Conclusion: We have found the unique regional subtype of CNO with early-onset in North Caucasian region with at least 10 times higher prevalence. We have not yet seen similar patients in other nationalities of Russia. Mutations in known genes were detected only in a minor fraction of CNO patients from Dagestan and Chechnya. This work supported by the Russian Foundation for Basic Research (grant No 18-515-57001) and by Japan Medical Research Foundation (grant No 18mrf001).

REFERENCES

Disclosure of Interests: None declared

AB0009
IDENTIFICATION OF A NOVEL POLYMORPHISM OF ERAP1 IN A GROUP OF ITALIAN PATIENTS WITH BEHÇET SYNDROME

Nancy Lascaro1, Pietro Lecceose1, Salvatore D’Angelo2,3, Teresa Carbone1, Angela Padula1, Giuseppe Martelli1, Maria Carmela Padula1,3.

Institute of Lucania (IReL), San Carlo Hospital, Potenza, Italy; Biomedica (BRB) Foundation, Matera, Italy; University of Basilicata, Department of Science, Potenza, Italy

Background: The endoplasmic reticulum aminopeptidase protein 1 gene (ERAP1) was associated to several human diseases, including Behçet syndrome (BS), a multisystemic disorder with unknown etiology. ERAP1 protein is involved in immune response and its role can be influenced by gene single nucleotide variations (SNVs) with an unclear mechanism [1-5].

Objectives: We aim to genotype ERAP1 whole structure searching for SNVs, in 50 consecutive BS patients and 50 sex and ethnically-matched healthy controls (HC) unrelated to each others and/or to BS patients.

Methods: We used both bioinformatics and molecular methodologies. Specific primers for the coverage of all ERAP1 regions were designed using the NCBI Primer-Blast tool. Genomic DNA was extracted from whole blood and amplified using in vitro PCR. Good-quality PCR amplicons were directly sequenced using the GATC Biotech Sanger sequencing service and bioinformatically analysed using Mutation Surveyor software and NCBI-Blat Nucleotide on line similarity search tool. SNV functional impact was predicted using on line PolyPhen-2 [6], while the 3D protein prediction was obtained using 3D Protean server [7].

Results: Our study was performed recruiting an explorative cohort of BS patients from Southern Italy, a population characterized by low disease prevalence. We identified a novel heterozygous SNV at 18169 nucleotide position (NG_027839.1: g.18169A>T; HGVS nomenclature) within ERAP1 exon 3 (Fig. 1a). It was found in 7% (15/400) of cases in BS patients and in none of HC. The novel polymorphism was submitted and released in GenBank Database (MK252970 accession number). The SNV was a missense variation responsible for the substitution glutamate to valine (hydrophobic amino acid) at 183 position (NP_057526.3:p.Glu183Val; HGVS nomenclature) (Fig. 1b). This is a conserved site involved in the substrate binding, due to its significant role in the anchorage of the N-terminal amine group of the peptides. Because of the different amino acid chemical features, the computational assessment of the protein structure was performed (Fig. 1c) recognizing a change in the protein energy and stability: the SNV was associated to a more stable protein chain (AE: -2.022), probably affecting the enzyme conformational state change and activity, as well as the substrate binding pocket. The amino acid change was predicted to be damaging with maximum score when PolyPhen-2 prediction software was queried (score: 1.00) (Fig. 1d).

Conclusion: We found a SNV not previously reported in literature in a relatively small group of Italian BS patients. Our data need to be tested in a larger case-control study. In particular, the link between our SNV and the protein stability is to be validated in future functional studies.

REFERENCES

Figure 1. a) Localization of our de novo SNV and nucleotide sequence (polymorphic site in bold font). b) amino acid sequence (the polymorphic sites in bold font. c) 3D Protein software of wild-type and p.Glu183Val polymorphic sequences. d) PolyPhen-2 output showing the SNV maximum score of pathogenicity.

Acknowledgement: Many thanks to Professor Olivieri for his “heredity”

Disclosure of Interests: Nancy Lascaro: None declared, Pietro Lecceose: None declared, Salvatore D’Angelo: None declared, Teresa Carbone: None declared, Angela Padula Speakers bureau: Lilly Italia EMS, Giuseppe Martelli: None declared, Maria Carmela Padula: None declared

AB0010
THE ASSOCIATION OF THE LT A AND PTPN22 GENES POLYMORPHIC VARIANTS WITH THE REDUCED IMMUNoglobulin A LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Lilija Nazarova1, Ksenia Danilko1, Viktor Malievsky1, Tatiana Viktorova1,2, Bashkir State Medical University, Ufa, Russian Federation; Institute of Biochemistry and Genetics, Ufa, Russian Federation

Background: Data from a number of studies indicate the presence of a genetic predisposition to the level of immunoglobulins [1]. The aberration in the distribution of serum immunoglobulin A (IgA) concentrations was previously shown in patients with juvenile idiopathic arthritis (JIA) [2].

Objectives: The goal of the study was to determine whether the LTA rs909253 and PTPN22 rs2476601 polymorphic loci variants are associated with the reduced IgA level in JIA patients.

Methods: The study included 234 JIA patients (154 girls and 80 boys) from the Republic of Bashkortostan, Russia. IgA levels were measured in serum by the radial immunodiffusion method and considered reduced when they were less than the lower limit of established age-dependent reference intervals. Genotyping was performed by the real-time PCR method, and statistical processing of the results – using the two-tailed Fisher exact test (p) and the odds ratio (OR) with a 95% confidence interval (CI).

Results: Reduced IgA levels were detected in 10.68% of patients with JIA (n=25), and the majority of them were girls (n=21). There were only four boys with the reduced IgA level, and therefore the isolated analysis was not carried out for them. The analysis of the LTA rs909253 polymorphic locus in the general JIA group, as well as in girls with JIA, showed that, in the presence of the reduced IgA level, the heterozygous genotype LTA rs909253*AG was significantly less common than in the absence of this IgA level abnormality (the general JIA group: 20.00% vs. 48.33%, p=0.010, OR=0.267, 95% CI 0.107-0.712; girls with JIA: 19.05% vs. 45.11%, p=0.031, OR=0.286, 95% CI 0.101-0.843, respectively).

The analysis of the PTPN22 rs2476601 polymorphic locus in the general JIA group, the risk markers for the formation of the reduced IgA level were not established (p>0.1). At the same time, it turned out that in girls with JIA with the reduced IgA level, the genotype PTPN22 rs2476601*AG was significantly more common than in girls with JIA with normal or elevated IgA levels (*GG: 95.24% vs. 73.68%, p=0.028, OR=7.143, 95% CI 1.162-76.405; *A: 2.38% vs. 14.66%, p=0.025, OR=0.142, 95% CI 0.014-0.865, respectively).

Conclusion: As a result of the study, the association of the LTA rs909253 and PTPN22 rs2476601 polymorphic loci variants with the reduced IgA level in girls with JIA was established.

REFERENCES