ADRENOCENTRO-RENAL DISORDER WITH SEVERE GROWTH FAILURE — A NEW DISEASE

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Many of the congenital adrenal disorders are combined with disorders of sex differentiation and maturation. The combination of the congenital adrenal disorder and genital dysfunction is also known to occur in some conditions like Denny Drash Syndrome, however, the combination of all three is not reported so far. We present a case with new disease which involves congenital adrenal, genital, and renal disorders with severe growth retardation. The patient (social sex: female) was born to unrelated healthy parents. She was noticed to have ambiguous genitalia with single genitai (genitalia) unusual labial fusion, unilatetral clinitorix, unappendate clitoris, palpable glands. She developed salt-losing adrenal failure with respiratory distress on day 8. ACTH was elevated, and serum cortisol and 17-OHP were not detectable. Chromosomal analysis revealed to be 46,XY karyotype. Intra-abdominal organs showed undifferentiated mass by biopsy. Mullerian structure of uterus and ovotestis was unregulated. Adrenal function was altogether disrupted, and there was no response of adrenal steroids to ACTH test. Serum Cr and BUN were constantly elevated, and low Cr and delay of renal excretion were observed. Bilateral kidney sizes were apparently smaller than normal, and renal biopsy showed diffuse glomerulosclerosis. LHBH test resulted in peak LH of 5.1 mIU/ml and peak FSH of 129 mIU/ml. She also showed asperacta and retarded growth. Her DNA from PMN was obtained and analyzed for the known genes; no significant mutation was found in SFI, WT-1, DAX-1, STAR, or CYP17 genes. In conclusion, we suppose that this is a new combined disorder. The gene defect responsible for this condition might be within the promotor region of known factors, or might be completely new factors.

OVARIAN CYSTS IN GIRL WITH PREMATURE THELARCHE

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[Aim] We studied the frequency of ovarian cysts in girl with premature thelarche.
[Discussion] Ultrasound examination was performed. We defined ≥5mm in diameter as "ovary cyst". LH, FSH, and estradiol level were at the first visit.
[Results] Four of the 15 patients showed the ovarian cysts at the first visit in our clinic. Seven of the 15 patients showed the ovarian cysts after one year. Three patients showed bilateral ovarian cysts. The size of the ovarian cysts was 5--12 mm in diameter. No relationship was found between the breast development and the ovarian findings. These ovarian cysts showed to be small and to be large in clinical course.

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THE ROLE OF KALI GENE AND KAL2 GENE (FGFR1) IN KALLMANN SYNDROME: MUTATION ANALYSIS AND CLINICAL ASSESSMENT IN 35 PATIENTS WITH KALLMANN SYNDROME


[Kalumman syndrome (KS) is defined by the combination of hypogonadotropic hypogonadism (HH) and hypothyroidism. It has been reported that mutations of the KALI gene on Xp22.3 result in the X-linked form and heterogeneous mutations of KAL1 (FGFR1) cause autosomal dominant form. Here, we performed mutation analysis of the KAL1 and KAL2 genes in 35 patients with KS, and assessed clinical features in mutation positive patients.]
[Method] Eleven familial cases from six families and 24 sporadic cases with KS were studied. Sequence analysis was performed for all the 14 exons of the KAL1 gene and 2--18 coding exons of the KAL2 gene.

[Results] KALI mutations and clinical features: Nine types of mutations, including six novel mutations, were detected in 15 males (10 familial and five sporadic cases). Two males aged 11 and 13 years had normal and borderline otilary function, respectively, and seven males exhibited exclusively right-sided renal lesion. KAL2 mutations and clinical features: Two novel heterogeneous mutations were detected in one familial case (mother, brother, sister) and a male sporadic case. They had typical KS phenotype, and the mother and the male became fertile after gonadotropin therapy.

[Discussion] The results indicate that KALI mutations account for 86% of familial cases and 21% of sporadic cases, and that KAL2 mutations account for 14% of familial cases and 4% of sporadic cases. In addition, the identification of nonsense mutation of KAL2 gene is consistent with haploinsufficiency of KAL2 gene being responsible for KS. Clinical assessment implies that KALI mutations permit normal otilary function in exceptional cases and cause renal lesion in roughly half of patients, and that patients with KAL2 mutations may respond well to gonadotropin treatment.