



POSTER PRESENTATION

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Comprehensive genetic analyses of primary adrenal failure without enzymatic defects

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Our objective is to estimate frequencies of mutations in *STAR*, *CYP11A1*, *NROB1*, *NR5A1*, *MC2R*, and *MRAP* in a cohort of Japanese patients with primary adrenal failure without enzymatic defects. Twenty-one patients were included, who were diagnosed as having primary adrenal failure without enzymatic defect, namely 21-hydroxylase deficiency, 3 β HSD deficiency, 11 β -hydroxylase deficiency, and P450 oxidoreductase deficiency. Sixteen patients presented with primary adrenal failure before the age of 2 years. Fourteen patients had apparent mineralocorticoid deficiency. Fourteen patients were 46, XY and 7 patients 46, XX. Three had 46, XY disorders of sex development. Mutation analyses of *STAR*, *NROB1*, *NR5A1*, *MC2R*, and *MRAP* were done by PCR-based sequencing and next generation sequencing. In case of no amplification of *NROB1* by PCR, we performed oligonucleotide array CGH. We described clinical findings in each patient and determined possible genotype-phenotype correlation. Five patients were diagnosed as having DAX-1 deficiency. *NROB1* mutations were found hemizygotously in 3 patients (c.116delG, c.846_865del, and p.Q283X). *NROB1* deletions were found in 2 patients (400kb deletion including *NROB1* and 2.4kb deletion of exon 1). Four patients presented with primary adrenal failure in newborn, and the other patient presented at the age of 6 years. *STAR* mutations were found in 3 patients. One patient was 46, XY, and 2 patients were 46, XX. One patient, who presented with primary adrenal failure in newborn, had c.712delA/p.Q258X. Two patients, who presented at preschool age, had p.Q258X/p.R272C and p.Q258X/p.R188H. No mutations were found in *CYP11A1*, *NR5A1*, *MC2R*, and *MRAP*. In conclusion, *NROB1* mutations and deletions are relatively common in 46, XY normal male phenotype

patients (5/11). *STAR* mutations might be found in cases, being older than 2 years of age. 3. *CYP11A1*, *NR5A1*, *MC2R*, and *MRAP* mutations are rare.

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