

Case report of SHOX gene haploinsufficiency diagnosed in early infancy

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OBJECTIVES

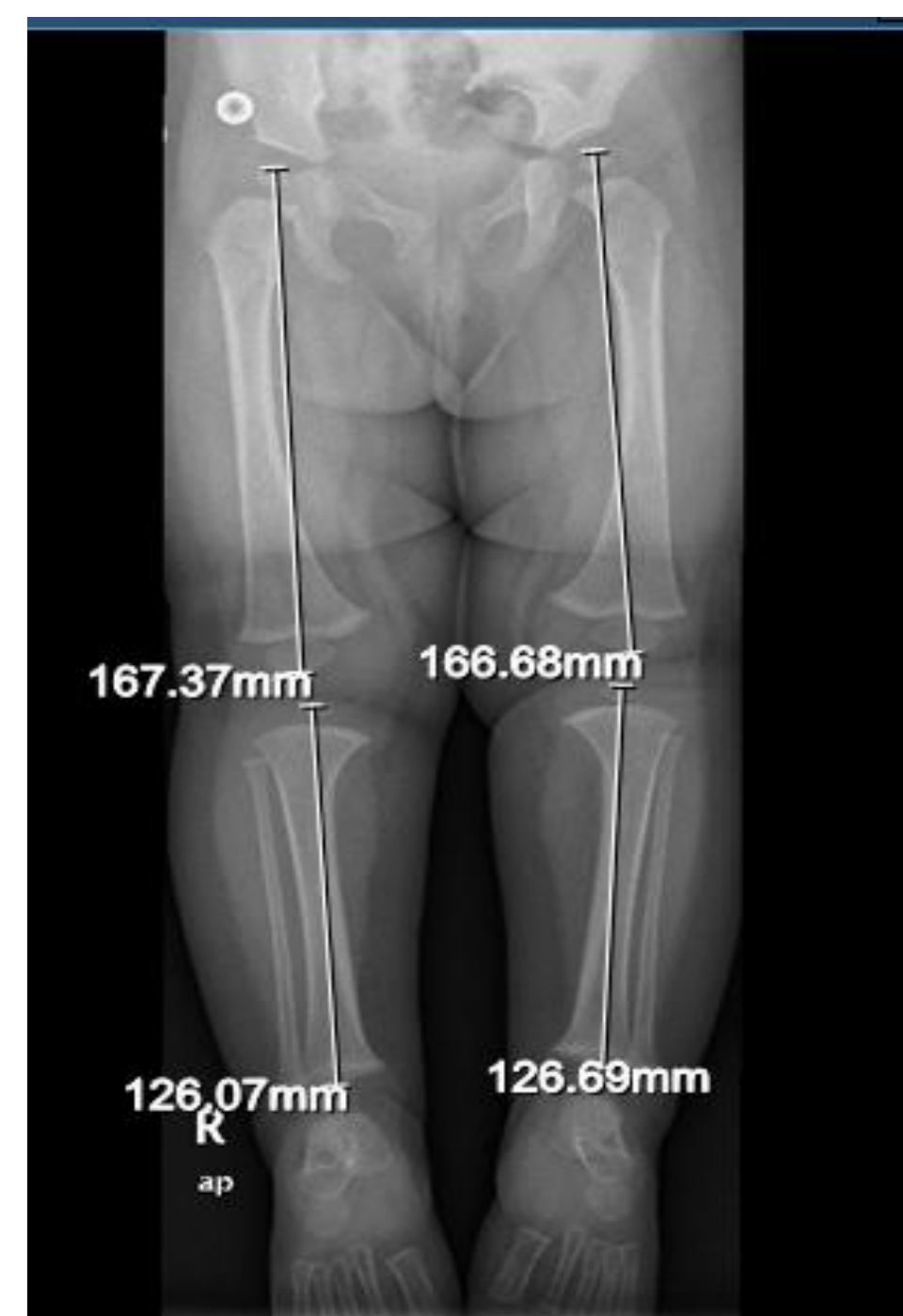
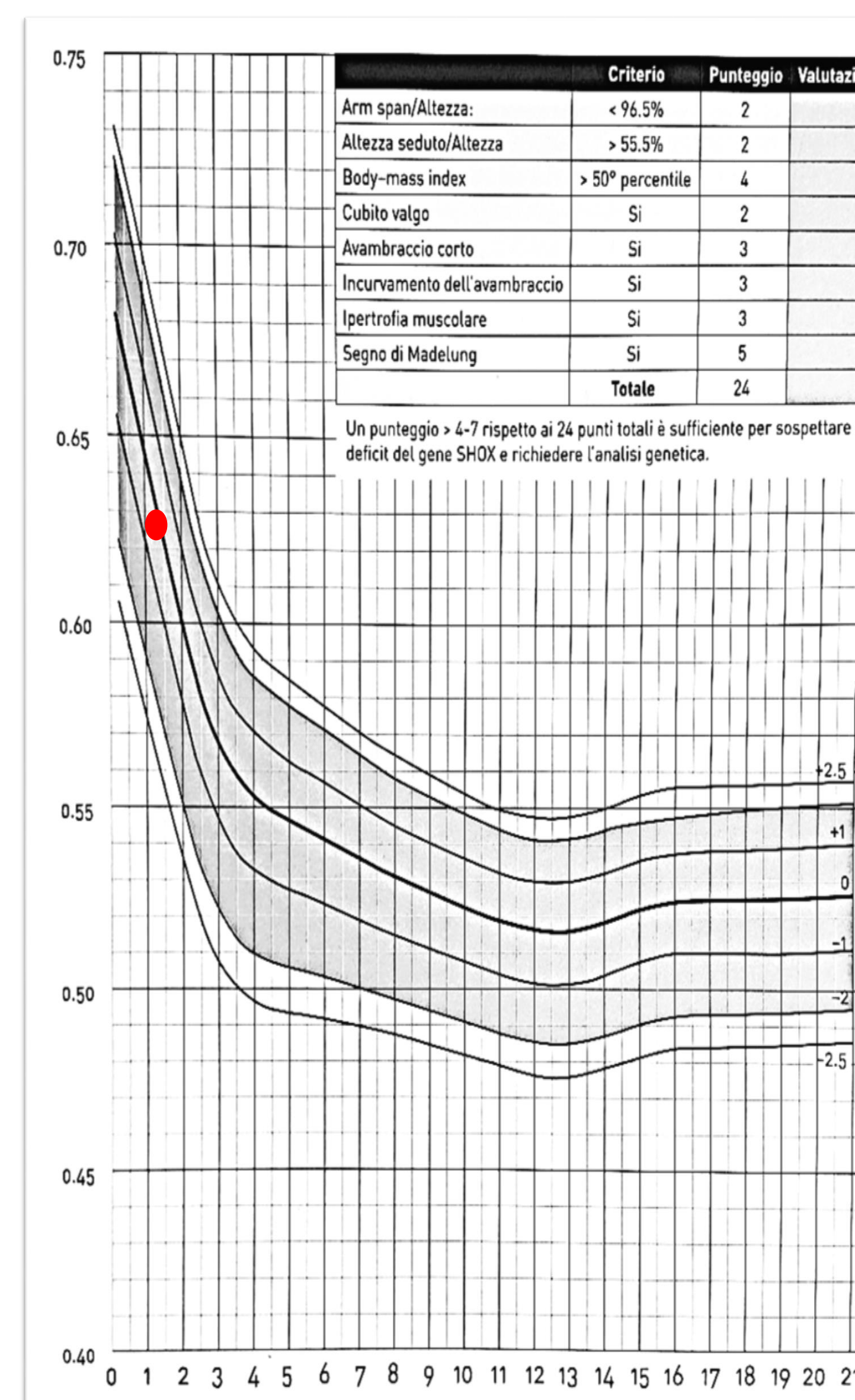
Describe clinical characteristics of two girls with an early diagnosis of Leri-Weill dyschondrosteosis, admitted to our hospital because of severe short stature.

