165.00

AUTOIMMUNE POLYGLANDULAR SYNDROME-1 (APS-1; APECED) IN CENTRAL AND EASTERN EUROPE: NOVEL MUTATIONS OF AIRE GENE AND P450 CYTOCHROME AUTOANTIBODIES

J. Lebl[1], D. Cihakova[1,2], K. Trebusak[3], M. Heino[2], T. Battelino[3], Z. Halasz[4], A. Tar[5], P. Blumel[6], V. Fadejev[7], A. Tyulpakov[7], K. Krohn[2], P. Peterson[2]

[1]Department of Pediatric, 3rd Faculty of Medicine, Charles University, Prague, Czech Republic [2]institute Medecin Technology, University of Tampere, Finland [3]University Children's Hospital, Ljubljana, Slovenia [4]2nd Department of Pediatric, Semmelweiss University [5]Madarasz Children's Hospital, Budapest, Hungary [6]Prayerisches Kinderspital, Vienna, Austria [7]Department of Endocrinol, Sechenov Moscow Medical Academy, Moscow, Russia

lebl@fnkv.cz

APS-1 is probably the most troublesome of all pediatric endocrine disorders. It is caused by mutations of AIRE (AutoImmune REgulator) gene and results in functional failure of endocrine glands and some non-endocrine organs. Within an international collaborative study, a total of 26 patient genomic DNA (incl. 2 pairs of siblings) and 16 patient sera were collected from 7 countries from Central and Eastern Europe. The prevalent R257X mutation was analysed by TaqI restriction digestions of PCR fragments. Deletion 1094-1106del was detected by fragment length analysis. The 14 exons of the AIRE were PCR-amplified from genomic DNA using the PCR primers, purified by Bandprep Kit and sequenced. Autoantibodies against P450c17, P450c21 and P450scc were tested by immunoblotting. The most common mutations were R257X in exon 6 (40/52 alleles) and 1094-1106del (4/52 alleles). Four novel mutations were detected: A large deletion of exons 2-4 in one Russian patient in the homozygous state, 156-179ins23bp in one Austrian and one Hungarian patient, W78R in a Czech patient and T16M in a Russian patient who all were compound heterozygotes. In two patients, no mutation was detected in one allele. 13 of 16 subjects (81 %) had antibodies reacting with one or more cytochrome P450 antigens. In this first large study of AIRE gene in patients from Central and Eastern Europe, we confirmed the high prevalence of the mutation R257X. Nevertheless, we detected four novel mutations.

Acknowledgements. The study was supported by a grant of MSM 111200001.