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Cns inflammatory (UK) problems: the neurologist's viewpoint, clinical approach and treatment

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INFECTIOUS OR NON-INFECTIOUS? THAT IS THE QUESTION...

Inflammatory CNS diseases are an extremely heterogenous group of diseases as far as their causes, pathological process involved and lesion distribution is concerned. Two distinct groups can be made: the meningoencephalomyelitis of unknown etiology and the infectious meningoencephalomyelitis.

Meningoencephalomyelitis of unknown etiology in the dog is commonly attributed to granulomatous meningoencephalomyelitis (GME) and the breed-specific meningoencephalitides. GME is an angiocentric, mixed lymphoid, infiltrative process that predominantly affects the CNS white matter and leptomeninges. The clinical signs are variable and reflect the morphologic type of disease and the site of the lesion. Three forms of GME have been described based on both morphological and clinical neurological abnormalities: disseminated, focal, and ocular. The disseminated form typically manifests with acute onset of rapidly progressive clinical signs suggestive of multifocal CNS disorder whereas focal GME is associated with clinical signs suggestive of a single space-occupying mass with an insidious onset and slowly progressive course. Ocular form of GME manifests with acute onset of visual impairment and dilated non-responsive pupils caused by optic neuritis. Dogs with the ocular form can subsequently develop CNS lesions. The cause of GME is not known with immune-mediated, infectious and neoplastic causes proposed as possible causes. Current thoughts are a non-specific neurotropic response of the canine immune system and multiple etiologies may be involved. The lesions associated with the breed-specific meningoencephalitides differ from those in GME in distribution and severity. Pug dog and Maltese encephalitis is characterized by extensive necrosis and non-suppurative inflammation of the cerebral gray and subcortical white matter (necrotizing meningoencephalitis or NME). The neurological signs are acute and progressive and reflect mostly forebrain disorder with seizures observed in most dogs. A necrotizing encephalitis is also described in Chihuahua, Shi Tzu and Yorkshire Terrier and characterized histologically by multifocal area of extremely severe mononuclear inflammation surrounding large malacic gliotic center predominantly affecting the brainstem and periventricular cerebral white matter (necrotizing leukoencephalitis or NLE). Brainstem signs with central vestibular dysfunction predominate frequently. A genetic basis is probable. Without histopathology, the antemortem diagnosis of GME or breed-specific meningoencephalitides is often presumptive. The terminology meningoencephalitis of unknown etiology should therefore be used for cases in which brain tissues have not been subject to histopathological evaluation.

Encephalitis and meningitis often exist concurrently in dogs and cats with infection of the central nervous system. Numerous infectious agents have been incriminated and include viral (distemper, rabies, parvovirus, pararinfluenza, herpes, feline leukaemia, feline immunodeficiency virus), bacterial (from direct inoculation, embolism from other source or extension of bacterial processes), rickettsial (Ehrlichia, Rocky Mountain spotted fever), protozoal (Toxoplasma, Neospora), fungal (Blastomycosis, histoplasmosis, cryptococcosis, aspergillosis, coccidiomycosis) and spirochaetes (Lyme disease, leptospirosis) agents. Adding to this list, a number of parasites have been reported to affect the brain during aberrant migration (Toxocara, heartworm,Cuterebra larvae). Their incidence depends mainly on geographic location. Disease tends to be acute on onset and progressive, with often a multifocal or diffuse distribution of lesions seen within the CNS.

DIAGNOSIS

A female predisposition for GME has been reported and the disease is most common in young to middle-aged dogs. Most cases of breed-specific meningoencephalitides described so far occurred in young and adult (6 months to 7 years) with no gender predisposition. Antemortem diagnosis of GME or breed-specific meningoencephalitides (NME, NLE) often lacks histopathological confirmation. Extraneural signs such as hyperthermia are rare. Blood examination may be normal or reveal a stress leukogram. CSF findings include a pure mononuclear pleocytosis or a mixed cell population (particular in acute cases). Although CSF mononuclear pleocytosis is a sensitive indicator for CNS inflammation, it cannot discriminate between immune-mediated, infectious, and neoplastic differential considerations for canine meningoencephalitis. The absence of CSF abnormality does not rule-out the possibility of GME, particularly in dogs pre-treaded with corticosteroids or where the lesions are not in close proximity to the ventricular system and subarachnoid space. CSF findings in dogs with NME or NLE reveal as well a moderate pleocy-

tosis with mononuclear cells or mixed cell pleocytosis and mild to marked elevation of protein concentration. Imaging findings in meningoencephalitis of unknown etiology are non-specific but can help to support the suspected clinical diagnosis. CT-scan may reveal hyperdense lesions after injection of contrast medium intraveinously. The most consistent MR imaging findings in dogs with multifocal form of GME are the presence of multiple hyperintense T2W or FLAIR lesions scattered throughout the cerebral white matter. Contrast-enhancement may or may not be present. Central nervous system lymphosarcoma, and less commonly glial neoplasms and metastatic neoplasia can present with similar clinical and imaging findings and should therefore enter in the differential diagnosis of this form of GME. The focal form of GME presents on CT or MR imaging as a non-specific single space-occupying mass. The more characteristic distribution of the lesions observed in breed-specific meningoencephalitis (NLE or NME) may aid in the imaging diagnosis of these conditions. As such, diagnoses of "GME" or "breed-specific meningoencephalitis" made from clinical signs, CSF, imaging and negative infectious disease titers are presumptive and histologic examination of the nervous tissue (brain biopsy or postmortem) is required for a definitive diagnosis. Combined intrathecal and systemic high IgA levels are also very useful for the diagnosis of aseptic suppurative meningo-arteritis.

