

Radial ray defects, growth hormone deficiency, and a novel PTPN23 variant: An unresolved genetic association

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Abstract

Background: Congenital radial ray defects with severe growth failure may indicate an underlying genetic disorder and require integrated endocrine and genetic evaluation.

Case summary: An 11-year-old boy presented with severe short stature and poor weight gain. Bilateral forearm and hand deformities had been present since birth. He was born to non-consanguineous parents and had normal cognitive and scholastic development. His height was 115 cm (height SDS -5.09), with microcephaly, chubby cheeks, depressed nasal bridge, downward-slanting palpebral fissures, delayed and malaligned dentition, and bilateral radial ray defects. Both forearms were markedly shortened with bowing, flexion deformities, radial deviation of the hands, and oligodactyly. The right radius was absent with a hypoplastic thumb, while the left radius was hypoplastic with an absent thumb. Bone age was approximately 4 years. Serum IGF-1 was low for age (78 ng/mL), and clonidine stimulation demonstrated a markedly subnormal peak GH of 1.05 ng/mL, consistent with severe growth hormone deficiency. Brain magnetic resonance imaging revealed pituitary hypoplasia. Abdominal imaging showed an ectopic/low-lying right kidney. Karyotype was 46, XY, and chromosomal breakage studies were normal. Whole-exome sequencing identified a novel heterozygous PTPN23 variant, c.695G>A (p.Arg232Gln). Segregation analysis showed the same mutation in the clinically unaffected father and brother but not in the mother, making its pathogenic significance uncertain. Recombinant human growth hormone therapy was initiated with multidisciplinary follow-up. At 3-month follow-up, the patient showed a favorable initial response to recombinant human growth hormone therapy, with a 2 cm increase in height.

Conclusion: The coexistence of bilateral radial ray defects, severe growth hormone deficiency, pituitary hypoplasia, and renal ectopia represents an unusual syndromic phenotype requiring integrated endocrine and genetic evaluation. Whole-exome sequencing identified a novel heterozygous PTPN23 variant; however, its presence in clinically unaffected first-degree relatives makes a causal relationship uncertain. This case underscores the importance of cautious variant interpretation and segregation analysis and highlights the need for continued phenotypic and genetic evaluation of children with congenital limb abnormalities and severe growth failure. [*J Assoc Clin Endocrinol Diabetol Bangladesh*, 2026;5(Suppl 1): S63]

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