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A novel nonsense mutation in the sedlin gene (*SEDL*) causes severe spondyloepiphyseal dysplasia tarda in a five-generation Chinese pedigree

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ABSTRACT. Spondyloepiphyseal dysplasia tarda (SEDT) is an X-linked recessive osteochondrodysplasia characterized by disproportionately short stature and degenerative joint disease. The objective of this study was to describe a novel nonsense mutation in the sedlin gene (*SEDL*) causing severe SEDT in a large Chinese pedigree. The clinical features of all affected individuals and female carriers were presented. Four affected males of the family were diagnosed with SEDT according to their clinical and radiological features. Direct DNA sequencing of *SEDL* was performed. Reverse-transcription polymerase chain reaction (RT-PCR) experiments of

total RNA from blood lymphocytes were performed to confirm the defect in *SEDL*. DNA sequencing revealed that all of the affected males carried a nonsense mutation (c.61G>T) in *SEDL* that has not been previously reported. The c.61G>T mutation resulted in a premature translation termination codon (GAG>TAG) at amino acid position 21 (p.E21*), and was predicted to initiate the degradation of mutant transcripts through the nonsense-mediated mRNA decay pathway. Two female carriers showed typical sequencing chromatograms of a heterozygote. Following genetic counseling, individual IV7 gave birth to a healthy baby. Therefore, identification of the novel nonsense mutation (c.61G>T) in the SEDT family enables carrier detection, genetic counseling, and prenatal diagnosis. The detailed genotype/phenotype descriptions contribute to the *SEDL* mutation spectrum. The continued identification of mutations in SEDT patients will greatly aid further elucidation of the role of the sedlin protein in normal bone growth.

Key words: Spondyloepiphyseal dysplasia tarda; *SEDL* gene; Nonsense mutation

