P-11-6

RHIZOMELIC CHONDRODYSPLASIA PUNCTATA (RCDP) TYPE I IN 2 THAI INFANTS: FIRST REPORTED CASE

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Rhizomelic chondrodysplasia punctata (RCDP) Type I (OMIM 215100) is a rare autosomal recessive peroxisomal disorder characterized by the presence of stippled epiphyses, coronal vertebral clefting, dwarfing, joint contractures, rhizomelia, congenital cataracts, ichthyosis and severe mental retardation. Biochemically, RCDP patients have submormal levels of red cells plasmalogens and progressive accumulation of phytanic acid starting from normal at birth and increasing to levels more than 10 times normal by age 1 year. Gene locus is mapped at 6q22-q24. It is caused by mutations in the PEX7 gene, which encodes the peroxisomal type 2 targeting signal (PTS2) receptor (OMIM-VA McKusick).

We herein report 2 cases of RCDP, first reported cases from Thailand. **Case 1**: One year and 3 month old boy (born in 1993) with history of bilateral congenital cataracts, delayed development, elevated plasma very long chain fatty acid; phytanic acid level was 25 times higher than normal (Kennedy Krieger Institute). Contractures and shortening of the proximal limbs; stippled epiphyses were observed. Peroxisomal plasmalogen synthesis enzymes were deficient. **Case 2**: Four-month-old girl (born in 1993) with bilateral congenital cataracts, delayed development, contracture and shortening of the proximal limbs, stippled epiphyses. Phytanic acid was 3 times higher than normal (Kennedy Krieger Institute). Both patients died before 2 years of age. Enzyme assay and mutation analysis are not available in Thailand.

P-12-1

A WHOLE YOUNG ALuYa5a2 INSERTION MUTATION CAUSES MENKES DISEASE IN A JAPANESE BOY

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Menkes disease (MNK) is a multi-systemic lethal disorder of copper metabolism dominated by neurodegenerative symptoms and connective tissue disturbances. The disorder is inherited as an X-linked recessive trait and the responsible gene, *ATP7A*, is located on Xq13.3. MNK results from mutations in the *ATP7A* gene. To date, chromosome mutations including translocation, gross deletions and point mutations have been reported. We present the first patient with MNK causing by an alu insertion. A whole young AluYa5a2 element, which was 382-bp long, was identified within exon 9 of the *ATP7A* gene, and all of exon 9 was aberrantly skipped in the cDNA, predicting severely truncated proteins. Using an exonic splicing enhencer finder the Alu element created two new high-score exonic splicing enhancer sequences in mutant nearby the site of insertion. Exon 9 is necessary for the normal function of ATP7A protein, because it encodes the first and the second transmembrane domains. Here, we present the first report of an Alu element insertion mutation causing Menkes disease by an Alu element's interfering with splicing regulatory elements.

P-12-2

IDENTIFICATION OF NOVEL MUTATIONS OF THE *ATP7A* GENE AND PRENATAL DIAGNOSIS OF MENKES DISEASE BY MUTATION ANALYSIS

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Menkes disease is an X-linkedrecessively inherited disorder caused by the mutation of the *ATP7A* gene encoding copper-transporting P-type ATPase. Mutation analysis has been carried out in 5 unrelated Korean Menkes patients using cDNA from cultured skin fibroblasts or genomic DNA from peripheral leukocytes. They presented with depigmented wool-like hair, progressive neurologic deterioration, and hypotonia in infancy. Serum copper and ceruloplasmin levels were decreased. Brain magnetic resonance imaging revealed tortuous intracranial vessels. One patient with deletion of exon 8 and 9 of the *ATP7A* gene died at the age of 4 years. Three novel mutations have been identified from three different families; c.3511+1G>A (p.E1099_N1171delinsMfsX18), c.4005+5 G>A (p.V1268_R1335del), and c.1870_2172del (p.S624_Q724del). The rest of the two mutations (c.3352 G>A (p.G1118S), and c.1933 C>T (p.V1268_R1335del))were previously reported. Prenatal diagnosis was performed in two cases using chorionic villi samples. One was diagnosed as normal, while the other turned out to be a female heterozygotewith p.S624_Q724del mutation of the *ATP7A* gene. Prenatal diagnosis in families at risk is critical in order to choose preventive options including an early treatment with copper-histidine therapy or therapeutic termination. In conclusion, most mutations of the *ATP7A* gene were frame-shift mutations and prenatal diagnosis has been successfully carried out.

P-12-3

COPPER AND ZINC CONCENTRATIONS IN THE BREAST MILK OF MOTHERS WITH WILSON DISEASE AND EFFECTS ON INFANTS

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This is only a model abstract. Female patients with Wılson disease who are being treated with a chelating agent or zinc can become pregnant. Most of the mothers want to breastfeed their infants while continuing their treatment for Wılson disease. However, the copper concentration has not been investigated in the breast milk of mothers with Wılson disease. We report here copper and zinc concentrations in the breast milk of mothers with Wılson disease and the effect of the milk on their infants. **Materials and Methods**: Using atomic absorption spectrometry, the copper and zinc concentrations in the breast milk from three patients with Wılson disease were analyzed at several times. A patient was sequentially treated with zinc and trientine. In addition, the infant's serum levels of copper and zinc were analyzed. **Results and Discussion**: Although the serum copper levels of the patients were significant lower than that of control subjects, the copper and zinc concentrations in the breast milk from the patients while they were taking zinc or trientine were normal levels. The serum copper and zinc levels were also normal in the infants receiving the breast milk from the patient taking zinc and trientine. However, the copper and zinc concentrations in the breast milk from the patients taking penicillamin were lower than those of controls. These results indicate that mothers with Wılson disease receiving zinc or trientine may safely breastfeed their infants.