Should we review clinical criteria to diagnose SHOX gene mutations?

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The mutation of the SHOX gene is a cause of short stature by varying frequency depending on the published work, but estimated at around 3-10 % of cases of short stature. The main diagnostic scheme for starting genetic testing is the Rappold score, which requires clinical and radiological criteria, under which this form of short stature is framed as a disharmonious. In our clinical experience, however, we also looked for mutations in the SHOX gene in patients with signs of growth hormone deficiency as defined by the Italian legislature with the note of the Italian drug agency AIFA (Agenzia Italiana del Farmaco), such as a defiance of stature growth speed, significant short stature or insufficient pubertal growth spurt. In the last ten years, we have assessed 496 boys and girls with the above criteria. We diagnosed GH deficiency in 50 cases and mutations in the SHOX gene in 10 cases, two of which achieved the minimum score predicted by the Rappold scheme. There was always at least one parent with short stature. Growth hormone was given at the dose of 0.035-0.05 mg/kg/die until the final stature (two cases) was reached, always with good stature response and with a final height within the genetic target (see table) . In our opinion, we need to review the criteria for accessing genetic diagnostics for SHOX mutations, performing this survey in all cases that require investigations for suspected GH deficiency.

Pt.	**Sex**	**Age of diagnosis**	**Rappold score**	**H SDS at diagnosis**	**Bone Age at diagnosis**	**Target height cm**	**H SDS at last visit**	**Final height cm**	**Gene anomaly**
1	M	2.04	2	-2,9	1.5	169.6	-2		microdupl
2	M	14.9	2	-2,4	13	170,5	-2		microdupl
3	M	12.35	0	-1,7	10.5	173.2	-1,2		microdupl
4	F	5.7	2	-1,4	4.5	157.6	-0,7		ENHANCER
5	F	3.5	0	-0,8	2.5	159.5	-0,6		del
6	M	7.7	0	-1,5	5.5	169.8	-1,1		del
7	M	12.6	2	-1,7	11	175	-0,2	174.6	microdupl
8	F	12,8	4	-2,7	13	149,4	-2,6	147.9	del
9	M	8.7	4	-1	7.5	161.4	- 0.9		del
10	M	10.4	6	-1,7	7,5	154	-1,2		del

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