Hypothyroidism and Growth Hormone (GH) Deficiency, A Spotlight on De Novo Chromosomal 20p11.2 Deletion

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Disclosure-None of the authors have any potential conflict of interest

INTRODUCTION

There are few reports describing proximal deletions of chromosome 20p, making it difficult to predict the likely consequences of the deletion in this area. Two reports have described a mosaic maternally inherited 20p deletion. The first report has described a proximal 20p11.2 deletion associated with panhypopituitarism, craniofacial dysmorphism, a small phallus with a semi bifid scrotum, and bilateral widely separated first and second toes inherited from a normal mosaic carrier mother with the same deletion [1]. The second case has reported Alagille syndrome with a submicroscopic 20p deletion (including the JAG1 gene) [2]. The only report describing a *de novo* 20p11.22-p11.23 haploinsufficiency, have described a phenotype of autism, craniofacial dysmorphism, and Hirschsprung disease in a 9- years old boy [3]. Herein, we report the smallest described *de novo* proximal 20p11.2 deletion in a 4-years old boy with dysmorphic features, GH deficiency and central hypothyroidism associated with a complex chromosomal rearrangement involving the short arm of chromosome 20 and *FOXA2*. Two studies have reported an association between *FOXA2* mutation and hyperinsulinism, hypopituitarism, craniofacial and Endoderm-derived organ abnormalities [4, 5].

CASE REPORT

The patient presented at the age of 4 years with short stature (Figure 1) and was noted previously to have multiple dysmorphic features. Investigations confirmed growth hormone deficiency and central hypothyroidism (Table 1). The patient has poor weight gain and repeated episodes of abdominal pain, vomiting, and diarrhea. He is on levothyroxine and somatropin injection.

