

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

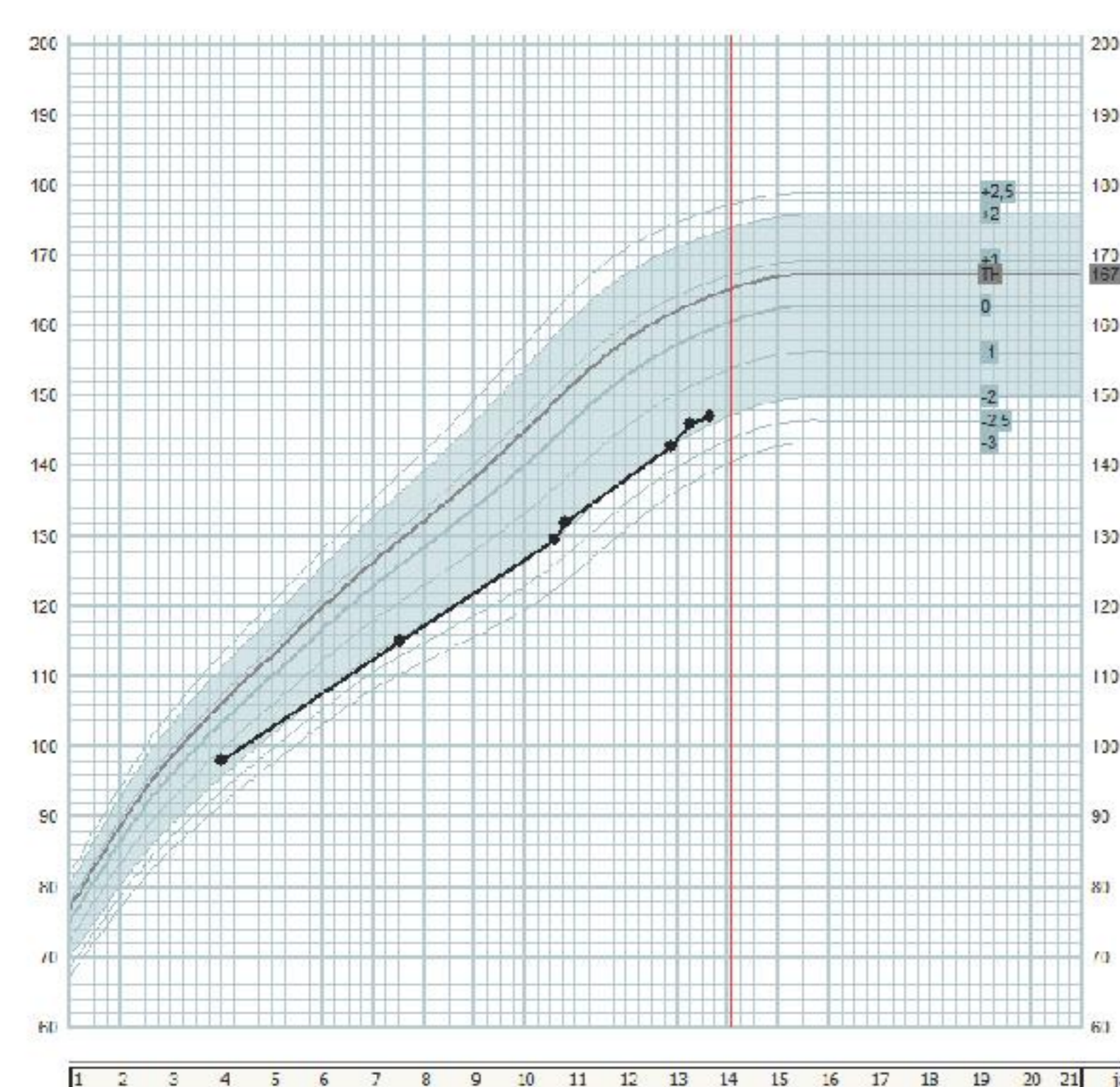
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Case presentation

