



SERUM AND CSF INFLAMMATORY MARKERS IN MULTIPLE SCLEROSIS



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INTRODUCTION:

Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system (CNS). Inflammatory and neurodegenerative processes appear in the early stages of MS. The immune system attacks the myelin, leading to nerve damage, and development of plaques in CNS. These processes are linked to the production of inflammatory and neurodegenerative markers. We hypothesized that concentration of some serum and cerebrospinal fluid (CSF) markers are changed in patients with MS in time of first clinical symptoms.

OBJECTIVES:

Compare and evaluate differences and possible similarities of several inflammatory markers in serum and CSF between a healthy control and a case group.

METHODS:

A control group of 84 healthy individuals with no inflammatory, neurological, or systemic disorders and no CNS lesions was compared to a case group of 84 newly diagnosed MS patients (patients were not treated by corticosteroids or disease modifying drugs before lumbar puncture). Serum and CSF samples were collected and analyzed using ELISA for interleukins (IL) 6,8,10, CXCL-13 and C3, C4 complement components and isoelectric focusing (IEF) for immunoglobulins (IgG, IgA, IgM) and light chains kappa and lambda. Tests were done at 0.05 significance level.

RESULTS:

There were no significant differences between MS and control group in demographic data (Table 6,7). Significantly higher levels of CSF IL-6 ($p=0,004$), IL-8 ($p< 0,0001$), IL-10 ($p=0,044$) (Table 1), CXCL 13 ($p<0,0001$) (Table 2) and C3 ($p=0,007$) (Table 3) were found in MS group. In the serum, significantly higher levels of IL-6 ($p=0,002$) (Table 1) were found in MS group. Furthermore, a moderate correlation IEF IgG (and also IEF kappa, IEF lambda) and CXCL 13 (CSF) and a weak correlation between IEF IgG (eventual IEF kappa, IEF lambda) and IL-10 (CSF) were demonstrated (Table 4). However, there was no significant relationship found between IEF IgG (eventually IEF kappa, IEF lambda) and IL-6,8 (CSF) (Table 4).

CONCLUSION:

Significantly higher levels of certain interleukins, chemokine ligand 13, and complement C3 were found in the multiple sclerosis group, primarily in the CSF but also in the serum. These results confirm the inflammatory processes in early stages of MS. These markers are also the subjects of research as possible prognostic markers of MS, markers of treatment effectiveness or possible target of biological treatment.

	Control			RS			Mann-Whitney U test p-value
	Median	Minimum	Maximum	Median	Minimum	Maximum	
IL-6(CSF)	2,99	2,0	26,4	4,4	2,0	152,0	0,004
IL-6 (s)	2,00	2,0	12,2	2,7	2,0	21,7	0,002
IL-8 (CSF)	42,9	11,4	85,8	55,8	30,2	337,0	< 0,0001
IL-8(s)	14,35	5,0	114,0	14,1	3,0	1024,0	0,617
IL-10(CSF)	5,00	5,0	5,0	5,0	5,0	7,2	0,044
IL-10 (s)	5,00	5,0	49,5	5,0	5,0	99,4	0,565

Table 1 – p-values (p) for IL-6,8,10 in both serum (s) and CSF

	Control			RS			Mann-Whitney U test p-value
	Median	Minimum	Maximum	Median	Minimum	Maximum	
CXCL 13 (CSF)	0,10	0,1	16,1	3,77	0,1	120,1	< 0,0001

Table 2 – p-value (p) for chemokine ligand 13 (CXCL13) in CSF

	Control			RS			Mann-Whitney U test p-value
	Median	Minimum	Maximum	Median	Minimum	Maximum	
S_C3	1,08	0,59	1,53	1,08	0,44	1,64	0,759
S_C4	0,24	0,14	0,51	0,25	0,06	0,41	0,925
CSF_C3	2,68	1,37	22,60	3,11	1,28	76,30	0,007
CSF_C4	1,36	0,92	6,91	1,51	0,92	18,90	0,067

Table 3 – p-values (p) for complement components 3 and 4 in both serum (s) and CSF

Age	Medián	Minimum	Maximum	Mann-Whitney U test p-value
Control	35,0	19,0	66,0	0,122
RS	37,0	18,0	71,0	

Table 7 – control and case groups age distribution

Soubor RS		IL-6(CSF)	IL-8 (CSF)	IL-10(CSF)	CXCL 13 (CSF)
IEF IgG CSF	Korelační koeficient	-0,111	0,145	0,298	0,475
	p-value	0,315	0,188	0,006	<0,0001
IEF kappa	Korelační koeficient	0,027	0,184	0,338	0,490
	p-value	0,807	0,093	0,002	<0,0001
IEF Lambda	Korelační koeficient	-0,050	0,083	0,242	0,556
	p-value	0,649	0,453	0,027	<0,0001

Table 4 – correlations coefficients and p-values between CSF IL-6,8,10, & CXCL13 with IEF IgG CSF, kappa, and lambda

Soubor RS		IL-6 (s)	IL-8(s)	IL-10 (s)
IEF IgG CSF	Korelační koeficient	-0,080	0,195	0,140
	p-value	0,468	0,076	0,203
IEF kappa	Korelační koeficient	0,090	0,061	0,073
	p-value	0,415	0,583	0,509
IEF Lambda	Korelační koeficient	0,061	0,095	0,060
	p-value	0,580	0,388	0,589

Table 5 – correlations coefficients and p-values of serum IL-6,8,10 with IEF IgG CSF, kappa, and lambda

	Female		Male		Chi-kvadrát test p-value
	počet	procento	počet	porocento	
Control	62	73,8%	22	26,2%	0,311
RS	56	66,7%	28	33,3%	

Table 6 – control and case groups gender distribution (no significant differences between MS and control group in demographic data)