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MYELITIS AND MENINGITIS

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Inflammation of the spinal cord parenchyma and support structures is termed *myelitis*. Parenchymal involvement can be subdivided into inflammation of the gray matter, called *poliomyelitis*, and inflammation of the white matter, called *leukomyelitis*. Astrocytes, oligodendrocytes, blood vessels, and other support structures are often involved in the inflammatory process. The dura mater, arachnoid mater, and pia mater compose the meninges that surround the spinal cord. The pia and arachnoid layers are morphologically similar and compose the leptomeninges. The cerebrospinal fluid (CSF) is contained between the pia and arachnoid layers. The dura mater is the thick, tough collagen outer membrane. Inflammation of the meninges is termed *meningitis*. Most inflammatory diseases involve the brain, spinal cord, and associated membranes, resulting in a *meningoencephalomyelitis*. Table 1 lists the common causes of meningoencephalomyelitis in companion animals. This article focuses on the inflammatory diseases that principally involve the spinal cord and meninges.

CLINICAL FINDINGS

The clinical signs associated with meningitis/myelitis are predicated on the location of the affected spinal cord segment(s) and the histopathologic features and cause of the inflammatory process. Evidence of paraspinal discomfort, paraspinal muscle rigidity, and decreased vertebral mobility are cardinal signs of meningitis. The cervical region is most commonly involved, but any cord segment can be affected.

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VETERINARY CLINICS OF NORTH AMERICA: SMALL ANIMAL PRACTICE

Table 1. CAUSES OF MENINGOENCEPHALOMYELITIS IN DOGS AND CATS

<i>Viruses</i>	<i>Fungi</i>
Distemper (D)*	Blastomycosis (D)*
Feline infectious peritonitis (C)*	Cryptococcosis (C)*
Panleukopenia (C)	Aspergillosis
Rabies	Histoplasmosis
Herpes (D)	Phaeohiphomycosis
Parvovirus (D)	Coccidioidomycosis
Adenovirus (D)	
<i>Rickettsia</i>	<i>Protozoa</i>
Erlichiosis (D)*	Toxoplasmosis*
Rocky Mountain spotted fever (D)*	Neosporidiosis (D)*
<i>Bacteria</i>	<i>Parasites</i>
<i>Staphylococcus*</i>	Dirofilaria immitus
<i>Pasturella*</i>	Cuterebriasis
<i>Idiopathic</i>	<i>Algae</i>
Granulomatous	Protothecosis (D)
meningoencephalomyelitis (D)*	<i>Spirochetes</i>
Steroid-responsive	Lyme disease (D)
meningoencephalomyelitis (D)*	
Pyogranulomatous	
meningoencephalomyelitis (D)	
Nonsuppurative	
meningoencephalomyelitis	

*Causes meningomyelitis most commonly (see text).

D = Most commonly affects dogs; C = most commonly affects cats.

Additional features of meningitis include fever; a stiff, short-strided gait, and reluctance to walk.

Frank neurologic deficits can occur with myelitis. Decreased or absent postural reactions and segmental reflexes are noticed with poliomyelitis. The clinical signs associated with leukomyelitis range from ataxia to paralysis, with segmental reflexes often being exaggerated. The gait and reflex abnormalities can involve the thoracic limbs, pelvic limbs, or both, based on lesion localization (see the article entitled "Approaches to the Patient with Spinal Diseases"). The distribution of lesions in gray matter or white matter is determined largely by the causative agent. Spinal cord inflammation in companion animals most commonly results in leukomyelitis.

DIFFERENTIAL DIAGNOSES

The list of differential diagnoses is formulated from the history, signalment data, and results of the neurologic examination. Animals with meningitis/myelitis are typically young to middle-aged, with an acute, progressive course. A breed or sex predilection is not recognized. Evidence of a diffuse or multifocal localization on the neurologic examination is supportive of inflammatory disease.

The differential diagnoses for animals with evidence of meningitis (paraspinal discomfort and muscle rigidity; decreased vertebral mobility;

and stiff, short-strided gait) include intervertebral disc herniation, discospondylitis, spinal cord and vertebral neoplasia, and vertebral fractures. The list of differential diagnoses for leukomyelitis is similar to meningitis if meningeal involvement and pain are present. If pain is absent, the differential list would also include diseases that can produce clinical signs, ranging from ataxia to paralysis, with exaggerated spinal cord reflexes. The list can be prioritized based on signalment data. For example, cervical malformation/malarticulation (wobbler) is most likely to occur in giant breed dogs like the Great Dane and Doberman, atlantoaxial subluxation in miniature and toy breeds like the Chihuahua and Yorkshire Terrier, and degenerative myelopathy in the German Shepherd and Miniature Poodle. Poliomyelitis is uncommon in small companion animals. The differential list includes diseases that produce lower motor neuron signs such as tick paralysis, polyneuropathy, polyradiculoneuritis, botulism, fibrocartilaginous emboli, ischemic neuromyopathy, and spinal cord and peripheral nerve trauma.

VIRAL INFECTIONS

Canine Distemper

Canine distemper (CD) can involve the brain, spinal cord, and meninges. The exact mechanism governing the eventual distribution of lesions and course of the disease in dogs with CD are unknown, but it is believed to be an interplay between virus factors and host immune factors that range from immunosuppression to autoimmunity.^{20, 32, 35, 38} Infection of the central nervous system (CNS) with CD virus usually results in polioencephalomyelopathy and high mortality in young (neonate) dogs, whereas older dogs infected with CD virus have lower mortality and principally develop leukoencephalomyelopathy.³² Dogs with CD-induced meningitis or myelitis are typically mature; however, in addition to signs of meningomyelitis (paraspinal discomfort and muscle rigidity, decreased vertebral mobility, and ataxia to paralysis), these dogs often have additional CNS dysfunctions (e.g., vestibular dysfunction, blindness).