Blood examination findings with infectious disease can range from leucocytosis with neutrophilia and left shift with bacterial infection, eosinophilia with increased muscle enzymes with protozoal diseases, lymphopenia with eventually leucopenia or leucocytosis with canine Distemper, hyperglobulinemia with feline infectious peritonitis. CSF and infectious titre (serology and/or PCR) performed on serum and/or CSF are the most reliable antemortem diagnostic test for identifying infectious CNS diseases. CSF findings in canine Distemper range from little changes in the acute phase to mononuclear pleocytosis and increased protein content in chronic inflammatory form. A marked neutrophilic pleocytosis is usually present with bacterial infection, feline infectious peritonitis (associated with marked increase in protein content) or aseptic suppurative meingoarteritis. A mild mixed pleocytosis and increase protein is often seen with protozoal disease. Bacterial cultures of CSF and blood are indicated on suspicion of bacterial meningoencephalitis but are often unsuccesfull.

TREATMENT

Immunosuppressive doses of corticosteroids have been the mainstay of treatment for presumptive GME, aseptic suppurative meningo-arteritis and the breed-specific meningoencephalitides. Response to corticosteroids has frequently been reported as variable and temporary with animals often having a dramatic initial response, but relapses are common. Long-term, high-dose corticosteroids treatment commonly causes adverse effects such as gastrointestinal ulceration, pancreatitis and iatrogenic hyperadrenocorticism. Radiation, azathioprine, procarbazine, cytosine arabinoside and cyclosporine as sole agent or as an adjunctive treatment with prednisone have been reported to be effective in some dogs with GME. Combined trimethoprim-sulfonamide, pyrimethamine and/or clindamycin are indicated for protozoal disease. Treatment of bacterial infection consists of high doses of broad-spectrum antibiotics known to penetrate the blood brain barrier. Glucocorticoids may be indicated during the first 48 hours of treatment. Treatment of viral diseases such as canine distemper or feline infectious peritonitis is essentially palliative.

PROGNOSIS

The prognosis for long-term remission in proven cases of GME and the breed-specific meningoencephalitides has been reported as being poor. However, such reports have been limited to histopathologically confirmed cases of GME that died or were euthanized as a result of the severity of their disease, so the poor prognosis in these studies may be biased. Others have reported greater than one year survival in dogs with suspected GME treated with aggressive immunosuppression including prednisone and azathioprine. The prognosis of aseptic suppurative meningo-arteritis is good with an early aggressive and sustained therapy.

Bibliography

Adamo FP, O'Brien RT. Use of cyclosporine to treat granulomatous meningoencephalitis in three dogs. J Am Vet Med Assoc. 2004;225:1211-1216

Bailey CS, Higgins RJ. Characteristics of cerebrospinal fluid associated with canine granulomatous meningoencephalomyelitis: a retrospective study. J Am Vet Med Assoc 1996;188:418-421

Braund KG, Vandevelde M, Walker, TL, et al. Granulomatous meningoencephalomyelitis in six dogs. J Am Vet Med Assoc 1978;172:1195-1200

Braund, K. G. Granulomatous meningoencephalomyelitis. J Am Vet Med Assoc 1985;186, 138-141

Cuddon, P. A., Coates, J. R. & Murray, M. New treatments for granulomatous meningoencephalomyelitis. American College of Veterinary Internal Medicine 2002

Cordy DR, Holliday TA. A necrotizing meningoencephalitis of pug dogs. Vet Pathol 1989; 26:191-194

De Lahunta A. Veterinary Neuroanatomy and Clinical Neurology. 2nd ed. Philadelphia: WB Saunders Co, 1983; 384-385

Dewey, C. W. Encephalopathies: disorders of the brain. In: A Practical Guide to Canine and Feline Neurology. Ed C. W. Dewey. Iowa State Press, Ames, Iowa. 2003;pp 99-178

Kipar A, Baumgartner W, Vogl C, et al. Immunohistochemical characterization of inflammatory cells in brains of dogs with granulomatous meningoencephalitis. Vet Pathol 1998; 35:43-52

Munana, K. R. & Luttgen, P. J. Prognostic factors for dogs with granulomatous meningoencephalomyelitis: 42 cases (1982-1996). J Am Vet Med Assoc 1998;212,1902-1906

Nuhsbaum, M. T., Powell, C. C., Gionfriddo, J. R. & Cuddon, P. A. Treatment of granulomatous meningoencephalomyelitis in a dog. Vet Ophthalmol 2002; 5, 29-33

Tipold, A., Fatzer, R., Jaggy, A., Zurbriggen, A. & Vandevelde, M. Necrotizing encephalitis in Yorkshire terriers. J Small Anim Pract 1993;34, 623-628

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