Identification of novel DYNC2H1 mutations associated with short rib-polydactyly syndrome type III using next-generation panel sequencing


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ABSTRACT. Short rib-polydactyly syndrome type III (SRPS3) is a perinatal lethal skeletal disorder with polydactyly and multisystem organ abnormalities. While ultrasound of the fetus can detect skeletal abnormalities characteristic of SRPS3, the syndrome is often difficult to diagnose before birth. As SRPS3 is an autosomal recessive disorder, identification of the gene mutations involved could lead to the development of prenatal genetic testing as an accurate method of diagnosis. In this study, we describe genetic screening approaches to identify potential abnormalities associated with SRPS3. Karyotype analysis, array comparative genomic hybridization (aCGH), and next-generation panel sequencing were each performed on a fetus showing signs of the disorder, as well as on the mother and father. Karyotype and aCGH results revealed no abnormalities. However, next-generation panel sequencing identified novel mutations in the DYNC2H1 gene. The fetus was compound heterozygous for both a missense mutation c.8313A > T and a frameshift mutation c.10711_10714delTTTA in the
DYNC2H1 gene, which were inherited from the mother and father, respectively. These variants were further confirmed using Sanger sequencing and have not been previously reported. Our study indicates the utility of using next-generation panel sequencing in screening for novel disease-associated mutations.

**Key words:** Short rib-polydactyly syndrome type III; DYNC2H1 gene; Next-generation panel sequencing