

97 A FEMALE INFANT WITH 21-HYDROXYLASE DEFICIENCY WHO HAD THE VAGINAL ENLARGEMENT

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[Background] Female patients with 21-hydroxylase deficiency (21OHD) often have urogenital sinus and stenosis at the distal end of vagina. They can develop GnRH dependent precocious puberty triggered by rapid decrease of excessive adrenal androgens with glucocorticoid treatment. We present a 2-month-old female infant with 21OHD who had vaginal enlargement and genital bleeding.

[Case report] A Japanese female baby was born with clitoromegaly, single perineal orifice, and hyperpigmentation. She was diagnosed as having 21OHD by high level of 17-hydroxyprogesterone (17OHP). Hydrocortisone and fludrocortisone acetate was started. She was referred to our service on day 70. She had weight gain of 34g/day. The laboratory data were as follows ; Na 133.5mEq/l, K 5.3mEq/l, ACTH 16pg/ml, 17OHP 6.4ng/ml, ARC 4412.8pg/ml, aldosterone 127pg/ml, LH 3.0mIU/ml, FSH 5.7mIU/ml, E2 1071pg/ml, and testosterone 0.2ng/ml. On day 74, she had the first episode of genital bleeding. Ultrasound findings : Day 77 ; right ovary with a cyst (3.3cm in diameter) and an enlarged vagina (4.0×2.4cm) with fluid. Day 119 ; enlarged vagina (5.81×3.05×3.19cm) with stenosis at the distal end. The vagina and uterus were filled with fluid, which increased at urination. MRI findings : Day 84; enlarged vagina (4.5×2.7×2.2cm) with fluid (mixture of blood and urine).

[Discussion] We thought that the stenosis at the distal end of vagina caused limited discharge of mixture of blood and urine, leading to the vaginal enlargement. The blood was due to withdrawal bleeding by GnRH dependent precocious puberty, and the urine was due to reflux from urethra into vagina.

99 THE SIDE EFFECTS OF DEXAMETHASONE (DEXA) MAY PERSIST AFTER DECREASING THE DOSE OF DEXA IN PATIENTS WITH CYP21A2 DEFICIENCY

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Background: In 2000, Rivkees et al. reported that children with CYP21A2 deficiency (CYP21A2D) treated with dexamethasone (DEXA) could achieve normal growth. Their mean dose of DEXA was 0.27 mg/m²/day. We tried to treat 6 CYP21A2D patients with DEXA. In 2 of them, skin striae, moon face, and excess weight gain were observed and those symptoms persisted after the doses of DEXA were decreased.

Cases: The first case was a 14.5 year-old boy with CYP21A2D. He began to be treated with 0.59 mg/m²/day of DEXA. Eight months later, the dose of DEXA had been gradually decreased into 0.15 mg/m²/day because of the development of moon face and skin striae on the thighs, but his daily urinary pregnanetriol (PT) level was 0.2 mg/day and skin striae were still observed. The second case was a 16.1 year-old girl with CYP21A2D. She had been treated with 22.0 mg/m²/day of hydrocortisone (HC) and her daily urinary PT level was 17.5 mg/day. She began to be treated with 0.55 mg/m²/day of DEXA. Her daily urinary PT level decreased into 0.5 mg/day. Five months later, DEXA was substituted for HC because of the development of skin striae and weight gain by 6 kg. Four months after the return to HC, her daily urinary PT level remained 0.5 mg/day, though the daily dose of HC was the same as before.

Conclusion: These observations showed 1) the side effects of DEXA might persist after the dose of DEXA was decreased and 2) the control of a patient with CYP21A2D was improved after a transient suppression of HPA axis by relatively high dose of DEXA.

98 A male-raised 46,XX case of congenital adrenal hyperplasia due to 21 hydroxylase deficiency

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Introduction: Most 46,XX patients with 21 hydroxylase deficiency (21OHD), if appropriately diagnosed, are raised as girls to preserve endogenous sex hormone production and fertility. Some patients who were born with markedly masculinized genitalia were assigned to the male gender. When, in such case, the correct diagnosed was made in infancy or early childhood, most patients were reassigned to the female gender with appropriate parental consent. However, a few with particularly strong degree of genital masculinization was deliberately assigned to the male gender. In such case, gender reassignment around puberty or later is very difficult because of confusion of self-gender identity and risk of social rejection. We present here a male-raised 46,XX patient with 21OHD until adulthood. **Case:** The patient is now a 27 year-old with 46,XX karyotype. The patient had severe virilizing genitalia of Prader stage 5 at birth and was assigned to the male gender. The patient had repeated adrenal crisis from infancy and was diagnosed as having 21OHD based on hormonal examination at 1 year of age. The patient was decided to be reared as a male with parental consent. At 5 years of age, breast budding and macrohematuria, suspected to be menarche, appeared because of poor compliance of steroid therapy. The patient is now under treatment of leuprolerin acetate for suppression of endogenous estrogen production. The physician has discussed with parent about sex reassignment to the female gender of the patient in several times until now, however, the patient has been reared as a male and not served a notice about genuine sex and sex assignment. **Discussion:** Theoretically, the patient and families themselves participate in decision making based on adequate informed consent would be ideal for any gender reassignment. However, it seems to be difficult in Japanese culture environment at present. Therefore, it will be necessary to make a guideline that gender reassignment can be done without an increase risk of conflict with gender wish of the patient and families.

100 ANALYSIS OF CYP21 GENE IN STEROID 21-HYDROXYLASE DEFICIENCY IN HIROSHIMA PREFECTURE

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Aim: Congenital adrenal hyperplasia (CAH) is a frequent autosomal recessive disease and almost cases are steroid 21-hydroxylase deficiency (21OHD). We analysed the mutation of 21-hydroxylase gene (*CYP21*) in 22 patients (17 families) that are cared in the Hiroshima University Hospital and Hiroshima JR Hospital.

Method: DNA samples were extracted from peripheral lymphocyte in 22 CAH patients (17 families). The *CYP21* gene were analysed by the method of PCR by miss-match primer and restriction fragment length polymorphism, allele-specific PCR. We took informed consent for families based on the decision of Hiroshima University Hospital Ethical Committee. The analysis were performed in our laboratory, but the case whose gene we could not detect were also re-analyzed in Sapporo City Health Laboratory Center simultaneously.

Results: We detected the mutation of *CYP21* in 91%. The most frequent mutation was the I2g (23.5%), followed by deletion/conversion (23.5%), the R356W mutation (14.7%), the exon6 cluster mutation (8.8%), the I172N and exon3 Δ 8bp mutation (5.9%), the P30L and Q318X and L307+T (2.9%), and unknown was 8.8%. Almost phenotype are salt lost type (20 cases, 91%), other cases are asymptomatic mild type with mild elevation of 17- α hydroxyprogesterone. They had the P30L/e6cluster and Δ el/I172N.

Discussion: In this study the frequent *CYP21* mutation are del/conv, I2g, R356W, but the exon6 cluster mutation are relatively common and the I172N mutation are uncommon compared to other laboratory.

Conclusion: There are regional characteristics in *CYP21* genotype (e.g. the high frequency of del/conv mutation in Kochi prefecture).