Detection of specific intrathecal antibody synthesis in multiple sclerosis and borreliosis using ELISA systems

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Introduction
In order to understand the specific humoral immune reaction in infections of the central nervous system (CNS), the concentration of pathogen-specific antibodies, the corresponding immunoglobulin class, and the concentration of albumin were determined in both the cerebrospinal fluid (CSF) and the serum of a patient. Using a EURO IMMUN ELISA system which has been specially developed for neurology, CSF/serum quotients of pathogen-specific antibodies, CSQ path-spec., were determined reliably.

Methods
Microplate wells coated with antigens from infectious agents were incubated in the first step with CSF (1:2) and patient serum (1:404) and in the second step with peroxidase-labelled anti-human IgA, IgG, or IgM. Tetramethylbenzidine was used as a detection reagent in the third step.

The concentration of pathogen-specific antibodies was determined for CSF and serum using the calibration curve produced from incubating the ready-to-use calibrators LA-LD and in the second step with peroxidase-labelled anti-human IgA, IgG, or IgM. Tetramethylbenzidine was used as a detection reagent in the third step.

| CSF/serum quotient diagram according to Reiber and Lange |

Reference range for normal values:
- Blood-CSF barrier dysfunction
- No Ig production in CNS
- Blood-CSF barrier dysfunction, additional Ig production in CNS
- Clear Ig production in CNS
- No disturbance in blood-CSF barrier function
- Error in blood extraction or analysis

The relative CSF/serum quotient (CSQrel.) is a measure of intrathecal pathogen-specific antibody synthesis. The determination of the CSQrel. for IgA and IgM is performed analogously. Normally immunoglobulins are used as a point of reference, but in polyspecific intrathecal antibody synthesis (e.g., in multiple sclerosis) the CSF/serum quotient of albumin (CSQ alb.) is used, since this protein is produced exclusively in the liver. The limiting quotient, (CSQlim.), can be determined from the CSQ alb. and the CSQrel. using the CSF/serum quotient diagram (according to Reiber and Lange). EURO IMMUN offers a program based on MS Excel for calculating the CSF/serum quotient and the limiting quotient.

Results
The CSQpath-spec. with respect to the MRZ reaction (anti-measles, rubella, and zoster) was examined in different patient collectives.

45% of patients with suspected multiple sclerosis and 85% of patients with clinically proven multiple sclerosis showed an CSQpath-spec. of >1.5 for one or more parameters. In 10 patients with hydrocephalus the CSQpath-spec. was <1.3.

Intrathecal production of antibodies was detected in 45% of patients with suspected neuroborreliosis and in 96% of patients with proven neuroborreliosis using the EURO IMMUN Anti-Borreliosis plus VlsE ELISA system.

Out of 9 patients who had specific antibodies against Borrelia in their serum but no signs of a neurological disease, none showed a positive CSF/serum quotient.

Conclusion
Determination of intrathecal antibody synthesis is an important criterion in the diagnosis of CNS infections. The ELISA systems described are simple to perform and provide reliable determination of pathogen-specific antibody concentrations in CSF and serum.