Genetic Investigation of Short Stature: A Case Report of Complex Constitutive Rearrangement Involving Chromosome 15

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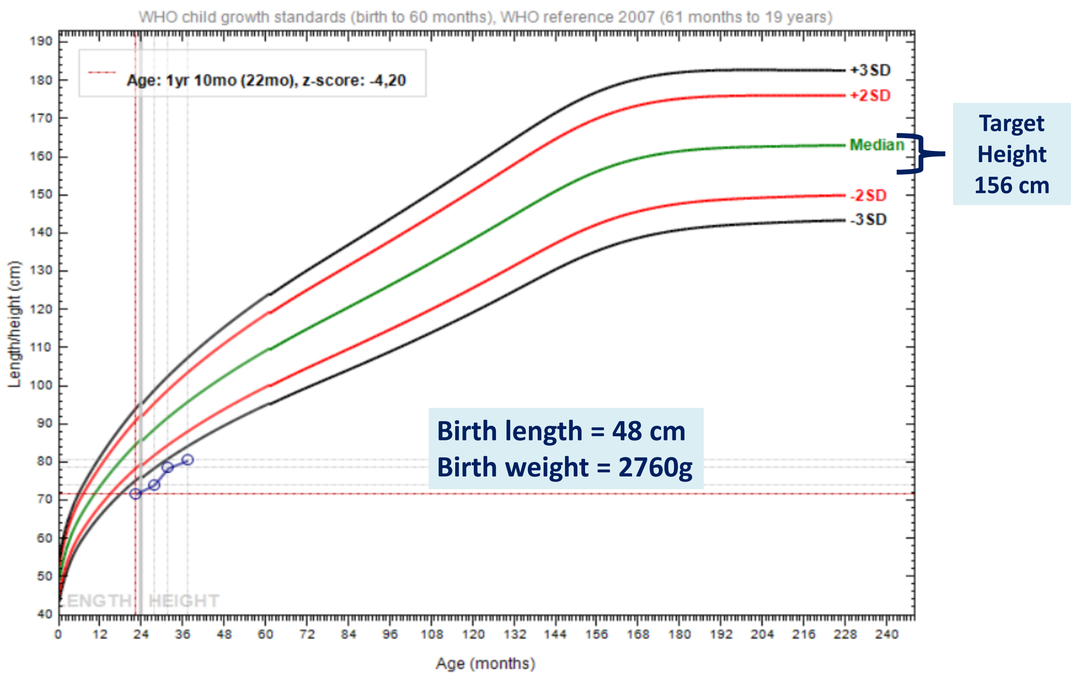
INTRODUCTION

- Growth is a complex process influenced by several genetic factors both pre and postnatal, in which 80% of the height variation is explained by genetic factors. Nevertheless, the standard medical evaluation of short stature (SS) relies upon physical examination and laboratory parameters and identifies a pathological cause of SS in 1–40% of individuals.
- Rearrangements affecting chromosome 15 are rare and affected patients show a variety of nonspecific features, including complex congenital malformations, growth deficiency, and developmental delay.

CASE REPORT

- LDG 1 year 11 months years old girl, first daughter of a non-consanguineous young couple presented to the Pediatric Endocrinology service with a short stature complaint.
- The height was 71 cm (−4,2 S.D.) weight 7000 g (−3,7 S.D.), cephalic perimeter 43,5 cm (−1,39SD).



- Physical examination
  - Brachydactyly
  - triangular face
  - prominent forehead
  - hypertelorism
  - bulbous nasal tip
  - long philtrum
  - thin upper lip
  - micrognathism

CASE REPORT

- G-banding karyotype analysis was performed, followed by FISH using probes 15q11-13 for Prader-Willi/Angelman and 15q26.3 for internal control.

46,XX,r(15)[64]

46,XX,r(15)dup(15)[16]

47,XX,+r(15)[5]

46,XX [9]

45,XX,-15[6].

- In r(15) was detected the absence of the 15q26.3 signal resulting in a genetic material loss, region that harbor IGF1R gene, which is responsible for the biological activity of IGF1.

CONCLUSIONS

- Ring chromosome results from breakage in both arms of a chromosome, with fusion of the points of fracture and loss of the distal fragments. In this context, a ring induces chromosomal instability, which in turn generates a diversity of cell lines harboring different chromosome configurations.
- In this case, we hypothesized that a 46,XX zygote acquired a r(15) leading to the instability subjacent to the other cell lines that had ring duplication, monosomy 15, trisomy 15, which included r(15), due to different approaches to restore balanced genome in the cells.
- Genetic diagnosis in cases of SS is important because it can end the diagnostic workup for the patient, it may alert the clinician to other medical comorbidities for which the patient is at risk, and it is extremely valuable for the genetic counselling.

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