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

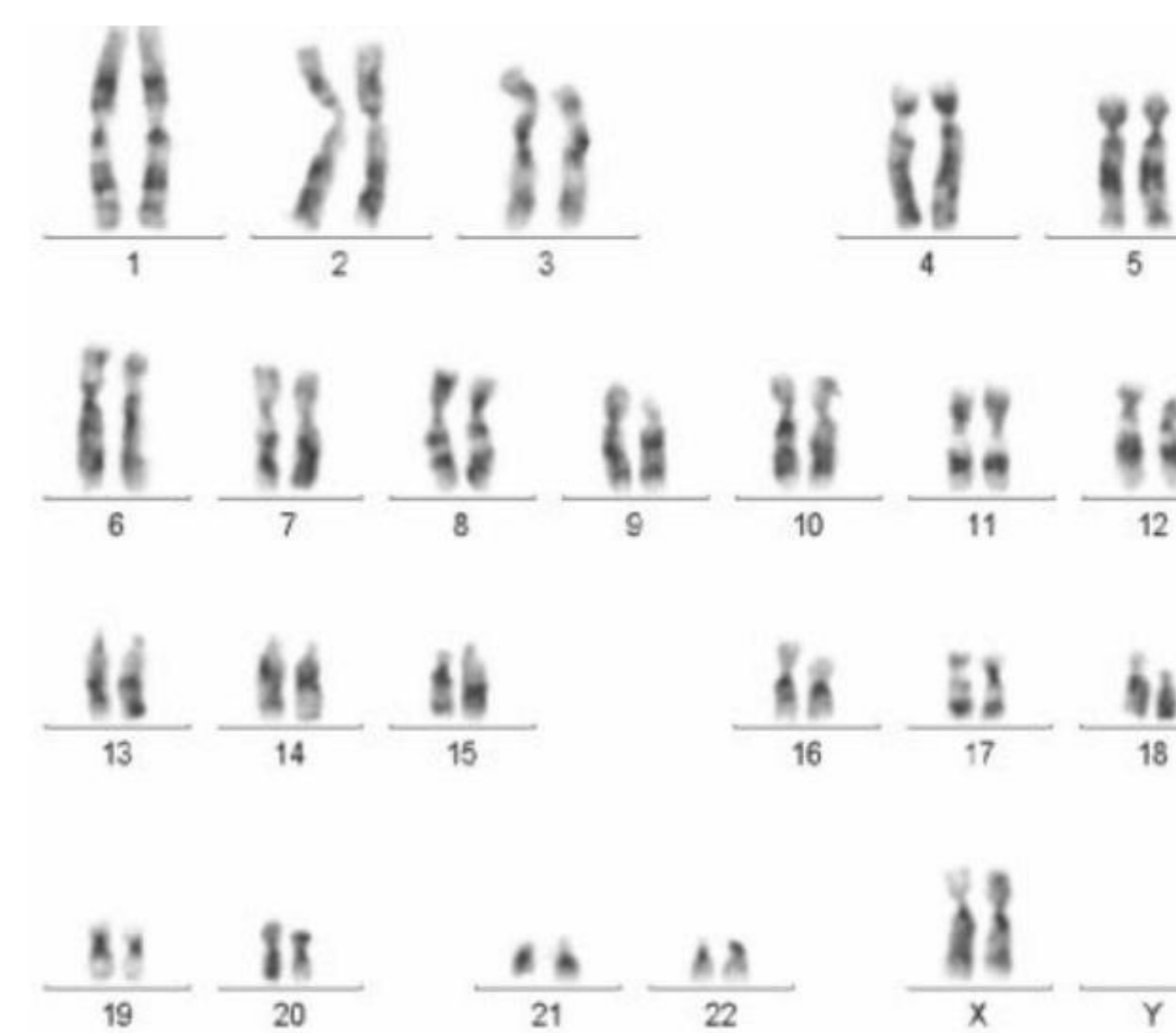


Clinical and radiological examination: Madelung deformity of the wrists.

Sitting height/height ratio was at + 2 SD



Karyotyping 46 XX



High suspicion of Short stature Homeobox (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

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

²Pediatr Endocrinol Rev. 2012 Aug;9(4):727-33 The SHOX gene and the short stature. Roundtable on diagnosis and treatment of short stature due to SHOX haploinsufficiency: how genetics, radiology and anthropometry can help the pediatrician in the diagnostic process Padova (April 20th, 2011). De Sanctis V(1), Tosetto I, Iughetti L, Antoniazzi F, Clementi M, Toffolutti T, Facchin P, Monti E, Pisanello L, Tonini G, Greggio NA