Unexpected growth patterns in branchio-oto-renal syndrome

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Introduction

• Branchio-oto-renal (BOR) syndrome is a rare inheritable condition affecting the ears, 2nd branchial arch structures and the urinary system.
• Recognised features include hearing loss, structural defects of the ear, branchial defects, and a variety of renal malformations.
• Causative genetic variants include SIX1 and EYA1 which cumulatively account for ~49% of all cases of BOR syndrome.
• Short stature has not commonly been described in BOR syndrome, but is associated with oculo-facial-cervical syndrome and oculoauriculovertebral syndrome, which have demonstrated allelism with BOR due to mutations involving the EYA1 gene.
• We present data from two unrelated pedigrees, seven individuals in total, who exhibit phenotypes clinically suggestive of BOR syndrome who demonstrate a pattern of delayed and suboptimal growth.

Methods

Data was collected on 2 probands and their siblings attending Paediatric Endocrinology for concerns regarding growth.

This included:
• Auxology data
• Annual growth velocity
• Final height where available
• Bone age
• Growth factors
• Midparental height (MPH)

Discussion

• These two families show similar patterns:
  • low height velocity
  • falling below centiles in later childhood
  • failure to reach the predicted mid-parental height
• This is suggestive of suboptimal late childhood and pubertal growth.
• The aetiology for this remains unclear.
• Genetic analysis is in process but yield in BOR syndrome is low.
• Sonic Hedgehog [SHH] mutations have been implicated in mouse studies of pituitary development. EYA and SIX1 are known to function as transcriptional regulators in SHH signalling and the associated GLI family of zinc finger transcription factors. We speculate that a disruption in this pathway could lead to growth reduction in BOR.

Conclusions

• Growth surveillance is advocated in children with BOR. Normal growth in the early childhood years does not guarantee final height attainment.
• We are pursuing auxology data on other families with BOR to ascertain if they display a similar phenotype.
• ? Value of GH replacement despite meeting criteria for same

References


This poster was funded by the Children’s University Hospital, Temple Street research travel grant.