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SCIENTIFIC LETTER

SEPN1-related Rigid Spine Muscular Dystrophy

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To the Editor: A 7-y-old boy, born to non-consanguineous parents, presented with low-grade fever and cough for the past 3 d followed by shallow breathing efforts and decline in sensorium. He had delay in the attainment of motor milestones since early infancy. On examination, he had reduced muscle bulk, neck stiffness with restriction of neck flexion movements, rigid spine, proximal limb-girdle and intercostal weakness, hyperlaxity at metacarpophalangeal joints, bilateral shoulder and ankle contractures, with diminished muscle stretch reflexes. A clinical diagnosis of collagen VI associated muscular dystrophy was initially considered. However, in view of the rigid spine, cervico-axial weakness and progressive respiratory insufficiency, rigid spine muscular dystrophy was also considered. Investigations showed mildly elevated muscle specific creatine phosphokinase (215 U/L), normal 24 h-Holter electrocardiogram, and echocardiography and compensated respiratory acidosis ($PaCO_2$ between 45 to 106 mmHg) with metabolic alkalosis. Muscle biopsy was normal. Limited electromyography (biceps brachii), and nerve conduction study were normal. Targeted next-generation sequence analysis for muscular dystrophy genes revealed a previously unreported homozygous three base pair insertion c.826_827insCCT in exon 6 of the selenoprotein N1 (*SEPN1*) gene on chromosome 1 which resulted in an in-frame insertion of serine between codon 276 and 277 (p. Ala276_Cys277insSer) which was confirmed by Sanger sequencing and found damaging by polyphen analysis. Both parents were detected to be asymptomatic carriers of this variation using Sanger sequencing. Another unreported heterozygous missense variation in exon 1 of the *KBTBD13* gene (chr15:65369293; A > A/G) was also detected that resulted in the amino acid substitution of Glycine for Glutamic acid at codon 47 (p.E47G; ENST00000432196). However, this variation in heterozygous condition was also detected in his unaffected father. Hence this variation was unlikely not to be associated with the clinical condition of the index patient. No mutations were identified in *COL6A1*, *COL6A2* and *COL6A3* genes. He required prolonged mechanical ventilation through tracheostomy tube and supportive care. Currently, at 3 y follow-up, he is well and needs intermittent positive pressure home ventilation.

SEPN1-related myopathy encompasses a group of 4 clinically overlapping entities including rigid spine muscular dystrophy, severe classic multi-minicore myopathy, desmin-related myopathy with mallory body inclusions, and congenital fiber-type disproportion myopathy which are believed to be part of the same disease spectrum and are caused by homozygous or compound heterozygous variations in the *SEPN1* gene (OMIM#606210) on chromosome 1p36 [1]. *SEPN1* variations are characterized by distinct features such as early-onset spinal rigidity secondary to contractures of spinal extensors, progressive scoliosis, life-threatening respiratory failure, absence of significant cardiac involvement, joint contractures especially the ankle and elbow, indolent clinical course, independent ambulation and limited clinical and laboratory evidence of progressive muscle damage such as normal or mildly elevated creatine kinase and non-specific muscle biopsy [1, 2]. They need to be differentiated from other conditions associated with rigid spine like Emery-Dreifuss muscular dystrophy, Bethlem myopathy, Ullrich congenital muscular dystrophy, and Dysferlinopathy [3].

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The largest series of *SEPN1*-related myopathy by Scoto et al., reported 48% missense, 18% splice site and 28% small deletions/insertions mutations at *SEPN1* gene in 41 patients [1]. To conclude, the authors report a novel insertion mutation in a young boy with *SEPN1* related rigid spine muscular dystrophy.

Compliance with Ethical Standards

Conflict of Interest None.

References

1. Scoto M, Cirak S, Mein R, et al. SEPN1-related myopathies: clinical course in a large cohort of patients. Neurology. 2011;76:2073–8.
2. Moghadaszadeh B, Petit N, Jaillard C, et al. Mutations in SEPN1 cause congenital muscular dystrophy with spinal rigidity and restrictive respiratory syndrome. Nat Genet. 2001;29:17–8.
3. Sponholz S, von der Hagen M, Hahn G, et al. Selenoprotein N muscular dystrophy: differential diagnosis for early-onset limited mobility of the spine. J Child Neurol. 2006;21:316–20.