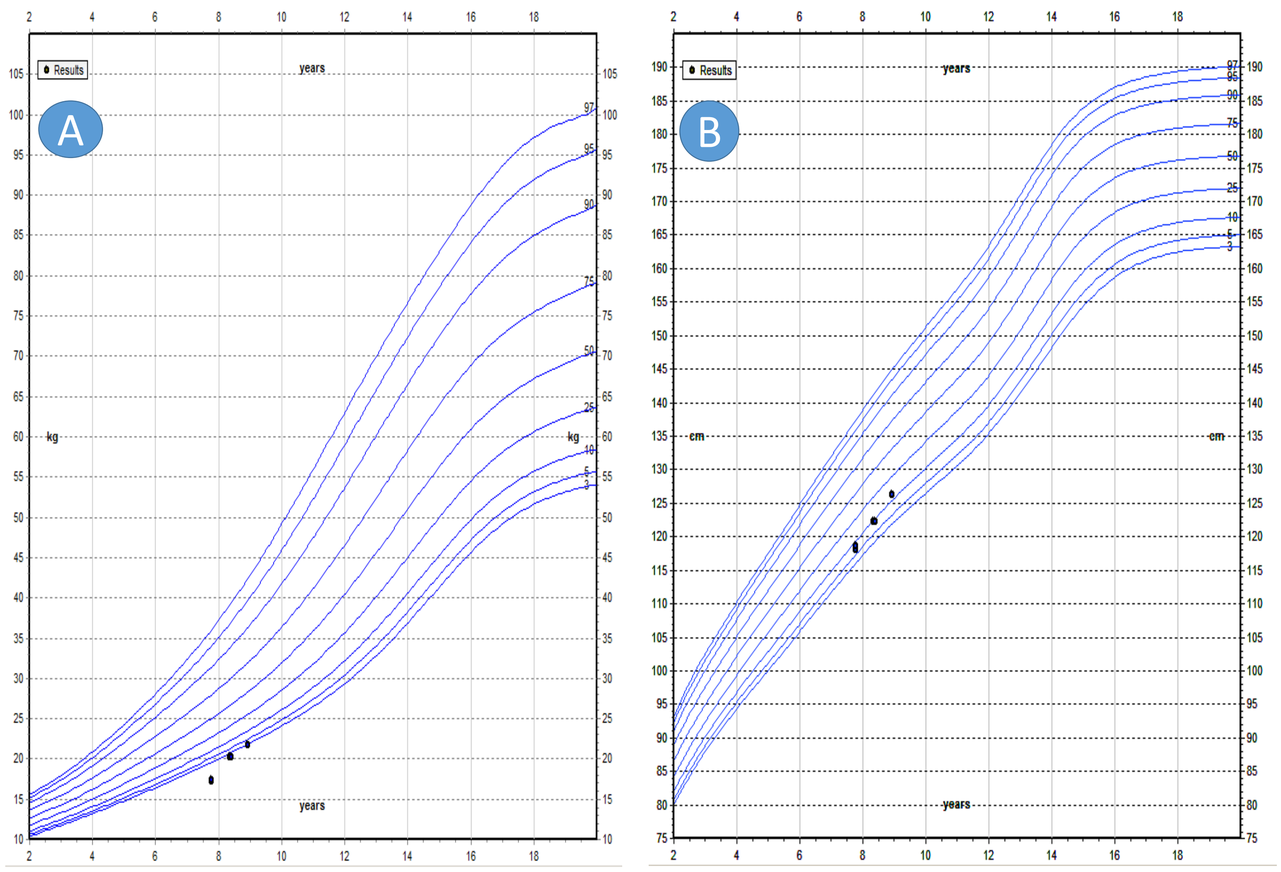

Figure 1. Growth chart- Illustration of growth abnormalities observed in the patient. Weight and height are below the 5th percentile.

A) Weight for age, 2-20 years, Boys
B) Stature for age, 2-20 years, Boys

METHODS

-G-banding chromosome analysis revealed a male chromosome complement with a reciprocal translocation between the short arm of chromosome 6 and 20 (karyotype: 46 XY, t (6; 20)(p11.2; p11.2)). The patient carries a deletion of around **969- kb** of the short arm of chromosome 20 within cytogenetic band 20p11. The parents had normal chromosomes. Microarray analysis was carried out using the Affymetrix CytoScan 750K platform. This array consists of 550,000 unique non-polymorphic probes and approximately 200,000 SNPs, mapped to GRCh37/hg19.

- Whole genome sequencing (WGS), Transcriptome and RNA-Sequencing done on an Illumina Hiseq sequencing platform.

RESULTS

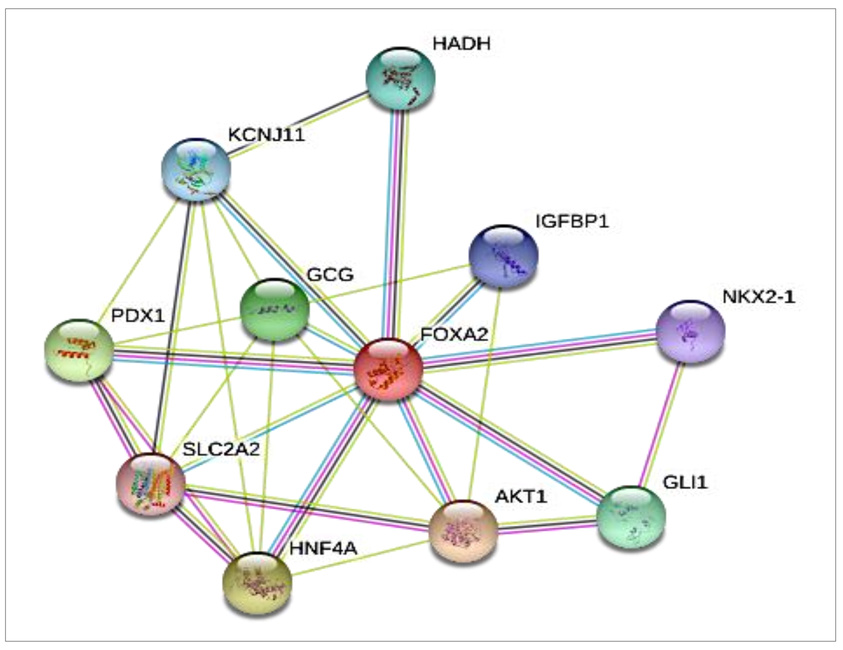

Figure 2. STRING network illustrating FOXA2 protein interaction network. Protein interaction map created using STRING database version 10.5 based on medium confidence events[6]

Table 1- Biochemical Investigations.

Endocrinology	
IGF1	46 ug/L (Low; reference 85-249)
IGFBP-3	1.1 mcg/mL (Low; reference 1.6-6.5)
Adrenocorticotropic hormone, P	41 pg/mL (Normal; 7.2-63)
General chemistry	
GGT	13 IU/L (High)
Glucose Fasting	4.5 mmol/L (Normal)
AST	40 IU/L (High)
ALT	31 IU/L (High)
Total bilirubin	9 mcmol/L (High)
Creatinine	54 mcmol/L (High)
BUN	8.7 mcmol/L (High)

CONCLUSION

Our patient carries a reciprocal translocation with a cytogenetic band 20p11.2, which is involved in the translocation and deletion of around 914-kb. The patient exhibited features related GH deficiency and hypothyroidism. Understanding the role of the deleted ***FOXA2*** gene might provide further insights into the regulation of GH and thyroid hormone secretion. Therefore, our patient expands the spectrum of phenotypes associated with proximal deletions of chromosome 20. Future direction will focus on the functional impact of the identified mutation.

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