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A Rare Cause of Short Stature : The Floating Harbor Syndrome. A Case Report.

Simon Kayemba-Kay's,[1,2] Odile Maillet[2] , Anne Heron[2]

1 . Pediatric Endocrinology Unit, Department of Pediatrics & Neontala Medicine ;

2. Unité de Recherche Clinique URC28, Centre Hospitalier Victor Jousselin,
28102 – Dreux, France skayembakays@ch-dreux.fr

Background: Short stature has several causes ranging from complex hormonal deficiencies mostly related to pituitary gland genetics, to idiopathic and environmental causes such as maternal smoking in pregnancy etc. Floating Harbor syndrome is a rare genetic disorder characterized by short stature, delayed bone age, mild to moderate mental retardation, retarded speech development and typical facial dysmorphic features. The syndrome is caused by heterozygous mutations in exon 34 of the Snf2-related CREBBP activator protein (SRCAP) gene encoding the core catalytic component of the multiprotein chromatin-remodeling SRCAP complex. The encoded ATPase is necessary for the incorporation of the histone variant H2A.Z into nucleosomes. It plays a key role in regulating cell growth and division, and is important for normal development.

Objective and hypotheses: Identify the cause of short stature in a child with dysmorphic features and delayed speech development.

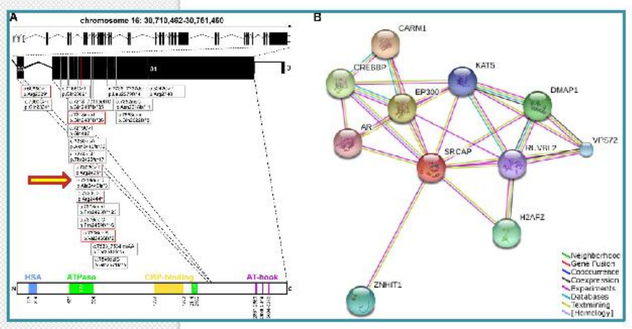
Method: We report the case of 53- month-old boy with severe short stature (-3.5 SDS), associated with micropenis, speech delay, hearing impairment and dysmorphic features compatible with Floating Harbor syndrome. He was term born with normal BW (3.220 kg), short BL (46 cm) and normal HC (36 cm). Family history was remarkable with two elder sisters aged 17 and 15 years who are short stature (145 cm). Endocrine screening revealed (peak GH:12.60 mUI/L; IGF-I:86 ng/mL; IGF-BP3:2640 ng/mL; normal urea and electrolytes, normal thyroid and liver function tests, LH:0.3 UI/L; FSH:0.5 UI/L; PRL 10 ng/mL; Cortisol:298 nmo/L; fasting blood sugar:4.47 mmol/L ; negative celiac screening, BA:3 years and normal head MRI.

Results: The SRCAP gene analysis by direct sequencing method was performed in all family members, but it revealed a previously described heterozygous c.7303C>T (p.arg2435*) mutation in the SRCAP gene (*De Novo*) only this patient. SHOX gene study was unremarkable. The child has been started on GH.

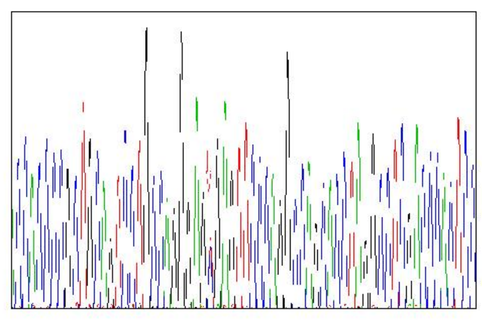
Where is the SRCAP gene located?

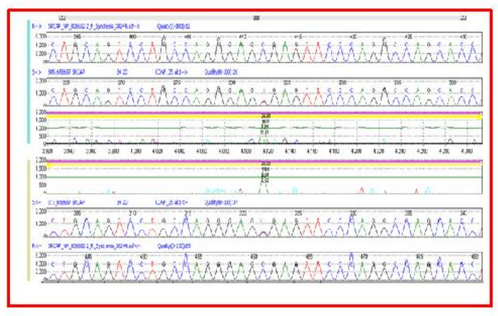
Cytogenetic Location: **16p11.2**

Molecular Location on chromosome 16: base pairs 30,699,140 to 30,740,128.

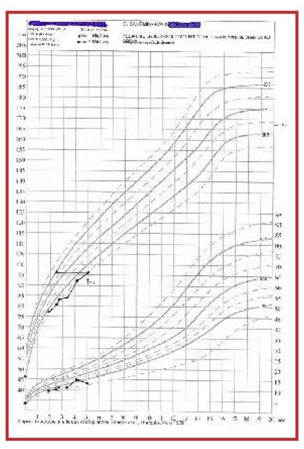


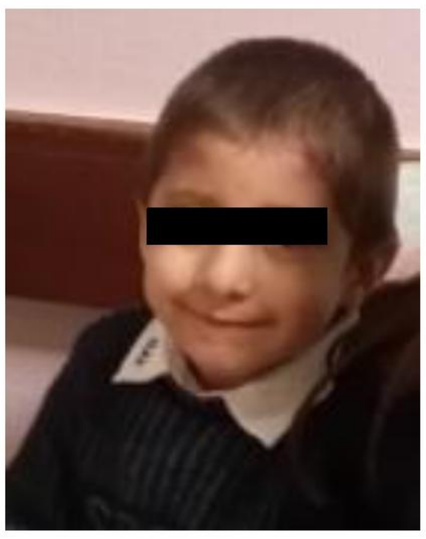
Schematic representation of the SRCAP gene and position of of known mutations.
(Seifert et al. BMC Medical Genetics 2014;15:127)

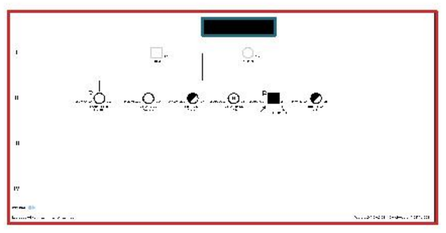




Heterozygous c.7303C>T (p.Arg2435*) mutation in the SRCAP gene.







Conclusion: Floating Harbor syndrome is rare, characteristic features are particular and should lead to its diagnosis.
GH therapy has proved beneficial in treated patients, regular screening for celiac disease is mandatory.

References:

Nikkel SM, Dauber A, De Munnik S, Connolly M, Hood RL et al.: The phenotype of floating-harbor syndrome: clinical characterization of 52 individuals with mutations in exon 34 of SRCAP. **Orphanet J Rare Dis 2013, 8(1):63.**

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Seifert W, Meinecke P, Kruger G et al. **BMC Medical Gentics 2014, 12:127**