

Comparison of antibody response in cerebrospinal fluid and serum in patients with Lyme neuroborreliosis and controls



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Introduction

- Lyme borreliosis (LB), caused by *Borrelia* species, is prevalent in Europe, including the Czech Republic, which reports approximately 4,000 cases annually and has the highest number of Lyme neuroborreliosis (LNB) cases among the countries submitting data to the ECDC.
- Clinically, only erythema migrans and/or facial palsy have positive predictive value.
- The definite LNB relies on laboratory testing.

Main goals

- The measurement of early antibody response of children with LNB and controls to recombinant *Borrelia* antigens in cerebrospinal fluid and serum.
- The prediction of active infection before calculating of antibody index.

Patients and methods

- Serum and cerebrospinal fluid (CSF) samples obtained from 90 children with definite LNB using EFNS criteria were evaluated.
- In control groups, samples of 90 pediatric controls and 85 adult controls with other neuroinfections were tested.
- Antibodies in the serum and CSF were analyzed using:
 - CLIA and ELISA recombinant assay IgM and IgG for screening
 - Microblot-Array (MBA) IgM and IgG for confirmation

Results

- Lymphocytic pleocytosis was found in the cerebrospinal fluid of all tested patients.
- The blood brain barrier (BBB) was disrupted in 58 LNB patients (64.4%).
- Intrathecal synthesis of IgG and/or IgM antibodies was demonstrated in 86 LNB patients (95.6%).
- No intrathecal synthesis was demonstrated in control groups.

group	IgG		IgM	
	serum	CSF	serum	CSF
LNB patients	93%	90%	66%	49%
pediatric controls	29%	21%	5%	0%
adult controls	24%	20%	5%	0%

Table 1: The detection of antibodies by screening methods (ELISA or CLIA)

