



Comparison of two CXCL13 assays for diagnosis of neuroborreliosis

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INTRODUCTION

Diagnosis of Lyme neuroborreliosis is based on three criteria:

- neurological symptoms
- cerebrospinal fluid (CSF) pleocytosis
- intrathecal *Borrelia burgdorferi* (BB) specific antibody production

However, 20% of early stage infections present without elevated antibody index and differentiation between passive diffusion and intrathecal synthesis of antibodies is sometimes difficult.

OBJECTIVES

- To evaluate the performance of two different CXCL13 assays.
- Comparing CXCL13 results with the results of BB immunoblot and clinical signs and symptoms.

MATERIALS AND METHODS

Patients were classified according to the European Federation of Neurological Societies (EFNS) criteria as definite LNB (dLNB), possible LNB (pLNB) or no LNB.

CXCL13 measurement in CSF was performed by both *recomBead* CXCL13 (Mikrogen GmbH, Germany) and Euroimmun CXCL13 ELISA (Euroimmun, Luebeck, Germany).

A) *Retrospective study*: samples were retrospectively selected based on results of BB IgM and IgG antibodies measured by Virotech Immunoblot (Sekisui, Lexington, USA). All samples were analysed with both CXCL13 kits.

B) *Prospective study*: prospectively, 47 samples of patients with suspected LNB were analyzed with both CXCL13 kits.

RESULTS

A) *Retrospective study*

- 63 CSF samples were analysed from 13 patients with dLNB, 5 with pLNB, 36 without LNB and 9 patients with other CSF infections (HIV (n=3) and herpes simplex (n=6)).
- According to the manufacturers' recommendations for interpretation, Euroimmun and *recomBead* assessed respectively 92% and 84% of the dLNB as suspicious for an acute LNB.
- In patients without LNB and patients with another diagnosed infection, Euroimmun and *recomBead* showed in respectively 73% and 84% of the cases a normal CXCL13 level.

Table 1: Results of CXCL13 Euroimmun and *recomBead* in cerebrospinal fluid of patients with and without Lyme neuroborreliosis (LNB) defined by EFNS criteria.

CXCL13 kit	result CXCL13	dLNB (n=13)	pLNB (n=5)	no LNB (n=36)	other CSF infection (n=9)
CXCL13 Euroimmun	normal <20 pg/mL	0	3	29	4
	borderline 20-30 pg/mL	0	0	2	0
	increased 30-100 pg/mL	1	1	3	2
	strongly increased >100 pg/mL	12	1	2	3
CXCL13 <i>recomBead</i>	normal <190 pg/mL	3	4	33	5
	borderline 190-300 pg/mL	0	0	2	0
	increased >300 pg/mL	10	1	1	4

B) *Prospective study*

- None of the 47 patients had LNB according to EFNS criteria. Forty-two patients had negative CXCL13, 2 patients had elevated CXCL13 with both tests, one patient had a borderline *recomBead* CXCL13 result and 2 patients had an increased CXCL13 with Euroimmun.
- The increased CXCL13 levels were detected in patients with diffuse-large B-cell lymphoma with central involvement (n=2), neurosarcoidosis (n=1) and in a patient with acute myeloid leukemia showing polyneuropathy.

Overall concordance (n=110) between the two kits (qualitative result) was 85%.

Different qualitative results between *recomBead* / Euroimmun were present in 16 samples:

- 10 normal (*recomBead*)/(strongly) increased (Euroimmun) CXCL13
- 2 normal (*recomBead*)/borderline (Euroimmun) CXCL13
- 2 borderline (*recomBead*)/(strongly) increased (Euroimmun) CXCL13

CONCLUSIONS

- ✓ Small differences in the determination of (acute) LNB between both CXCL13 kits may be due to different cut-offs and different standardizations.
- ✓ Both *recomBead* and Euroimmun CXCL13 kits show good performance in LNB.
- ✓ CXCL13 is a promising additional marker in the diagnosis of active LNB, as in the case of borderline BB immunoblot results.