

IS GROWTH HORMONE DEFICIENCY THE CAUSE OF SHORT STATURE IN FLOATING-HARBOR SYNDROME?

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Introduction:

Floating Harbor syndrome (FHS) is a dominant autosomal genetic disorder characterized by facial dysmorphism, delay in language development and short stature associated with delayed bone age. The genetic defect is a mutation in the SRCAP gene, one of the several proteins that help activate a gene called CREBBP which produce a protein that plays a key role in regulating cell growth and division and is important for normal development.

Currently there are about 100 cases reported worldwide. Although the short stature is one of the main features of the FHS, its etiology is poorly understood. A limited number of cases reported growth hormone deficiency as a cause of short stature in FHS and the evolution during treatment.

Therefore the aim of our case report is to present the evolution during somatropin treatment of a case with FHS and short stature due to growth hormone deficiency.

Case report

- Boy, 3.3 years at admission, urban environment.
- Admission grounds: severe short stature H=82cm (-4 DS), delayed bone age (1.5 years), particular phenotypic features for FHS, delay in language development.
- History: gestational age=39 weeks, birth weight=2800g, Birth length=51cm;
- Hypospadias and astigmatism;
- Frequent upper respiratory tract infections;

TSH= 2.84uIU/ml, freeT4=1.15ng/dl
Maximum GH during Clonidine stimulation test=8,77ng /mL, low IGF-I levels.
Celiac disease antibodies negative, normal karyotype.
Bone age=1,5 years.
Normal pituitary-hypothalamic MRI scan.

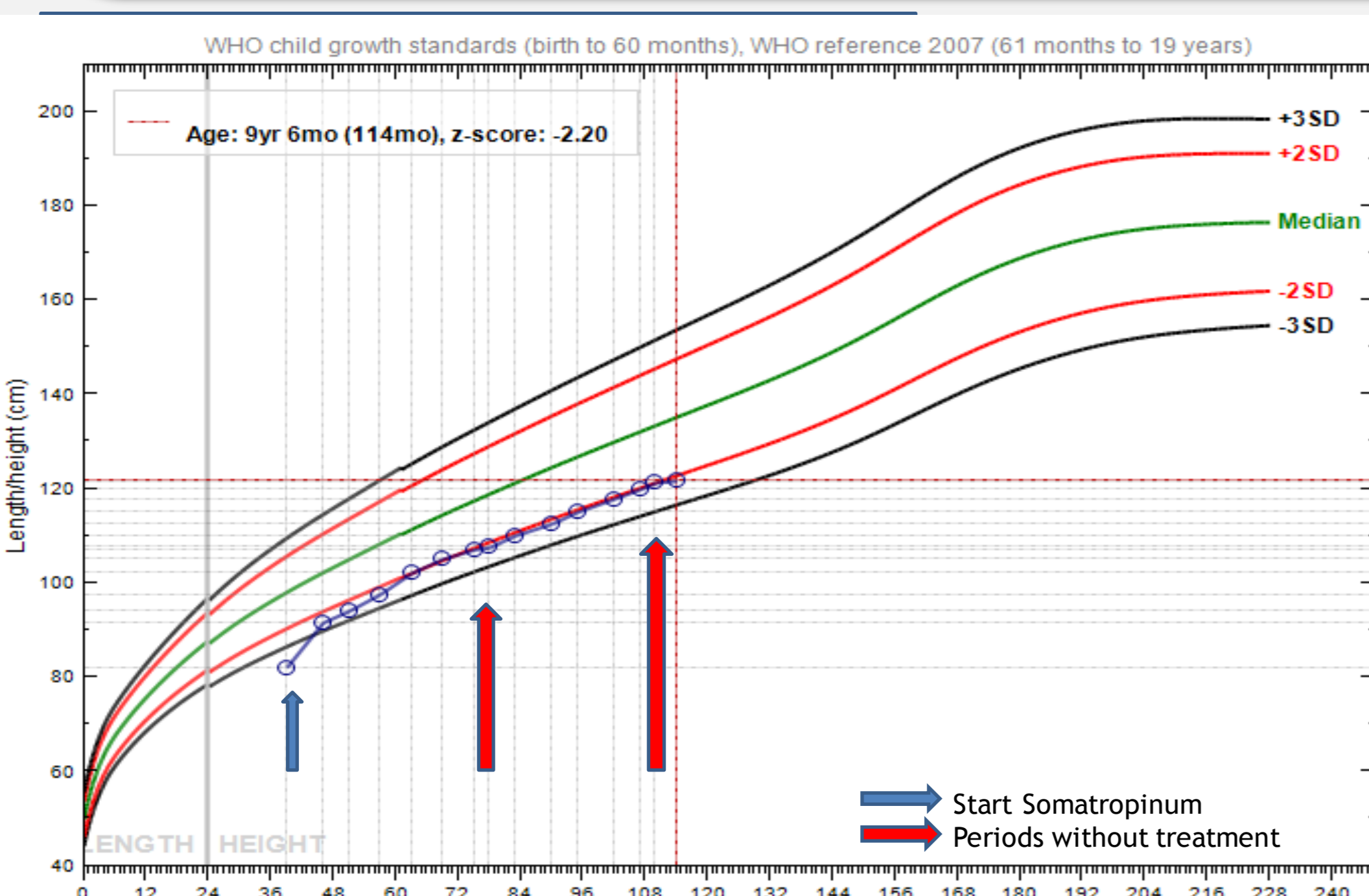
Genetic consultation:
Floating Harbor Syndrome?
↓
Genetic test
↓
mutations in the SRCAP gene

Diagnosis: Growth hormone deficiency. Floating Harbor Syndrome.

Start treatment with somatropin
0.035mcg/kg/day

initial response

increase of 1.7 SD during first 2.5 years of treatment



Growth history:

Start Somatropin
0.035 mg/kgc/day
low IGF1

Increase 1.7 SD

High IGF1
STOP
SOMATROPIN

REEVALUATION
Maximum GH during
Clonidine test 8.55ng/ml
START SOMATROPIN
0.03mcg/kg/day

High IGF 1
IGFBP3 at the upper limit
Bone age delay 3.5 years
STOP SOMATROPIN

Growth
chart:

| | | | | | | | | |
|-------|---------|---------|---------|---------|--------|---------|---------|---------|
| 82cm | 91.5cm | 94cm | 102cm | 105cm | 107cm | 107.5cm | 121.6cm | 121.8cm |
| -4 SD | -3.22SD | -3.13SD | -2.53SD | -2.36SD | -2.6SD | -2.6SD | -2.84SD | -2.9SD |

Time from
start of
treatment

Start 6 months 12 months 24 months 30 months 36 months 39 months 6 years 6,5 years

Discussion

Start treatment with GH 0,035mcg/zi.

The initial response was favorable with an increase of 1.7 SD during first 2.5 years. Subsequently the response to treatment decreased and SDS for height did not additionally improved although the IGF1 levels were increased and IGFBP3 level were at the upper limit of normal values.

However the attempt to discontinue the somatropin treatment was followed by a stationary height.

Conclusions:

- Floating Harbor syndrome is a rare cause of short stature that should be considered in a child with early onset short stature, facial dysmorphism, delay in language development and short stature associated with delayed bone age.
- This case suggests that growth hormone deficiency may be a cause of short stature in FHS patients. However the response to somatropin treatment and long-term evolution should be clarified by further studies.

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