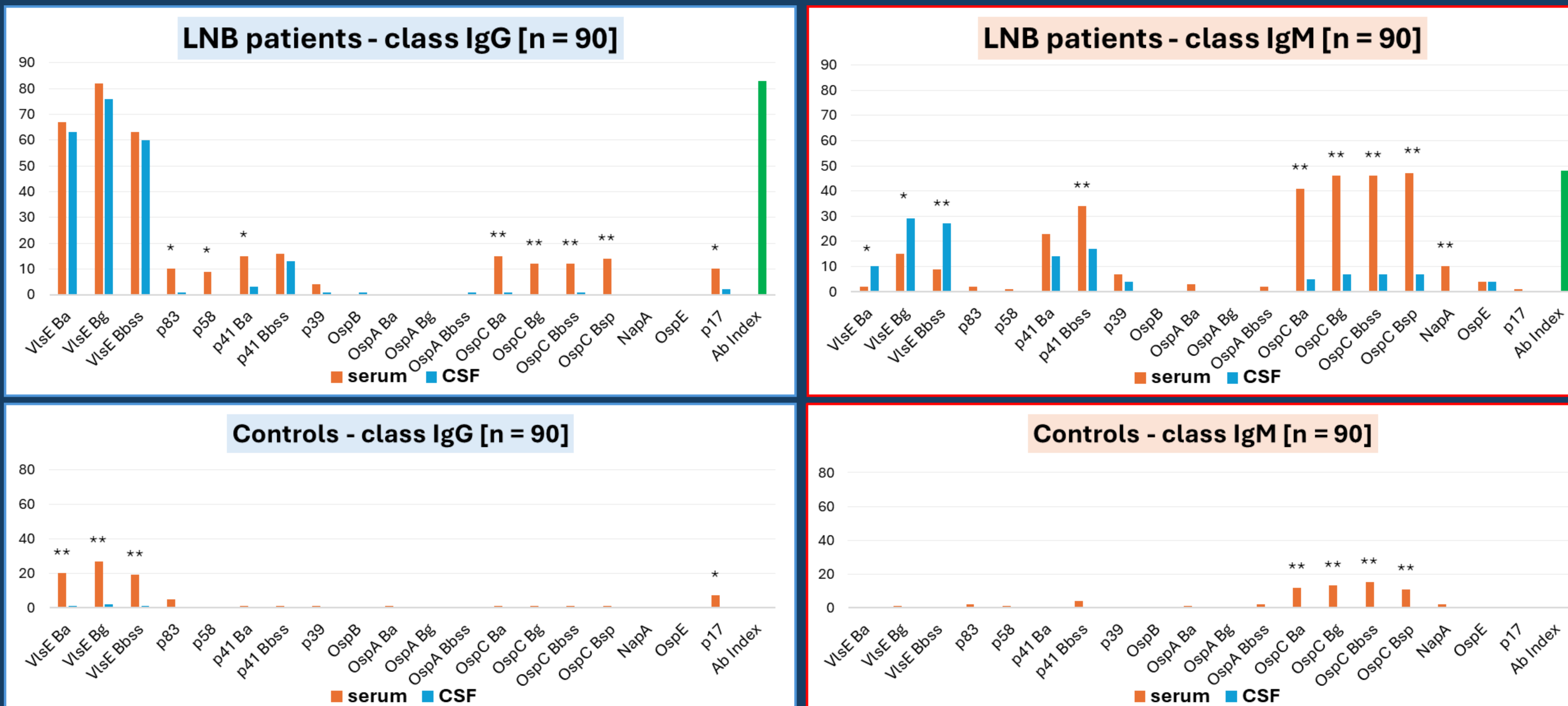


Figure 1: Reactivity of antibodies against *Borrelia* antigens in LNB patients and control group in serum and CSF compared with positivity in the antibody index (Ab Index); * $P \leq 0.05$; ** $P \leq 0.01$

Table 2 summarizes differences in antigen reactivity between serum and CSF samples from LNB patients.

In LNB patients:

- Statistically significant differences were mainly observed in favor of serum (black values).
- An exception was VlsE in the IgM class, where higher reactivity was detected in CSF (highlighted in red).

In the control group, statistical differences between serum and CSF were detected only for VlsE ($P \leq 0.0001$) in IgG and OspC ($P \leq 0.001$) in IgM.

Antigen	IgG	IgM
	SERUM vs CSF	SERUM vs CSF
VlsE Ba	ns	$P \leq 0.05$
VlsE Bg	ns	$P \leq 0.05$
VlsE Bbss	ns	$P \leq 0.01$
p83	$P \leq 0.05$	ns
p58	$P \leq 0.05$	ns
p41 Ba	$P \leq 0.05$	ns
p41 Bbss	ns	$P \leq 0.01$
p39	ns	ns
OspB	ns	ns
OspA Ba	ns	ns
OspA Bg	ns	ns
OspA Bbss	ns	ns
OspC Ba	$P \leq 0.0001$	$P \leq 0.0001$
OspC Bg	$P \leq 0.001$	$P \leq 0.0001$
OspC Bbss	$P \leq 0.01$	$P \leq 0.0001$
OspC Bsp	$P \leq 0.0001$	$P \leq 0.0001$
NapA	ns	$P \leq 0.01$
OspE	ns	ns
p17	$P \leq 0.05$	ns

Table 2: Statistical comparison of antibody detection in serum and CSF (IgG/IgM) for LNB patients; ns = not significant

