

Analysis of association of single nucleotide polymorphism in the promoter region of the CD209, IL-10, IL-28 and CCR5 D32 genes with human predisposition to development of tick-borne encephalitis

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Objectives

In the pathogenesis of tick-borne encephalitis (TBE) plenty various molecules play a significant role. The most prominent factors include IL-10, IL-28B, CD-209 and CCR5. It is reasonable to search for genetic predispositions to development of various clinical forms of TBE related to the genetic variation of IL-10, IL-28B, CD-209 and CCR5. We aimed to search for association of single nucleotide polymorphism in the promoter region of the CD209, IL-10, IL-28 and 32 base pair deletion in CCR5 coding region (Δ 32) with human predisposition to development of various clinical presentations of TBE. We tried to assess the relation between the presence of particular alleles and genotypes and laboratory and clinical parameters.

Methods

59 patients with TBE and 57 people, who never developed TBE were included in the study.

The detection of TBE virus infection was performed with SERION ELISA classic TBE Virus IgG/IgM (Institut Virion/Serion GmbH, Germany) diagnostic kit twice in patients with meningitis or encephalitis after tick bite: at the moment of admission to the hospital and 2 weeks later. Anti/ TBEV antibodies level dynamics was observed. A level of viral specific IgM and IgG antibodies was marked according to manufacturer's recommendations.

To assess the distribution of single nucleotide polymorphisms, TaqMan SNP (Life Technologies, USA) genotyping assays were used for IL10: rs1800872 and rs1800896, for CD 209 rs4804803 and rs287886, rs12979860 for IL 28B SNPs according to the manufacturer's protocol using real-time PCR technology on the StepOne thermal cycler (Applied Biosystems/Life Technologies, Foster City, CA). Genotypes were called using TaqMan Genotyper Software v1.0.1 (Applied Biosystems/Life Technologies, Foster City, CA), calculation of Hardy-Weinberg equilibrium for each analyzed set of genotypes was performed by this software.

Results

Comparison between TBE patients and CG showed that in SNP rs287886 CD 209 AG heterozygotes were more frequent in TBE group, while homozygotes GG were more frequent in CG group.

Conclusions

SNP rs287886 CD 209 AG heterozygotes predispose to develop TBE. No predisposition to severe forms of TBE and single nucleotide polymorphism in the promoter region of the CD209, IL-10, IL-28 and CCR5 D32 genes was stated.



http://pasozyty.org.pl/attachments/Image/kleszcz_najedzony.jpg

Table 2. Genotype frequencies for the CD209 rs2287886, CD 209 rs4804803, IL 10 rs1800872, IL 10 rs1800896, CCR5 Δ 32, IL B28 rs12979860 single nucleotide polymorphisms (SNPs) in tick-borne encephalitis (TBE) patients with different clinical manifestations and control group (CG)

Table 1. Laboratory test results

	Examination 1		Examination 2		Examination 3	
	Mean	SD	Mean	SD	Mean	SD
ESR (mm/h)	32.72	20.38	-	-	-	-
CRP (mg/dl)	12.3	14.6	1.7	2.1	-	-
WBC ($10^3/\mu$ l)	10.7	4.6	9.4	6.3	-	-
Lymphocytes	1.96	3.17	3.76	6.01	-	-
PLT ($10^3/\mu$ l)	197.72	52.27	230.8	63.4	-	-
Pleocytosis (cells/ml)	135.5	192	55.93	29.21	22.21	17.85
Mononuclear cells (cells/ml)	91.66	120.57	52.29	29.53	18.7	16.22
Neutrophil cells (cells/ml)	44.5	152.9	3.8	13.93	3.5	10.95
Lymphocytes (cells/ml)	81.5	120.95	49.66	29.8	28.1	14.8
Monocytes count (cells/ml)	15.17	16.27	4.43	3.61	4	7.24
Protein concentration (mg/dl)	62.5	24.82	65.37	30.74	47.89	24.46
Albumin concentration (mg/d)	43.88	19.63	42.89	20.6	33.91	18.7

	CG	TBE	p	TBE1	TBE2	p
CD 209 rs2287886						
AA	9 (15.8%)	9 (15.3%)	0.9	3	6	0.49
AG	21 (36.8%)	34 (57.6%)	0.02	14	20	0.61
GG	27 (47.4%)	16 (25.4%)	0.02	9	7	0.25
CD 209 rs4804803						
AA	38 (66.7%)	38 (64.4%)	0.8	15	23	0.34
AG	14 (24.6%)	19 (32.2%)	0.36	10	9	0.37
GG	5 (8.8%)	2 (3.4%)	0.22	1	1	0.88
IL 10 rs1800872						
TT	1 (1.8%)	2 (3.4%)	0.59	1	1	0.88
TG	22 (38.6%)	18 (30.5%)	0.36	10	8	0.25
GG	34 (59.6%)	39 (66.1%)	0.48	15	24	0.23
IL 10 rs1800896						
TT	13 (22.8%)	12 (20.3%)	0.82	5	7	0.89
TC	32 (56.1%)	28 (47.5%)	0.42	14	14	0.46
CC	12 (21.1%)	19 (32.2%)	0.3	7	12	0.53
CCR5Δ32						
wt/wt	42	49	0.2	23	26	0.33
wt/ Δ 32	15	10	0.2	3	7	0.33
IL B28						
CC	27	20	0.14	10	10	0.51
CT	20	30	0.09	13	17	0.91
TT	10	9	0.74	3	6	0.48