11β- hydroxylase deficiency due to a novel compound heterozygous mutation and literature review

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Background

The incidence of 11β-hydroxylase deficiency is 1/100,000～1/200,000. However, according to the former report, only 15 cases were reported in China, less was reported about the gene mutation and none for the novel mutations.

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Objective

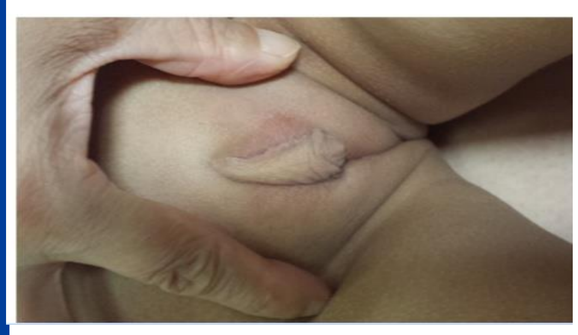
To analyze the clinical features and CYP11B1 gene mutations of a family with 11β-hydroxylase deficiency (11β-OHD) and literature review were also included.

Method

Physical examination and laboratory tests were done on a 4 years old girl and gene mutation screening was conducted in her and her parents.

Results

The adrenocorticotropic hormone (ACTH), 17-hydroxyprogesterone(17-OHP) were normal and testosterone, DHEA, estradiol, serum sodium levels increased while potassium and renin levels decreased. Bilateral adrenal enlarged according to CT scan. A novel compound heterozygous mutation R453Q/R374W was found in the patient and the mother was found to carry R374W allele and the father was found to carry R453Q allele. R453Q was a missense mutation previously reported to cause the disease. R374W was a novel missense mutation that was predicted to lead to decreased 11β-hydroxylase activity. The indicators of the patient recovered and keep normal under hydrocortisone. According to the literature review, the prevalence of the disease is likely to be lower in China than previously reported in other countries.



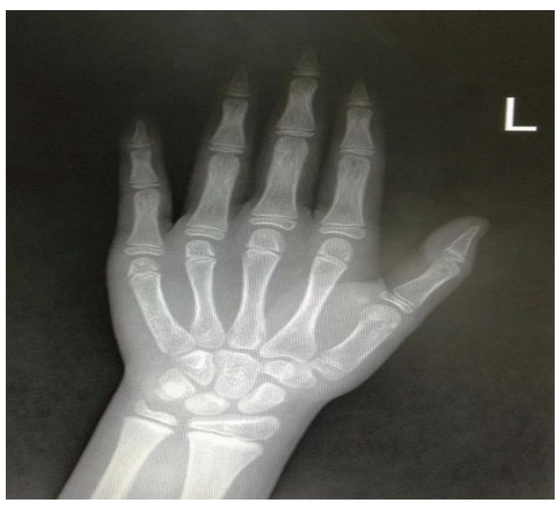


Fig.1：

Pigmentation of nipple and areola

Clitoral hypertrophy

Bone age advance

Conclusion

A novel compound heterozygous mutation was found to be a disease-causing mutation. Hydrocortisone is suggested other than dexamethasone in treating 11β-OHD in Child.

Acknowledgements

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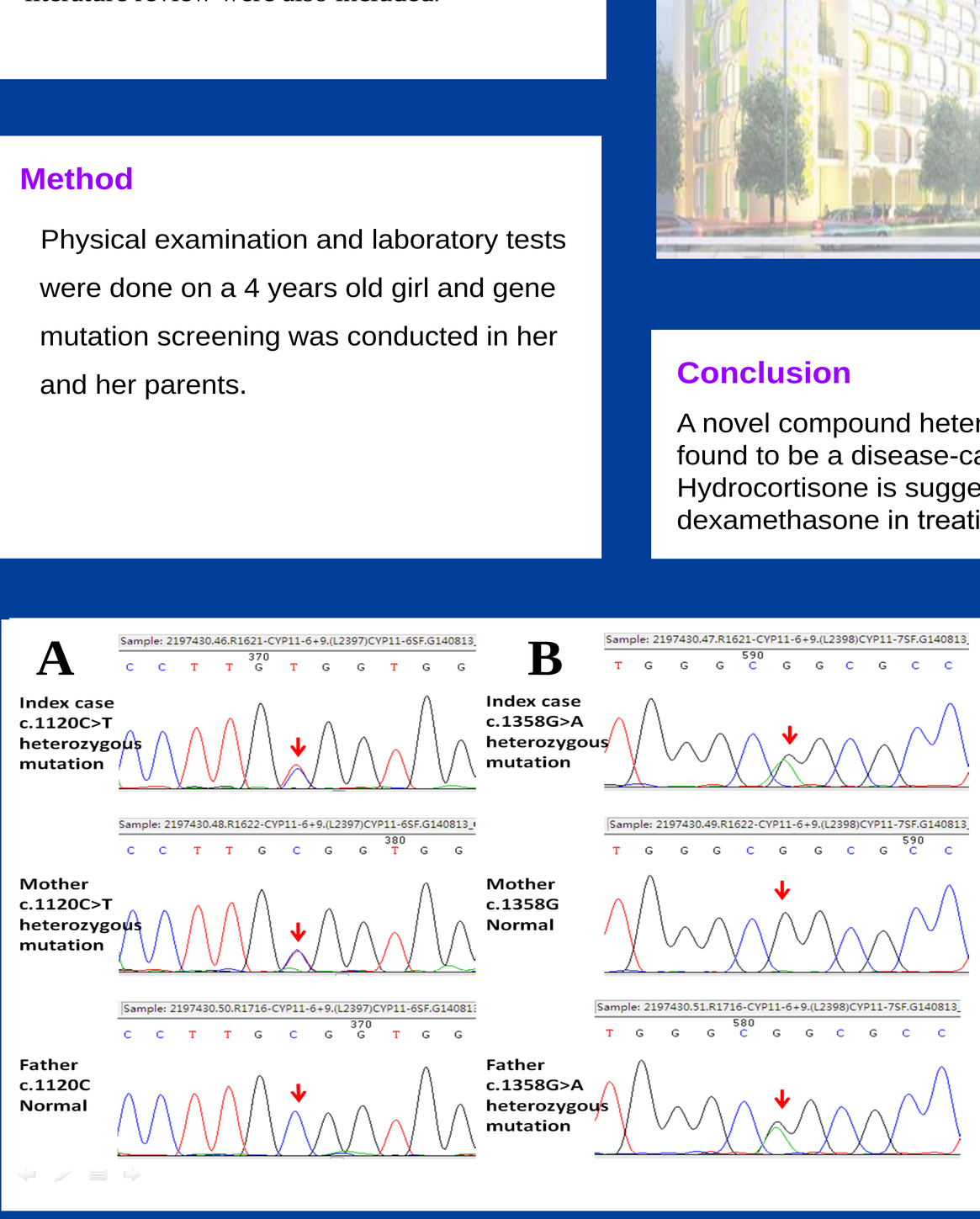

Fig.2 Mutation analysis by direct DNA sequencing

A*:The novel mutation from mother were localized in exon 6. The base change from C to T at position pb 1120 leads to the substitution from arginine to tryptophan (R374W)*

The mutation from father were localized in exon 8. The base change from C to G at position pb 1358 leads to the substitution from arginine to glutarnine (R453Q) The index case was heterozygou for both mutations

B: *Pedigree illustrating the segregation of the mutant alleles to the index patient. The arrow shows the proband.*

55ESPE 94--P2

Adrenal

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