

Jones et al 2016 ⁹	Multiplex ELISA	CSF	30 varicella vasculopathy	30 MS, 20	IL-1b, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, IL-13, IFN-γ TNF-a),	Yes	Yes	Yes	Yes	Yes	No	No				Yes		No
Losy et al 2001 ¹⁰	ELISA	CSF	23	15	CCL2/ MCP1												Yes	
Beridze et al 2011 ¹¹	ELISA	CSF	95	25	IL-1β, IL-6, TNF-a and IL-10		Yes	Yes	Yes		No							

Suppl Table 2: Demographics and investigations details of encephalitis and non-inflammatory neurological controls.

Clinical syndrome (n)	Control (20)	Encephalitis (43)
Gender, female/male	9F, 11M	29M/43F
Age, median (range), y	4.9 (0.3-14) [#]	4.9 (1.3-14)
Timing of CSF from onset of neurological symptoms, median (range), d	NA	5 (1-24)
CSF Pleocytosis (Elevated >5x10 ⁶ cells/L), n	0	32 (74%)
CSF Pleocytosis, median (range), 10 ⁶ /L	0 (0-3)	16 (0-175)
CSF neutrophils, median (range), 10 ⁶ /L	0 (0-1)	1 (0-25)
CSF protein, median (range), mg/dl	NA	0.3 (0.1-1.3)
Neopterin (Elevated >29 nmol/L), n	1 (6PTPS deficiency)	40 (93%)
CSF Neopterin median (range), Nmole/L	12.75 (4.9-166.7)	94.8 (26.1-1399.7)
Intrathecal oligoclonal IgG bands (positive), n	NA	7/36 (19.4%)

Supplementary Table 3: CSF cytokine/chemokine* concentrations (median and range) in non inflammatory neurological controls, encephalitis and focal cerebral arteriopathy. This table shows predominant elevation of CSF IL-6, IL-8, CXCL10, CXCL1 and paradoxical decrease CXCL12 in children with acute stroke due to FCA.

Cytokines pg/ml	Control	Encephalitis	FCA	Ctrl vs FCA	Ctrl vs Enceph	FCA vs Enceph
	Median (Range)			P values		
CXCL9/MIG	26.9 (13.4-143.7)	139.9 (4.3-15123.9)	48.83 (48.83-249)	0.3	<0.0001	0.0001
IP-10/CXCL10	666.2 (327.4-985.6)	3654.3 (0-268417.3)	1759 (383.9-7719)	0.05	<0.0001	0.06
CXCL11	5.1 (0.4-8.2)	5.8 (0-114.7)	5.2 (1.95-71.3)	0.4	0.11	0.2
IL-6	0.3 (0-5.6)	15.4 (0.9-745.4)	21.4 (3.2-53)	0.006	<0.0001	0.2
IL-8	32.4 (19.6-77.3)	61.8 (6.5-2165.6)	181.7 (128.1-303.3)	0.002	0.0009	0.2
G-CSF	15.4 (5.9-36.2)	65.4 (1.7-7378.6)	35.9 (8.3-38.2)	0.15	<0.0001	0.02
MIP3b/CCL19	108.8 (37.7-320.6)	270.6 (1.4-2598.8)	182.8 (42.2-316.7)	0.06	0.0003	0.2
BCA.1/CXCL13	1.8 ((0-8.4)	17.8 (0-1000)	1.4 (1-18.2)	0.4	<0.0001	0.0004
CXCL12	1543.8 (981.5-3117)	1122.6 (0-4081.6)	456 (116.9-1045)	<0.0001	0.01	0.008
GRO/CXCL1	0 (0-97.40)	27.1 (0-793.1)	40.9 (24.2-83)	0.002	0.0018	0.2
IFN- α	0 (0-25.4)	18.7 (0-128.7)	3.2 (3.2-24)	0.2	<0.0001	0.003
MCP-1/CCL2	995.2 (633-3238)	716.5 (37.5-9859.6)	655.9 (584.9-5158)	0.5	0.18	0.2

*Detectable above lower limit on multiplex assay.

Th1 (IFN- γ , TNF- α) Th2 (IL-2, IL-4, IL-13, Eotaxin, CCL17), Th17 (IL-17A, GM-CSF, IL-21, IL-23) and other cytokines (IL-1 β , IL-1ra, IL-12 (p70), IL-12 (p40), IL-10) and chemokines (MIP-1 α /CCL3, MIP-1 β /CCL4, RANTES were below detectable level in FCA group, hence not presented in the table.

p calculated using Kruskal-Wallis test. Non FCA stroke cases were not included in statistical analysis due to small number of cases.

Abbreviations: Th, T helper cell; IL-, interleukin; IFN-, interferon; TNF, tumor necrosis factor; MIG, monokine induced by IFN- γ ; IP, IFN- γ inducible protein; G-CSF, granulocyte colony stimulating factor; MIP, macrophage inflammatory protein; GM-CSF, granulocyte monocyte colony stimulating factor; BCA-1, B cell attracting chemokine, GRO, melanoma growth stimulating activity alpha; MCP, monocyte chemotactic protein; RANTES, regulated on activation normal T cell expressed and secreted.

Supplementary Figure Legends:

Supplementary Figure 1: CSF cytokine/chemokine concentrations of all measured cytokines and chemokines in CSF of non inflammatory neurological controls, encephalitis, FCA stroke and non FCA stroke according to T and B cell subsets. Compared to controls, CSF IL-6, IL-8, CXCL1 and CXCL10 were elevated in FCA stroke, and were comparable to encephalitis. The other cytokines/chemokines were not elevated in FCA group, but most/many cytokines/chemokines are elevated in the encephalitis group.

Dotted lines represent medians. The 95th centile of the 20 non-inflammatory controls is presented (P95 Co). Detection limits are presented as DetL

*Non FCA stroke cases are represented by empty triangle symbol

Supplementary Figure 2: Correlation of a) NIHSS score and b) PSOM score with CSF cytokine/chemokine concentrations.

Supplementary Figure 3: Comparison of infarct size with CSF concentration of cytokine/chemokines. There is no apparent correlation between cytokines and severity of stroke. For example IL-6 and CXCL1 are higher in case 3 with smaller infarct compared to case 1 with larger infarct size. Similarly despite similar CSF timing and smaller infarct size, cytokine concentrations (CXCL1, IL-6, CXCL10) are higher in case 2 compared to case 1.

References:

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