scivac
SOCIETÀ CULTURALE ITALIANA
VETERINARI PER ANIMALI DA COMPAGNIA
SOCIETÀ FEDERATA ANMVI

in collaborazione con

RICHIESTO ACCREDITAMENTO

scivac

56th INTERNATIONAL CONGRESS

organizzato da certificata ISO 9001:2000

RIMINI 1st-3rd June 2007

PALACONGRESSI DELLA RIVIERA DI RIMINI

INFORMATION
SCIVAC Secretary
Palazzo Trecchi, via Trecchi 20 Cremona
Tel. (0039) 0372-403504 - Fax (0039) 0372-457091
commscientifica@scivac.it www.scivac.it

In: 50° Congresso Nazionale Multisala SCIVAC, 2005 – Rimini, Italia

Cerebrospinal Fluid Assessment in Dogs and Cats

William Vernau BSc, BVMS, DVSc, PhD, Diplomate ACVP Assistant Professor of Clinical Pathology, Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine, UC Davis, Davis, CA. USA

The analysis of cerebrospinal fluid (CSF) has been described as the central nervous system equivalent of the complete blood count (CBC), and the comparison is appropriate.[1] A CSF analysis provides a general index of neurologic health and often provides evidence of the presence of disease. Given the restricted number of parameters that are measured in routine CSF analysis, the possible alterations of CSF are relatively limited compared to the variety of neurologic diseases that occur. Therefore, similar to a CBC, CSF analysis has reasonable sensitivity but low specificity. Additionally, the type and degree of CSF abnormality is dependent not only on the cause and severity of the disease process, but also on the location of the lesion; meningeal and ventricular / paraventricular diseases generally produce greater abnormalities in CSF than deep parenchymal lesions. The presence of CSF abnormalities is also dependent on the collection site with respect to the lesion location: CSF collected caudal to a lesion is more likely to be abnormal.[2, 3] It is also important to note that previous therapy may also affect the type, degree and duration of CSF abnormalities. CSF analysis only occasionally provides a specific diagnosis – for example, if infectious agents (bacteria, fungi, protozoa) or overtly neoplastic cells are observed. The primary function of CSF analysis in most instances is to assist in the diagnostic process by **excluding** the likelihood of certain diseases being present. As is the case with all tests that have relatively low specificity, CSF analysis is only useful when the results are correlated with the history, clinical findings, imaging studies and ancillary laboratory tests.

CSF IN HEALTH AND DISEASE

Many analytes have been measured in CSF. However, from a diagnostic perspective, the most useful things to measure in CSF are a total nucleated cell count and differential cell count, total protein concentration and cytologic examination. Normal nucleated cell counts for dogs are 0-2 cells/ul, with 3 cells/ul being in a “gray” zone and 4 cells/ul or more being abnormal.[1, 4] In cats, 3 cells or more /ul is considered abnormal.[4, 5] In dogs and cats, monocytic type cells predominate (unreactive macrophages), with lesser numbers of small, mature lymphocytes.[2, 5] Rare neutrophils can be seen in normal CSF but should not exceed 1-2 % in non-blood contaminated CSF. Large foamy activated macrophages or phagocytes are not seen in normal CSF and their presence is non-specific evidence of an inflammatory disorder.[6] However, low numbers of large foamy activated macrophages may be seen as an artefact of cytocentrifugation. Plasma cells are not seen in normal CSF either.[4] In animals, plasma cells may be observed in the CSF in various diseases, including distemper, other viral meningitis, rabies, granulomatous meningoencephalitis (GME), neoplasia and abscessation.[4] Therefore, although the presence of plasma cells in CSF is abnormal, there is little specificity to this finding. Similarly, reactive lymphocytes are not found in normal CSF, but their presence has no specificity.[4]

Measurement of total protein concentration in CSF is important in the diagnosis of neurologic disease. In our laboratory, the protein concentration of CSF in normal dogs and cats is < 30 mg/dl (0.3 g/L). Although the total protein concentration in CSF does increase along the neuraxis from rostral to caudal (ie. lumbar puncture CSF has a higher protein concentration than cerebellomedullary cisternal CSF), this reference value tends to be used regardless of the origin of the CSF (cisternal or lumbar puncture).[4, 7, 8] This may reduce the sensitivity of diagnosis of cisternal CSF, but good studies are not available to confirm this.

A normal CSF analysis does NOT exclude the presence of disease. However, abnormal CSF findings always indicate the presence of pathologic abnormality. An increase in the cellularity of CSF is termed pleocytosis. The proportions of the different cell types present in CSF in disease vary according to the nature of the disease process and provides useful information for the differential diagnosis of neurologic disease.

Bacterial Disease

A marked pleocytosis with neutrophil predominance is often present in bacterial meningitis.[9] Total leukocyte counts in excess of 2000 cels/ul are often encountered in these diseases and may even exceed 10,000 cells/ul. Observation of bacteria or a positive culture confirms septic meningitis. However, in my experience, bacteria are not commonly observed in the CSF of dogs and cats with confirmed septic meningitis and the neutrophils are frequently non-degenerate.

