Clinical follow-up of an Adrenal Hypoplasia Congenita patient with a novel mutation in NR0B1

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INTRODUCTION

Gene disturbances of NR0B1 (nuclear receptor subfamily 6, group B, member 1) mediated by the point (missense) mutation, Frameshift mutation, nonsense mutation, and/or gene deletions is directly associated with the adrenal hypoplasia congenita (AHC) disease and gonadotropin hypogonadotropic hypogonadism. NR0B1 (DAX-1) gene located on the short arm of the chromosome X (Xq21) classified as a dosage-sensitive sex reversal gene associated with the X-linked adrenal hypoplasia. Like the NR0B1 gene, the SF-1 (NR5A1) gene on X chromosome plays a significant role in the human adrenal, pituitary, and gonadal development. Since the first description of the AHC in 1959, numerous mutations have been recorded on this gene. As per the information recorded from the Human Gene Mutation Database (HGMD) database, till April 2018, there are 255 mutations (in total) have been identified with the NR0B1 gene. NR0B1 (DAX-1) gene encodes a nuclear receptor protein that plays a central role in the normal development of the gonadal and endocrine system. The NR0B1 protein expression markedly regulates the synthesis of steroid hormones and its associated organ development. Consequently, the NR0B1 gene-protein, and the steroidogenic factor-1 (SF-1) protein mediate the differentiation and development of the adrenal cortex and reproductive axis.

CASE PRESENTATION

A young male boy aged about 5.3 years and 9 months old was admitted in the Department of Endocrinology and Metabolism, Zhengzhou Children's Hospital in the year 2007 with these noticeable clinical symptoms: emerging skin hyperpigmentation, penis enlargement, enhanced growth hormone secretion, male pseudohermaphroditism, and pubertal signs. The patient was examined by the Department of Endocrinology and Metabolism for Adrenal Insufficiency (AHC). The testicular volume was 0.15 ml. The patient showed signs of hypocalcemia, hypokalemia, and hypogonadotropic hypogonadism. The patient showed a remarkable enlargement in the skin which can be explained early precocious puberty followed by HH. (2) NR0B1 inhibits the reproductive axis before puberty, and its loss-of-function to distribution which may be related to CPP. But this does not explain the spontaneous remission of precocious puberty. (3) There are a large number of chromophobe cells in the middle section of pituitary that can differentiate into cells such as gonadotropes and thyrotropes. This results in unknown if NR0B1 has any regulatory effect on the differentiation of these chromophobe cells. (4) There is a setting of NR0B1-expressing mutant NR0B1 exhibit an age-dependent decline in functions, which can explain early precocious puberty followed by HH. (5) NR0B1 inhibits the reproductive axis before puberty, and its loss-of-function to distribution which may be related to CPP. But this does not explain the spontaneous remission of precocious puberty. (6) There are a large number of chromophobe cells in the middle section of pituitary that can differentiate into cells such as gonadotropes and thyrotropes. This results in unknown if NR0B1 has any regulatory effect on the differentiation of these chromophobe cells. 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