Novel ACAN mutation in a SGA short stature without accelerated skeletal maturation

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Introduction

Heterozygous mutations in the ACAN, encoding for aggrecan or cartilage-specific proteoglycan protein, exhibit a broad phenotypic spectrum of non-syndromic short stature associated with advanced bone maturation, osteochondritis dissecans (OCD), early-onset osteoarthritis, and mild dysmorphic features including mid-facial hypoplasia, brachydactyly, broad great toes, and lumbar lordosis, with no genotype-phenotype correlations.

Some reports ACAN mutation is a relative common cause of familial severe short stature without advanced bone age.

Others presented that ACAN mutations in children born SGA with persistent short stature, advanced BA, and midface hypoplasia, joint problems, or broad great toes are highly prevalent.

We report a case of novel ACAN mutation in a severe short child born as small for gestational age without accelerated skeletal maturation, showing incomplete penetrance.

Methods

A 2 years 7 month-old girl born as small for gestational age presented with proportionate short stature (height 79.9cm, SDS -3.23).

She was born as small for gestational age, GA38+5 weeks, birth weight of 2.3 kg (SDS, -2.25), birth length of 44.6 cm (SDS, -2.44) and head circumference of 30.4cm (SDS -2.94).

She didn’t show dysmorphic features. She has no history of arthralgia or other joint problems and developmental delay.

Her father and mother’s height (SDS) are normal, 166 (-1.57), and 158 (-0.63) respectively. However, her grandfather and late grandmother’s height (SDS) are extremely short, 150 (-4.83) and 140cm (-4.73) respectively.

Bone age x-ray, chemical and genetic test were performed.

Results

Two unprimed GH stimulation tests with glucagon and clonidine administration showed a peak GH value of 10.7 ng/mL

BA was delayed about 1 year less than her chronologic age

Karyotype test showed normal 46, XX.

Her father denying joint problem showed the same mutation. A genetic test is underway for her short grandfather without joint problem.

Conclusions

A novel ACAN (c.1927T>C) mutation showed incomplete penetrance in this family.

Our findings extended the known clinical phenotypic spectrum of heterozygous ACAN mutations and suggest that this diagnosis should be considered in children without a family history of short stature and in children born as SGA without advanced bone age.

Bibliography