A Case Of Hoarseness, Dysphagia And Weakness In Twin

Doha Ayish MD, Thy Nguyen MD, Aziz Shaibani M.D

Department Of Neurology

University Of Texas Health Science Center At Houston

McGovern Medical School

Introduction

Desmin-related myofibrillar myopathy is a rare condition that primarily affects skeletal muscles. Phenotypes include distal weakness, distal and proximal weakness, scapuloperoneal weakness and significant respiratory involvement. So far, less than 200 cases have been identified. Inheritance can be autosomal dominant, autosomal recessive or sporadic, due to de novo mutations.. Only rare cases of desmin myopathy associated with hoarseness have been reported in literature. Our case revisits the differential diagnosis of neuromuscular disorders presenting with dysphonia.

Objective

To report a rare case of desmin related myofibrillar myopathy associated with hoarseness and dysphagia.

Case Summary

An 80 year old Caucasian male presents with a 20 years history of slowly progressive, bilateral, distal legs weakness. His wife started to notice his feet “slapping on the floor” when he walked. He subsequently had trouble arising from a chair. He also recounted 12 years of dysphagia and progressive hoarse voice. Both the patient’s twin and older brothers had similar symptoms. They passed away from congestive heart failure and aspiration pneumonia respectively. Physical exam was significant for hoarseness. Strength examination revealed symmetric, distal>proximal, anterior compartment predominant, lower extremity weakness.

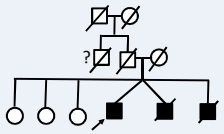

Fig.1. Patient’s family pedigree

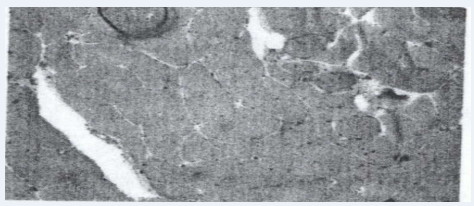

Fig.2. H&E stain showing variation of fiber size

Diagnostic Work Up

Creatine kinase (CK) levels were normal, 142. EMG showed evidence of irritable myopathy. His twin brother had a muscle biopsy which showed mild variation of fiber size, several rounded and split fibers, lobulated fibers, and increased internal nuclei suggesting a chronic myopathic process. Genetic studies were negative for myotilin, oculopharyngeal muscular dystrophy and matrin-3 gene mutations. Patient had a comprehensive muscular dystrophy/myopathy panel which revealed a heterozygous mutation in the desmin gene (pathogenic missense variant C. {1243C>T}). Pulmonary function tests showed moderately severe restrictive lung disease. Echocardiogram showed moderate left ventricular hypertrophy, normal ejection fraction and atrial enlargement. Modified barium swallow showed mild aspiration. Laryngoscopy revealed poor adduction of the cords bilaterally.

Gene	Position	Exon	Variant	Amino Acid Change	Zygosity	Inheritance
DES	Chr2: 220286281	6	c.[1243C>T]	p.Arg415Trp	HTZ	AD, AR

Fig.3. Patient’s CMDM panel results

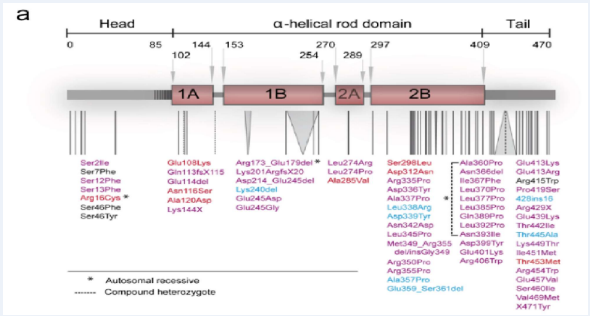

Fig.4. Different locations of desmin gene mutations(Hnia, K., Ramspacher, C., Vermot, J. et al. Cell Tissue Res (2015) 360: 591)

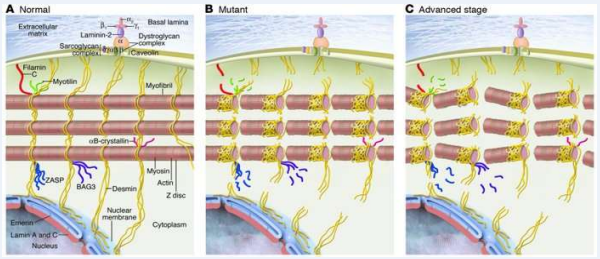

Fig.5. The pathophysiology of desminopathy

Conclusion

Desmin related myofibrillar is a rare genetic neuromuscular condition that involves both proximal and distal muscles. Our patient has a strong positive family history with similar symptoms that suggests a familial inheritance rather than sporadic inheritance. Also, dysphonia due to vocal cord palsy has been reported in vocal cord and pharyngeal weakness with distal myopathy. Only one similar case of desmin-related myofibrillar myopathy with hoarseness has been reported in literature(1). This occurrence expands the phenotype of this myofibrillar myopathy subgroup.

Neuromuscular differential diagnosis of hoarseness		
Nerve Related	**Muscle Related**	**Other**
Hereditary motor sensory neuropathy Distal HMN VII Scapuloperoneal SMA Neuromyotonia HSN + cough and GE reflux HNA Recurrent laryngeal lesion	Distal myopathy+ vocal cord and pharyngeal weakness Williams Beuren syndrome Myotonic dystrophy **Desmin- related myofibrillar myopathy**	Myasthenia Gravis SMA

Table.1. Neuromuscular differentia diagnosis of hoarseness

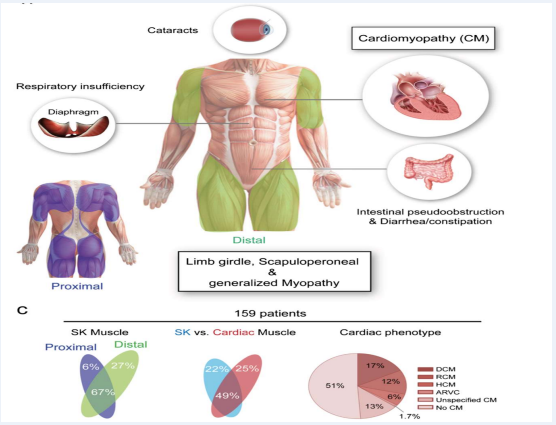

Fig.6. Phenotypic variations of desminopathies(Hnia, K., Ramspacher, C., Vermot, J. et al.Cell Tissue Res (2015) 360: 591).

1. Albertyn C, Maguire C, Murphy RP
PONMM Myofibrillar myopathy caused by a mutation in the desmin gene: expanding the phenotype
Journal of Neurology, Neurosurgery & Psychiatry 2010;81:e61