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ALTERATIONS OF SHOX AND ITS ENHANCERS AS A CAUSE OF SHORT STATURE: EVOLUTION OF OUR CASES

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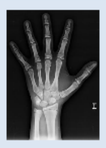
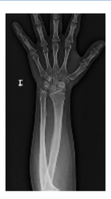
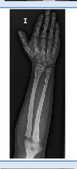
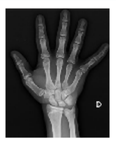
Background: Heterozygous alterations of **SHOX** and its **regulatory region PAR1** are identified in approximately **70% of Léri-Weill dyschondrosteosis** and **2–5% of idiopathic short stature** cases. Identification of a SHOX mutation enables GH treatment to be offered to the patient.

Objective: To evaluate the **clinical characteristics** of **seven patients** with SHOX haploinsufficiency suspected and their evolution.

Method: **Retrospective analysis** of patients with a genetic study of SHOX and the regulatory regions. Analysis of medical records.

Results: **N= 7** (3 female, 4 male). Mean age at **first visit 8.0 years** (4.9–11.7). **Referrals for short stature** (7).
-Personal history: SGA (2), preterm (1), obesity (1).
-Family history: short stature and alteration of body segments in parents (7).
-Physical exam: mesomelic limb shortening (7), Madelung deformity (2).
-Radiological study: pathological in all patients.
-GH deficiency in 3 patients (two GH functional tests <10 ng/ml).
-Genetic study: 3/7 presented with a heterozygous mutation, 1 stop mutation (c.79G>T (p.G27X)), two common 47.5 kb downstream enhancer deletions. **Cosegregation** of the mutation with the phenotype was confirmed when possible (**2 families**)

Gender & Age First Visit	Age at Genetic Diagn.	Genetic Study	GH Secretion Study	Target Height (SDs)	Height At First Visit	GH Treatment				Height Last Consultation
						Inicial Age	Inicial Height	Height After 1 Year	Increase (SDs & cm/year)	
 Female, 5.1 y	10.5 y	Common 47.5 kb downstream enhancer deletions. Cosegregation: father +	Normal	-1.7	93.6 cm **(-3.9 SDs)**	6.0 (SGA)	98.3cm **(-4.1 SDs)**	108.1cm **(-3.3 SDs)**	+0.8 9.8 cm/y	135.9 cm **(-1.8 SDs)**
 Male, 10.6 y	11.7 y	stop mutation (c.79G>T (p.G27X)	GH deficiency	-1.0	127.8 cm **(-2.5 SDs)**	11.9 (SGA)	133.6 cm **(-2.3 SDs)**	140.9 **(-1.7 SDs)**	+0.6 7.3 cm/y	150.7 cm **(-1.8 SDs)**
 Female, 11.7 y	13.4 y	Common 47.5 kb downstream enhancer deletions Cosegregation: father +	GH deficiency	-1.9	135.6 cm **(-2.3 SDs)**	12.4 (BA 13)	138.7 cm **(-2.1 SDs)**	142.7 c **(-2.0 SDs)**	+0.0 4.0 cm/y	144.6 cm **(-2.7 SDs)**
 Male, 4.9 y	9.0 y	SHOX: no alterations	Normal	-1.6	100.3 cm **(-2.5 SDs)**		Start of treatment: pending			124.5 cm **(-2.4 SDs)**
 Male, 11.0 y	17.4	SHOX: no alterations NPR2: c.1262C>T(p.Thr421Met)	Normal	-1.9	130.1 cm **(-1.9 SDs)**		Start of treatment: pending			155.5 cm **(-2.9 SDs)**
 Female, 5.8 y	9.0 y	SHOX: no alterations	GH deficiency	-2.1	101.0 cm **(-3.3 SDs)**	9.9	122.4 cm **(-2.5 SDs)**	not meet 1 year of treatment		123.9 cm **(-2.5 SDs)**
 Male, 7.2 y	14.4 y	SHOX: no alterations NPR2: c.1641_1643del (p.Val548del) Cosegregation: mother+	Normal	-1.9	108.4 cm **(-2.9 SDs)**	13.4	135.2 cm **(-3.0 SDs)**	144.0 cm **(-2.6 SDs)**	+0.4 8.8 cm/y	157.6 cm **(-3.0 SDs)**
Mean	**8.0 y**			**-1.7**	**-2.75 SDs**		**-2.8 SDs**	**-2.4 SDs**	**+0.45 SDs**	**-2.4 SDs**

Conclusion: The study of short stature should include a comprehensive **physical examination** to analyse **body segments** and **skeletal dysplasias**, requesting radiological study where appropriate. An **early genetic study** based on clinical suspicion (physical exam and family history) leads to **early treatment** with **better response.**

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