Shox Gene Pathologies In Children With Short Stature And Madelung Deformity

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INTRODUCTION

SHOX deficiency is the most common cause of monogenic short stature and results in short stature with a highly variable phenotype.

AIM

In this study, we aimed to detect SHOX gene pathologies in patients who applied to the pediatric endocrine outpatient clinic with short stature and who were found to have Madelung deformity on hand-wrist radiography, and to evaluate the clinical, laboratory features and responses to growth hormone (GH) treatment.

METHOD

- SHOX gene FISH analysis was performed in 21 of 23 cases who applied with short stature and who were found to have Madelung deformity on hand-wrist radiography, and microarray test was performed in 2 cases.
- For Madelung deformity; the criteria were triangularization of the distal radial epiphysis, lucency of the ulnar border of the distal radius, enlarged diaphysis of radius plus bowing of radius, shortening of the 4th and 5th metacarpals, pyramidalization of the carpal row, and convexity of distal radial metaphysis.
- SHOX gene sequence analysis and MLPA test are planned to be performed for cases where deletion was not found in the FISH analysis.

RESULTS

- Deletion in SHOX gene was found in 13 (56%) of 23 patients.
- Clinical characteristics of the patient are presented in Table 1.
- Nine of the 13 cases (69.2%) were female and 4 were male.
- Nine cases were prepubertal, 4 cases were pubertal.
- There were 2 cases with short stature and Madelung deformity in the mother.
- Body proportions of the cases are given in Table 2.
- There were scoliosis in 1 case, muscular hypertrophy in 3 cases, cubitus valgus in 3 cases, short neck in 3 cases, and mesomelia in 7 cases.
- GH treatment was given to nine patients. The characteristics of the patients who received treatment are given in Table 3.
- GH treatment onset mean age was 6.6 years (2.4-10.6), mean height SDS was -2.8.
- In patients who had received growth hormone treatment median first-year change-in-height SDS was + 0.53.
- Treatment of three patients was completed, and the mean duration of treatment was 24.6 months (12-58), and the mean final height was 143 cm (133.3-160).

Table 1. Clinical characteristics of patients

	Mean (± SD) n:13	(Minimum/Maximum)
Age, years	6,4 ± 4,3	2,4/14,3
Birth weight, gr	2671 ± 440	2000/3310
Height SDS	-2,97 ± 1,3	-4,88/-0,56
Weight SDS	-1,03 ± 1,9	-3,46/2,39
BMI SDS	1,06 ± 1,3	-0,8/3,69
Bone age-Chronological age	-0,7 ± 1,3	-2,5/2,4

Table 2. Body proportions of the cases

Arm span/height ratio, mean % (n:8)	93
Arm span/height ratio <%96,5, %	75
Sitting height/height ratio, mean % (n:7)	56
Sitting height/height ratio >%55,5, %	42

Table 3. The characteristics of the patients who received treatment

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Gender/Tanner stage	F/1	M/1	F/3	M/1	F/3	F/1	M/1	F/1	F/1
Age, years	5,3	7,1	10,6	9,2	9,1	7,4	3,6	2,4	5,1
Height SDS	-2,54	-3,31	-1,85	-2,81	-0,45	-2,38	-4,2	-4,74	-3,46
GV with treatment (cm/year)	6,9	9,2	5,4	7,2	10	10,2	8,5	10,6	8
First year gain in height SDS	-	0,9	-0,55	0,41	0,84	0,33	0,7	1,1	0,55
Final height (cm)/SDS			135,9 / -2,4	160 / -1,74		133,3 / -2,97			

CONCLUSIONS

In our study, we found SHOX gene pathology in 56% of cases with short stature and Madelung deformity. MLPA test and gene sequence analysis studies continue in cases with normal FISH analysis. There is a need for increased experience with early growth hormone therapy in SHOX deficiency.

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