Identification of one novel homozygous mutation in the \textit{NPR2} gene in a patient from Taiwan with acromesomelic dysplasia Maroteaux type

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Acromesomelic dysplasia Maroteaux type (AMDM) is a rare autosomal recessive skeletal disorder characterized by disproportionately short stature, predominantly affecting the acromesomelic sections of the limbs. AMDM results from a mutation in the natriuretic peptide receptor 2 (\textit{NPR2}) gene, located on chromosome 9p13.3, and impairs skeletal growth.\(^\text{1}\) We report a 29-year-old woman with short stature and small hands and feet. Her height, 125.5 cm, was below the third percentile. She was born without complications after a full-term pregnancy from healthy, non-consanguineous Taiwanese parents of normal stature. She is the third child in the family; her elder siblings are of normal stature. Her intelligence and cognitive development are normal. Physical examination revealed noticeably short upper and lower extremities, brachydactyly, elbow extension limitation, macrodactyly of big toes, relatively small toes, and radial head dislocation (Fig. 1A). The skeletal changes were compatible with AMDM. Apparent mesomelic shortening was observed, with pronounced forearm bone shortening. The phalanges and metacarpals/metatarsals were short and dysplastic. The metatarsals and assorted phalanges of the big toes were relatively extended. The vertebral bodies were flattened and more pronounced posteriorly. The vertebrae showed posterior wedging as dorsal parts were shorter than the ventral parts. The hips displayed bilateral dysplastic acetabula, although the iliac wings and sciatic notches appeared normal (Fig. 1B).

To identify the possible \textit{NPR2} exonic mutations responsible for AMDM, coding exons and splice junction sites were amplified from genomic DNA and sequenced. One novel missense homozygous C-to-T mutation, causing a proline to serine substitution at codon 879 (p.P879S) was detected at nucleotide 2635. Her parents and brother are carriers, unlike her sister, and this mutation was not detected in a

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group of 100 healthy control subjects. An NPR2 gene mutation that lead to a loss-of-function is responsible for AMDM, but a gain-of-function leads to overgrowth. We confirmed this is the first case reported of AMDM in Taiwan.

Conflicts of interest

The authors declare no conflict of interest.

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References


Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.pedneo.2017.11.017.