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Allan-Herndon-Dudley Syndrome with New SLC16A2 Mutation : A Case report

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Indroduction
Allan-Herndon-Dudley syndrome (AHDS) is a disease that prevents absorption of thyroid hormone and leads to developmental disorder of the brain due to the problem of MCT8 expression process caused by mutation of SLC16A2 (Monocarboxylate transporter 8; MCT8) gene of X-chromosome. Clinical findings include motor weakness, muscle atrophy, hypertelorism and mental retardation. Laboratory findings include increased T3, decreased T4 and borderline or increased TSH levels. We report a case of new mutations in Allan-Herndon-Dudley syndrome.

Case report
The 26-month-old boy admitted the department of rehabilitation medicine for evaluation due to developmental delay. He was the first child of healthy parent and born in the 40th week of gestation after an uncomplicated pregnancy; birth weight was 3500g (50-75th centile). At birth, mother and father were 34 and 39 years old, respectively. He could not head control at 4 months, and developmental delay with progressive muscle weakness was seen from 8 months. On physical examination at the age of 26 month, height was 100cm (>97th centile), weight 12kg (25th centile) and occipital-frontal circumference was 47cm (5th centile). He had hypertelorism, ptosis, a broad and flat nasal bridge. Both upper and lower extremities strength was grossly grade 3 by manual muscle test and showed muscular hypotonia. He still could not head control. Further investigations, routine laboratory tests, brain magnetic resonance imaging, electroencephalogram, chromosomal microarray, spinal muscular atrophy test and joint x-rays did not reveal abnormality. Thyroid function test were T3 1.67(0.87~1.78)ng/dL, free T4 0.45(0.58~1.64)ng/dL, TSH 5.44(0.34~5.6)U/mL. T3 showed a result on the high borderline of the normal range, low on the freeT4, and high on the borderline of the normal range of TSH. The NGS (Next generation sequencing) panel test, a genetic test, found NM_006517.4(SLC16A2):c.455G>A, p.(Gly152Asp), hemizygote, a rare mutation in the SLC16A2 gene. The result is an X-linked recessive disorder of chromosome Xq13.2, located in the mutated hot span region of exon 2, and the mutation was not previously reported. Family NGS Panel Test showed that the father was negative, and the mother was a heterozygote mutant of SLC16A2 and was a carrier without clinical symptoms. (Fig. 1)

Conclusion
This is a case of AHDS diagnosed by a new SLC16A2 mutation through genetic testing in patients with developmental delay and muscular hypotonia. Physiatrists are likely to be

the first to encounter with these patients, so careful physical examination with gathering detailed information on family history and appropriate genetic analysis should be considered in patients with unexplained developmental delay or muscular hypotonia to ensure a correct diagnosis.

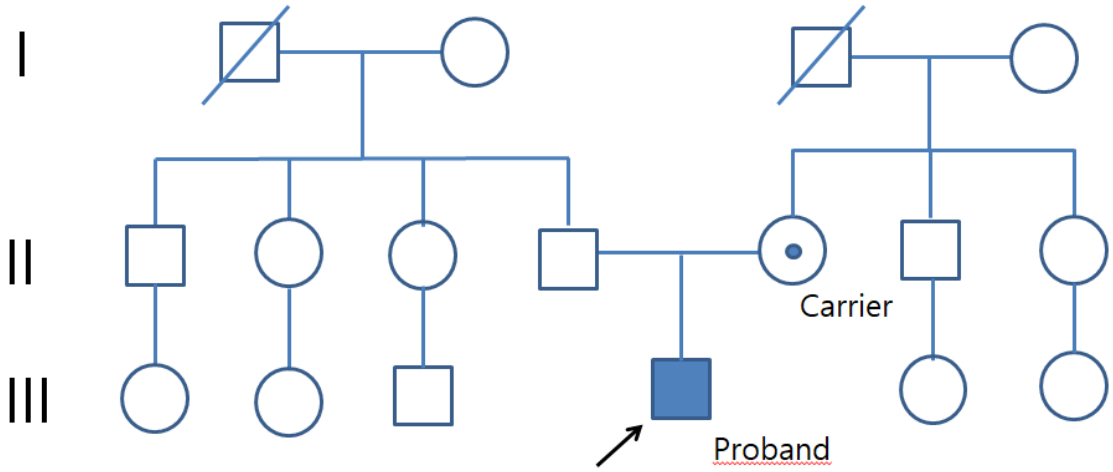

Figure 1. Three generation pedigree of the patient's family. Filled symbols represent affected members, open symbols represent unaffected members. Circles and squares represent females and males, respectively.