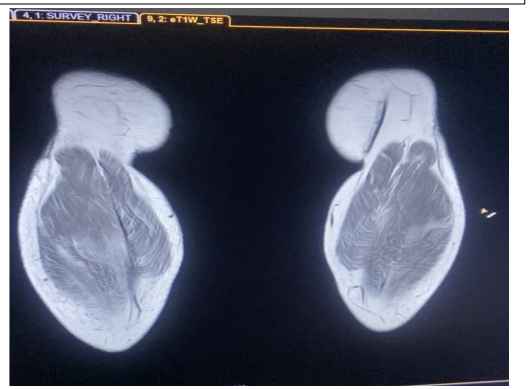




RESULTS & DISCUSSION

Routine blood Investigations are normal. Serum CPK is 24U/L, normal. NCS showed mild demyelinating neuropathy. CSF analysis is normal. 2D Echo is normal. EMG showed myopathic pattern. MRI spine showed mild disc bulge at L3/L4, l4/L5 with adequate spinal canal and neural foramen. MRI of bilateral calf muscles showed diffuse fatty infiltration involving intramuscular planes of both legs suggestive of atrophy. With the above findings we considered a differential diagnosis of distal myopathy as a first possibility and sent for genetic analysis which showed GNE gene mutation, confirming diagnosis of Nonaka myopathy.





CONCLUSION

Discussion: The typical presentation is bilateral foot drop caused by weakness of the tibialis anterior muscles in early adulthood. The disease slowly progresses over the next decades to involve all skeletal muscles, with relative sparing of the quadriceps until late stages. The upper extremities are affected 10 years later and do not follow the distal to proximal progression seen in the lower extremities. The disease does not affect swallowing or facial muscles, neck muscles can be involved at advanced stages. Serum CPK levels may be mildly elevated or within the normal range. Muscle biopsies of affected muscles show variation in muscle fiber size, atrophic fibers, characteristic rimmed vacuoles, and typically lack of inflammation. Sialylation increasing therapies like ManNAc and sialic acid, and highly sialylated glycoproteins, such as siallylactose and intravenous immunoglobulin (IVIG)can be tried.