KEY WORDS: cattle, cerebrospinal fluid, S-100B.

ABSTRACT. We measured the concentrations of S-100B, a marker protein used in humans to detect brain damage, in the cerebrospinal fluid (CSF) of clinically normal cattle (n=15, mean ± SD: 31.8 ± 37.5 months) and of cattle with various inflammatory disorders (n=43, 70.6 ± 31.9 months). The mean ± SD CSF S-100B level was 2.9 ± 1.6 ng/ml in the normal group and 7.0 ± 7.4 ng/ml in the diseased group. Thirteen diseased cattle that had developed no obvious neurological signs showed abnormally high S-100B concentrations (> 8.0 ng/ml), whereas the two cattle with neurological disorders did not. No particular disease could be related to the S-100B rise. Therefore, it remains inconclusive whether measurement of CSF S-100B concentration is useful in veterinary neurological diagnosis.

S-100B is a calcium-binding protein found in the central nervous system [1]. This neurotrophic protein is primarily synthesized in the brain by astrocytes [7] and appears in the cerebrospinal fluid (CSF), the fluid within the subarachnoid space, the central canal of the spinal cord, and the brain ventricles. Therefore, CSF S-100B is used as a marker protein in humans to detect brain damage. Increased concentrations of CSF S-100B have been reported in patients with brain injury [10] or with Creutzfeldt-Jakob disease [4, 6]. In veterinary diagnosis, Green et al. [2] first used this CSF protein in the assessment of cattle with suspected bovine spongiform encephalopathy (BSE). However, to our knowledge, no further veterinary application of this protein has been reported since.

In this study we measured CSF S-100B concentrations in normal cattle and in cattle with various inflammatory diseases in order to elucidate the diagnostic relevance of CSF S-100B.

CSF samples representing a normal group were obtained from 15 clinically healthy Holstein calves and cows ranging in age from 0.25 to 114 months (mean ± SD: 31.8 ± 37.5 months). These animals had been kept at our institute and were sacrificed to serve as controls for other experiments. Just before euthanasia, a sample was collected from the medullary cavity of the spinal cord of the ventral medulla. The CSF samples were kept frozen at –80°C until assay for S-100B concentrations. Protein levels were evaluated by a sandwich ELISA method [3], using mouse anti-bovine S-100B monoclonal antibody (clone SH-B1, Sigma, St. Louis, U.S.A.) and horseradish-conjugated rabbit anti-bovine S-100 serum (Dako, Copenhagen, Denmark) as the first and second antibodies, respectively. Measurement was performed in duplicate on each sample.

Figure 1 shows scatter plots of individual CSF S-100B concentrations in normal cattle and in cattle with various inflammatory diseases in order to elucidate the diagnostic relevance of CSF S-100B. CSF samples representing a disease group (43 cattle, largely cows ranging in age from 6 to 168 months, mean ± SD: 70.6 ± 31.9 months) were kindly supplied by five livestock hygiene centers. Disease types were classified on the basis of clinical examination at the hygiene centers. CSF samples were collected immediately from the medullary cavity of the ventral medullary fissure. All animals aged 24 months or more, or with suspected neurological abnormalities, underwent the compulsory post-mortem ELISA screening test for bovine spongiform encephalopathy (BSE), and all were diagnosed as BSE-negative.

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The mean CSF S-100B concentration in the normal group was close to that of non-BSE diseased control cattle, reported by Green et al. [2]. We set a cut-off to distinguish abnormal S-100B levels in the diseased group. Even though our cut-off value was twice as high as that used in the previous report [2], almost 30% of the diseased cattle showed abnormally high CSF S-100B concentrations. It remains unexplained why those cattle without apparent neurological signs showed an increased level of S-100B. In contrast, although the concentration of this protein tends to be increased in patients with meningitis [5, 8], we failed to confirm such an increase in our bovine case. We were unable to identify any association between disease type and an increased level of S-100B. Green et al. [2] reported that when compared with non-BSE diseased cattle, only 50% of animals with BSE developed abnormally increased S-100B.
concentrations. The concentration of S-100B may be affected by various factors such as the severity of brain damage, the interval between the damage onset and CSF sampling, or the method used for sampling. Further research will be needed to clarify the reason for the increased level of S-100B in cattle and whether measurement of CSF S-100B concentration is useful in veterinary neurological diagnosis.

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