References:


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ALLELIC POLYMORPHISM OF PROINFLAMMATORY CYTOKINE GENES AS A BASIS FOR THE FORMATION OF PHENOTYPES OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: The pathological process of juvenile idiopathic arthritides (JIA) largely depends on pro-inflammatory cytokines, the polymorphism of the alleles of some genes of which we have the opportunity to study. No studies have been conducted on the dependence of certain features of the pathological process of JIA on the polymorphism of the IL-6 (G-174C) and TNF (G308A) genes.

Objectives: To reveal the dependence of JIA phenotypes and its course on genetic polymorphism of alleles IL-6 and TNF.

Methods: Polymorphism of the IL-6 and TNF genes was studied by PCR-method using allele-specific primers 44 patients 1-7 y.o. (24f, 20m) with JIA. The level of IL-6 and TNFα in the serum was determined using ELISA and CLIA methods.

Results: There were 73% cases with an unfavorable course of the disease (UCD) in the patients with the CC allele of the IL-6 gene, for most patients average activity was JADAS27 13.5±16.0, JIA (50%) & uveitis (30%) were the most frequent among subgroups. The level of serum IL6 was 74.1±89.5 pg/ml, TNFα 274±173 pg/ml (ratio IL6/TNFα=4.3±2.1). Among patients with GC IL6 70% female, 79% with UCD. More often pJIA (36%, including all RF+) and eJIA (35%) were noted with the largest frequency of inclusion of the hip joints (33%), spine (35%), detection of secondary osteoporosis (43%). The metabolic changes were registered on the ECG in 82% cases. The serum IL-6 level was 11.3±2.95 pg/ml, TNF 241.75 pg/ml (IL-6/ TNFα=0.047, p<0.05 vs CC allele). Children with GA IL-6 (wild allele) with a more favorable course of the JIA (31%, less than in the CC and GC groups (p<0.05), only 8% had the highest disease activity), the largest number of patients with sJIA (25%) was registered in this group. The detection of HLA B27 was significantly lower (p<0.05) than in other alleles, while 60% cases were ANA+ (more than in the group GC, p<0.05). The highest level of serum IL6 (35.3±18.9 pg/ml) & the highest average number of mutations in folate metabolism genes (4±0.51) were revealed in this group. The wild allele ILG prevailed (n=32) among the TNF gene alleles, sex ratio 1:1, UCD in 70%. The number of active joints, ESR, CRP, ANA-a positivity (50%), HLA B27+ (53%) were unsignificantly higher than in GA TNF allele, while serum IL6 level (22.8±9.8 pg/ml) & TNFα (12.3±4.1 pg/ml) were lower. In patients with the GA TNF gene allele, an UCD (73%), eJIA (36%) were noted slightly more often. By such parameters as the patient’s gender, the presence of uveitis, damage to the hip joints, the type of synovitis, metabolic changes on the ECG, indicators were observed comparable with the wild allele group. IL6 level was 48±39.2 pg/ml (TNFα 636.5±520.1 pg/ml, IL6/TNFα=0.07±0.06 (vs 1.9±0.5 in GG group, p<0.05). The genotype of two wild alleles TNF GG with IL6 GG apparently showed the smallest proportion of the UCD (33%, p<0.05), the most frequent polymorphism of ANA positivity (71%), with no uveitis and RF-pJIA in this group. All cases of RF+pJIA had TNF GA and IL6 GC. oJIA prevailed (57%) in the TNF GG&IL6 GC group, there was not a single case of sJIA, and the AJ number was the smallest (2.8±0.5). The largest group was TNF GG & IL6 GC (n=14). 91% of cases had UCD, AJ=6.6±2.4, damage to the hip joints (40%), ESR 23.7±6.7 mm/h, CRP 14.5±5.4 mg/l, metabolic changes on the ECG in 100%, but ANA+ only at 13%. In general, there was no correlation between the cytokine content in the blood serum during of active disease in the examined children with features of allelic polymorphism of these genes.

Conclusion: Depending on the allele polymorphism of the IL-6 and TNF genes, certain phenotypes of the JIA course emerge. Thus, revealing the polymorphism of these alleles in patients at the onset of the disease, we can predict to some extent its course and take this into account when choosing treatment tactics.

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T REGULATORY CELLS LEVEL IN PERIPHERAL BLOOD OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND ITS RELATION WITH DISEASE ACTIVITY

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