METHODS

Clinical suspicious of SHOX-D was made using Shox scoring system (Rappold et al). Hand and wrist X-ray was performed. Mutation screening of SHOX and its regulatory regions was performed by MLPA and gene sequencing. Family analysis was undertaken.

RESULTS

The first 1.3 ys girl was born on term, SGA for weight (-1.9 SDS) and length (-1.77 SDS) with a family history of short stature in both parents (T-Ht -2.6 SDS). At first evaluation physical examination revealed rhizomelic body disproportion, no macrocephaly, H -3.96 SDS, Span/H ratio 90%, SH/H ratio 63%. Hypochondroplasia was ruled out by Rx vertebral column and limbs, that didn't reveal any radiological sign. Laboratory tests and karyotype resulted normal. SHOX gene MLPA in her and her father revealed c.463G>C mutation in heterozygosis, already described in X-chromosome gene database.



The second 1.2 ys girl was born on term, AGA. At 33 week of gestation prenatal finding of short femur (5° p). Physical examination revealed relative macrocephaly, prominent frontal bossing, depressed nasal root and rhizomelic aspect of upper limbs, L -2.11 SDS, no family history of short stature (T-Ht 0.18 SDS), SH/H ratio 50%, Span/H ratio 98%. Height velocity - 0.7 SDS- 2.1. Laboratory findings resulted normal, except for low IGF-1 level. Karyotype resulted normal. She undergone FGFR3 analysis which resulted normal. SHOX gene analysis showed c.728 dup in heterozygosis cause of frameshift de novo mutation. SHOX gene analysis (MLPA and Sequencing) resulted normal in both parents.

CONCLUSIONS

SHOX deficiency phenotype is variable and frequent non specific in early childhood. At this age SHOX-D diagnosis is a medical challenge, since typical mesomelia and radiological findings of LWS are still not apparent. Thus Rappold score system lose his predictive value. Different clinical criteria are still lacking, enhancing the role of familiarity of short stature as the only diagnostic tool for clinical suspicion at this age. Early genetic study could lead to early treatment with better response.

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