ABSTRACT BOOK

SLAVIC FOUNDER MUTATION P.S44R IN IL7RA GENE IN CHILDREN WITH POSTMORTEM DIAGNOSIS SEVERE COMBINED IMMUNODEFICIENCY

POSTER DISPLAY 06: GENETICS IN IEI

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Background and Aims: Severe combined immunodeficiency with IL-7Rα-chain deficiency has immunologic phenotype T-B+NK+, frequency∼10% of SCID cases.

Methods: We conducted a multicenter retrospective study, enrolling patients' DNA with clinically suspected-SCID without genetic confirmation from Belarus(n=22) and Ukraine(n=24); children were selected from the mortality lists who died before the age of 1 year due to complications from generalized infections in infants (21–DNA was obtained from newborn cards, 16–FFPE, 2–FFT,1–FT,6–PB). We investigated a NGS PID panel of 102-SCID/CID genes.

Results: We studied DNA from 20 females and 26 males. In 19/46 patients' DNA TREC/KRECs were determined, TRECs–mediana-4.2x10^3(0-2.0x10^4)/10^6leukocytes) and KREC–mediana-4.6x10^3(0-3.9x10^4)/10^6leukocytes). In three patients with T-B+SCID, TREC were undetectable and KREC-normal were (8.2x10^3(2.7x10^3-2.1x10^4)/10^6leukocytes). In 2/4 patients, the genetic variant of p.S44R in the IL7Ra gene was detected in the homozygous state, in 2 of patientsin the heterozygous state, one patient had heterozygous compound with other mutations in the IL7Ra gene. p.C57R, p. R206Q, which is described by Clivar database as Uncertain significance. Variant p.S44R is not annotated in ClinVar database. According to Mutation Taster, SIFT, and PolyPhen-2 programs predicting the functional consequences of non-synonymous substitutions, this variant is classified as probably pathogenic by Pathogenicity Scores (9/10). The patients with homozygous p.Ser44Arg were born in Western part of Ukraine (n=1) and Belarus (n=1) from unrelated families, heterozygous state in 2 patients from Belarus.

Conclusions: Based on our data, a repeated substitution in the IL7Ra gene may be classified as mutation and may have the "founder effect" in East Slavic countries.

Disclosure: No.

Keywords: SCID, IL-7Rα, founder mutation