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SCIENTIFIC LETTER

A Novel Biallelic Splice Site Variant in the *SPARC* Gene Causing Severe Osteogenesis Imperfecta

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To the Editor: Osteogenesis Imperfecta (OI), characterized by decreased bone density leads to bone fragility and deformity [1]. We report a novel homozygous splice site variant in the *SPARC* gene from India and the sixth case in the world with a severe OI phenotype.

A three-year-old boy born to consanguineous parents, weighing 3.2 kg had no birth fractures or limb deformities but presented with severe motor delay. His first fracture occurred at 1.3 y in his right femur, followed by 15 more fractures in the lower limbs. Physical examination revealed normal dentition, mild blue sclera, and joint hyperlaxity (Wynn-Davies) score of 5/5. His weight was 10 kg, and his height was 81 cm.

Radiographs showed multiple vertebral compression fractures, thoracic kyphosis, and thoracolumbar scoliosis. His bone density was 0.237 g/cm^2 at the radius and 0.203 g/cm^2 at the lumbar spine on the DXA scan. His Quality of life (PedsQL^{TM}4.0) [2] assessment revealed a 68.75% physical functioning score, 40.38% psychosocial score, and 54.56% of health-related quality of life, which was poor.

A homozygous novel variant c.451+1G>A (NM_001309444.1) was identified in intron 6 of the *SPARC* gene, which was predicted as disease-causing by MutationTaster and class 5 splice variant causing exon skipping by VarSEAK tool. Segregation analysis showed parents and another sibling as heterozygous.

Delayed motor development with neuromuscular weakness, scoliosis and multiple compression fractures as common phenotypes in *SPARC* gene mutation have been reported recently and expand the phenotypic spectrum of similar neuromuscular patterns with a presumed diagnosis of myopathy [3, 4]. Our child's significant motor delay and hypotonia through grade 3 power are consistent with previous reports.

To conclude, muscular weakness with significant generalized hypotonia associated with low trauma fractures and early scoliosis seems to be an initial presentation in the previously published cases resulting in a significant motor delay and should alert the clinician to *SPARC* gene associated OI.

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Declarations

Conflict of Interest None.

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