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INFECTIOUS DISEASE

# CXCL13 is a potential biomarker for Lyme neuroborreliosis

Levels of the chemokine CXCL13 in the cerebrospinal fluid (CSF) show high sensitivity for acute, untreated Lyme neuroborreliosis (LNB), according to a recent prospective study. The disorder is caused by infection of the CNS with tick-borne *Borrelia* spp. (bacteria of the spirochete phylum) and is diagnosed on the basis of *Borrelia*-specific antibody levels and CSF pleocytosis. However, a time lag is observed between infection and antibody production, and antibodies may persist after the infection is cleared. A biomarker with higher sensitivity and specificity is, therefore, needed.

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Several lines of evidence from previous studies suggested CXCL13 as a promising biomarker candidate, including high concentrations in the CSF of patients with LNB and in vitro studies showing the role of this chemokine in attracting antibody-producing B cells to the CSF in patients with LNB. However, "due to the lack of a prospective study, a definitive recommendation for routine clinical use could not yet be given," explains Tobias Rupprecht, the senior author of the current study.

The study involved a cohort of 192 patients with pleocytosis and suspected LNB at a single center in Germany. Of this cohort, 14 patients were confirmed as having LNB, four of whom had not previously received *Borrelia burgdorferi*-specific antibiotic treatment. Owing to these low numbers of patients with LNB, the researchers also included CSF samples—collected and frozen up to 9 years previously—from patients with acute, untreated LNB.

In the group of untreated patients with LNB, CSF levels of CXCL13 were markedly increased (mean 15,149 pg/ml). By contrast, treated patients with LNB did not show substantially elevated CXCL13 levels, and the CXCL13 levels were normal in most of the 178 patients with diagnoses other than LNB. However, five patients with white blood cell malignancies and two patients with bacterial meningitis, none of whom had LNB, exhibited CXCL13 levels above the cut-off of 1,229 pg/ml and, therefore, "have to be considered a possible 'confounding' group," says Rupprecht. Nevertheless, "our prospective study confirmed the high sensitivity (94.1%) and specificity (96.1%) of CXCL13 as a diagnostic marker for acute LNB," he adds.

*B. burgdorferi*-specific antibody levels showed the same specificity as CXCL13 but lower sensitivity (85.7%) because two false-negative results were obtained, presumably owing to the delay in antibody production following infection. As shown in previously studies, CXCL13 production occurs at an early stage of CSF infection, which could represent an advantage of assessing CXCL13 levels rather than antibody indices for diagnosing infection. CXCL13 levels could also be used to discriminate between an active infection and a subsided infection, when antibodies still persist.



Further studies are needed to determine whether the species of *Borrelia*—which varies across continents and influences the inflammatory process—affects the CXCL13 response profile.

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