Fungal disease

Fungal infection of the CNS is relatively uncommon, although *Cryptococcus neoformans* has a predilection for the CNS. The CSF associated with neural cryptococcosis is quite variable. Counts vary from marginally to markedly increased and are typically mixed with a majority of neutrophils.[4] However, mononuclear CSF has been reported, as has predominantly eosinophilic fluid.[4] Cryptococcal organisms are commonly seen in the CSF and cultures are often positive. Latex agglutination tests for cryptococcal antigen in the CSF may also be positive. The reports of the CSF abnormalities associated with neural aspergillosis, blastomycosis, coccidioidomycosis or histoplasmosis are sporadic. With these mycoses, the CSF tends to have a mixed pleocytosis of neutrophils, macrophages, lymphocytes and eosinophils (often in this order of frequency).

Protozoal Disease

Both *Neospora* and *Toxoplasma* can invade the CNS, usually resulting in a multifocal, granulomatous meningoencephalitis. *Neospora* seems to have a greater predilection for the central nervous system than *Toxoplasma*, particularly in young dogs.[10] The CSF associated with neural protozoal infections typically has a mild to moderate, mixed pleocytosis with monocytes, lymphocytes, neutrophils and eosinophils present in order of decreasing percentage.[4] However, I have seen eosinophil predominance in some cases of confirmed Neosporosis.

Viral Disease

The CSF associated with viral disease is typically characterized by nonsuppurative inflammatory changes. The cell count and protein concentration are often mildly to moderately elevated. The pleocytosis may be entirely mononuclear (mostly small lymphocytes with lesser numbers of macrophages) or mixed with a predominant mononuclear component. Rarely, especially in the early stages of disease, neutrophils may predominate.

Granulomatous meningoencephalitis (GME)

The CSF associated with GME is usually abnormal. The total nucleated cell count is moderately to markedly elevated. Typically, small, mature lymphocytes predominate, with macrophages and neutrophils making up the remainder in about equal percentages.[11] However, there is some variability in the cytologic findings and the leukocyte differential can range from 95% neutrophils to 100% mononuclear cells.

Necrotizing encephalitis of Pug dogs, Maltese dogs, Yorkshire terriers and Chihuahuas

A necrotizing encephalitis of unknown cause has been identified in Pugs, Maltese, Yorkshire terriers and Chihuahuas.[4] The lesions are similar in each breed although the distribution of lesions varies, being multifocal and brainstem in the Yorkshire terriers and diffuse and cerebral in the other breeds. A marked, predominantly lymphocytic, pleocytosis is typical of the disease.

Steroid-responsive meningitis / arteritis

This disease has been reported in Beagles, Bernese mountain dogs, German short-haired pointers and sporadically in other breeds.[12] A marked neutrophilic pleocytosis is characteristic of this disease, provided it has not been attenuated by therapy.

Feline Infectious Peritonitis (FIP)

FIP coronavirus may cause a multifocal, pyogranulomatous meningitis, choroids plexitis and ependymitis. The CSF has a moderate to marked pleocytosis and increase in protein concentration (> 2g/L) that is characteristic.[13] The pleocytosis is dominated by non degenerate neutrophils and lesser numbers of activated macrophages, appearing pyogranulomatous.

Disk herniation / trauma

CSF abnormalities associated with trauma and / or compression are variable, depending on the rate at which the insult developed, the severity of the insult, the location of the lesion (and site of CSF collection), the time between insult and collection and the maintenance or progression of the insult. With acute trauma, there is typically suppurative inflammation and hemorrhage. With spinal cord injury, lumbar CSF is more consistently abnormal than cerebellomedullary CSF.[3] Chronic disease tends to produce milder change that is typically more mononuclear. Chronic type I disk disease can occasionally result in moderate lymphocytic inflammation (unpublished observations).

Neoplasia

The CSF changes associated with neoplasia are variable, reflecting the variety of tumors, locations and tissue reactions to the disease. The most common abnormality is increased protein concentration, with choroid plexus tumors producing the most marked increases.[4] Pleocytosis may occur, and is typically mononuclear, although meningiomas may have >50% neutrophils.[14] The observation of neoplastic cells in the CSF from animals with central nervous system neoplasia is rare but somewhat method dependent.[4] Neoplastic cells are more likely to be seen in the CSF with lymphoma and meningeal tumors than gliomas, which often don't reach the meninges or ventricular system. When neoplastic cells are present, determining their origin can be difficult. Immunocytochemistry is a very useful adjunct in these instances.[4]

Polymerase Chain Reaction (PCR)

PCR methodology has the potential to dramatically increase the diagnostic sensitivity and specificity of CSF. It is uniquely suited to the small volumes and low cell numbers frequently present in CSF. In people, it has been used to confirm the presence of lymphoma (via PCR detection of clonal antigen receptor gene rearrangements) and a variety of infectious agents.[4, 15] In veterinary medicine, PCR has been used to detect several infectious agents in CSF, including sarcocystis neurona, toxoplasma and listeria.[16, 17]

REFERENCES – available on request: wvernau@ucdavis.edu