New point mutation in short stature homeobox (SHOX) gene leads to phenotype of Lery-Weill dyschondrosteosis

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Case presentation

We present an 11 year old girl of Moroccan descent with non-familiar short stature.

High suspicion of Short stature Homebox (SHOX)-related haploinsufficiency (Lery-Weill dyschondrosteosis) However: MLPA-analysis of the SHOX gene detected no deletions.

Sequence analysis of the SHOX gene was then requested and identified heterozygosity for:

a de novo c.836T>G p.(Leu279Arg) unclassified, but likely pathogenic variant in the SHOX gene

This confirmed the diagnosis of Lery-Weill dyschondrosteosis. Growth hormone therapy was initiated at the age of 13 years.

Background

Point mutations in SHOX account for 30% of the SHOX-related haploinsufficiency disorders¹

Standard analysis for point mutations after negative screening for deletions is not always common practice.

Recommendation

Because of the implications for growth hormone therapy, sequence analysis or mutation scanning of the SHOX gene should always be performed in children with a clinical phenotype of SHOX-related haploinsufficiency, when deletion/duplication analysis of the SHOX gene does not confirm the diagnosis, to detect possible (new) point mutations².

References

¹GenetReviews.org: SHOX-Related Haploinsufficiency Disorders, Last Update February 1, 2008