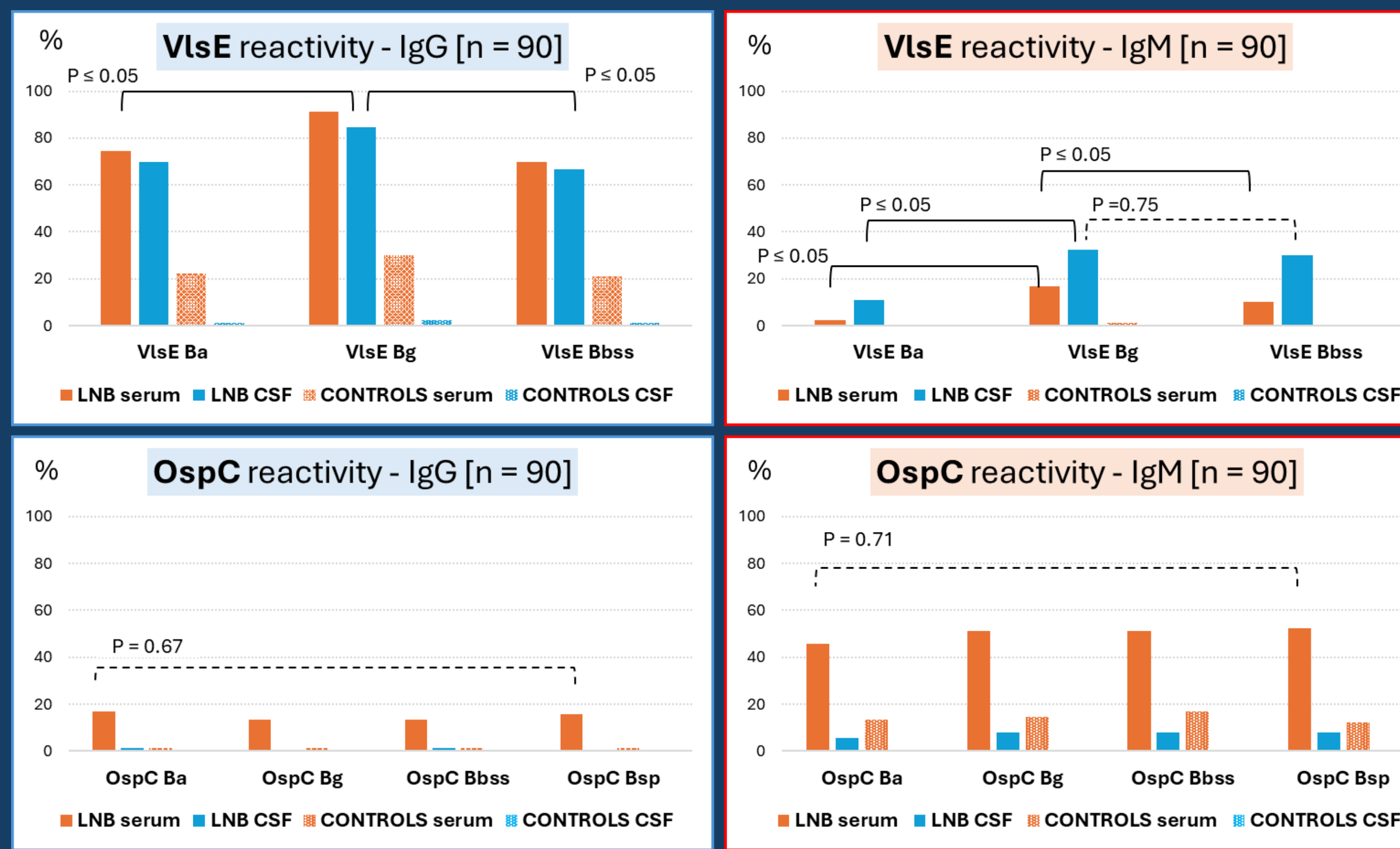


Figure 2: Statistical comparison of antibody reactivity against VlsE and OspC antigens from different *Borrelia* species in LNB patients and control group. Species: *Borrelia afzelii* (Ba), *Borrelia garinii* (Bg), *Borrelia burgdorferi sensu stricto* (Bbss), *Borrelia spielmanii* (Bsp).

Reactivity of antibodies against *Borrelia* antigens (Figure 1)

Specific antibodies were detected in serum in LNB patients to:

- VlsE, p83, p58, p41, OspC and p17 antigens in IgG
- VlsE, p41, p39, OspC and NapA antigens in IgM

The reactivity in CSF in LNB patients was as follows:

- VlsE and p41 antigens in IgG
- VlsE, p41 and OspC antigens in IgM

Correlation of antigens in serum or CSF with positivity of antibody index (Ab index):

- Serum: IgG – VlsE, IgM – OspC
- CSF: IgG – VlsE, IgM – VlsE

VlsE and OspC species reactivity in groups (Figure 2)

- Significant difference in the reactivity of VlsE Bg was compared to VlsE Ba or VlsE Bbss in IgG in serum and CSF ($P \leq 0.05$).
- No significant difference was found in VlsE Bg and VlsE Bbss in CSF IgM ($P > 0.05$).
- No significant difference was observed in OspC reactivity both IgG and IgM across all *Borrelia* species ($P > 0.05$).

Control groups reacted to individual antigens in serum and CSF only rarely (1-4%), except for VlsE in IgG and OspC in IgM in serum samples. No intrathecal synthesis was demonstrated in control groups.

Conclusions

- Acute CSF reactivity of VlsE in both IgG and IgM was consistent with intrathecal synthesis.
- Cerebrospinal fluid VlsE reactivity in IgM class was superior to serum IgM reactivity ($P \leq 0.05$).
- B. garinii* VlsE antigen dominated in LNB patients.
- Sensitivity was 93% for serum IgG, 66% for serum IgM, 90% for CSF IgG and 49% for CSF IgM. Specificity was 71%, 80% for serum, and 96% and 100% for CSF, respectively.

References

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