Confirmation of CD-induced meningitis or myelitis is achieved by ruling out other differential diagnoses. A gastrointestinal or respiratory illness that precedes evidence of multifocal neurologic dysfunction is suggestive of CD infection. A thrombocytopenia or lymphopenia may be noticed, but hematologic results are typically nondiagnostic. Fluorescent antibody (FA) testing for viral antigens in conjunctival smears can be positive in dogs with CD. False-positive and false-negative results, however, are common, and interpretation of FA test results should always be in association with the appropriate clinical neurologic signs. Dogs with CD-associated encephalitis can have electroencephalographic abnormalities characterized by increased voltage and decreased frequency with spike and sharp waves. Chorioretinitis charac-

terized by depigmentation and hyperreflectivity is noticed principally in dogs with CD-induced leukoencephalomyelopathy.³³

The most sensitive means of antemortem confirmation of CD virus meningoencephalomyelitis is by CSF analysis.^{1, 32, 33} Dogs with principally leukomyelopathy often have a lymphocytic pleocytosis (15 to 60 white blood cells (WBCs)/mm³; normal = 0 to 4 WBCs/mm³), increased total protein (35 to 55 mg/dL; normal = 20 to 25 mg/dL), and increased gamma globulin (9 to 11 mg/dL; normal = 5 to 7.5 mg/dL).³² CD virus antibody normally is absent in CSF and when present is highly diagnostic of CD virus infection of the CNS. A false-positive result can occur, however, if the CSF is contaminated by serum CD virus antibody following either iatrogenic or pathologic blood-brain barrier (BBB) disturbance. All CSF values are typically normal to below normal in young dogs with principally polioencephalomyelitis.^{32, 33}

Treatment of CD-induced meningomyelitis is symptomatic. The lymphocytic response noticed in CSF is found on histopathologic examination to extend into the subarachnoid spaces as a mononuclear inflammatory infiltration and into the spinal cord as mononuclear perivascular cuffing with attendant edema, gliosis, and microglial proliferation.³⁷ Prednisolone or prednisone can be administered to reduce inflammation. Treatment is generally long-term or continuous. Treatment starts at 1 to 2 mg/kg daily, divided into 12-hour doses. Typically signs improve within the first 24 to 48 hours of treatment. The dose is then decreased by 50% every 4 to 5 days until the lowest maintenance dose is determined. Long-term or continuous management is based on alternate-day therapy. The lowest daily maintenance dose or next higher dose is typically used.¹¹ Hemorrhagic gastroenteritis, colitis, pancreatitis, and hepatopathy are complications associated with glucocorticoid administration, especially at higher dosages. A combination of cimetidine (Tagamet), 4 mg/kg orally every 6 to 8 hours, followed in 2 hours by sucralfate (Carafate), 250 to 1000 mg orally, is recommended to prevent gastrointestinal complications.

The prognosis is poor for recovery in dogs with CD-induced neurologic dysfunction. Some dogs can be maintained on glucocorticoid therapy, but the disease is typically progressive, which necessitates an increase in medication or if seizures occur the addition of anticonvulsant medication. Euthanasia is advised for dogs with inexorable progression of clinical signs.

Feline Infectious Peritonitis

Feline infectious peritonitis (FIP) results in multiorgan system involvement following coronavirus infection. An effusive and non-effusive form occurs with a multifocal pyogranulomatous meningoencephalomyelitis typically associated with the non-effusive form. Affected cats are usually young and come from a cattery or multiple cat household. No sex predilection exists, and purebred cats are more

commonly affected. The cerebral cortex, cerebellum, brain stem, spinal cord, and associated meninges are consistently involved, producing seizures, ataxia, vestibular dysfunction, and varying degrees of paresis and paraspinal discomfort. Nonneurologic signs include anterior uveitis, depression, anorexia, and pyrexia. An acute onset and progressive course are typically noticed.^{17, 19, 28}

FIP is suspected in young cats with evidence of progressive multiorgan system involvement, including evidence of multifocal CNS involvement. Differential diagnoses include systemic diseases such as toxoplasmosis, systemic fungi, feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infections, and congenital storage diseases. A definitive antemortem test for FIP is not available. The diagnosis can be aided by evidence of lymphopenia and nonregenerative anemia. Hypergammaglobulinemia often occurs. Increased serum FIP titers can indicate CNS infection; however, benign enteric coronavirus antibody may cross react, yielding a false-positive result. Evidence of an abnormal electroencephalogram (EEG) and anterior uveitis is supportive of FIP. CSF analysis yields the most reliable antemortem evidence of FIP infection of the CNS. CSF protein is typically elevated greater than 200 mg/dL (normal = 6 to 36 mg/dL). The total WBC count is markedly elevated (500 WBCs/mm³; normal = 0 to 2 WBCs/mm³) with a severe neutrophilic pleocytosis. Compared with cats with other CNS viral infections, cats with FIP had markedly elevated values for CSF protein and WBCs.²⁸ CSF titers may be more sensitive compared with serum titers in diagnosing FIP infection of the CNS; however, FIP infection cannot be ruled out with a negative titer.

There is no effective therapy for FIP, and the prognosis is poor. Many cats with FIP have concurrent infections with FeLV, FIV, and toxoplasmosis, making the clinical signs and prognosis more grave.^{17, 19, 28}

IDIOPATHIC INFLAMMATIONS

Granulomatous Meningoencephalomyelitis

Granulomatous meningoencephalomyelitis (GME) is an idiopathic disease of the CNS characterized by varying numbers of histiocytes (macrophages), lymphocytes, monocytes, and plasma cells arranged in a whorling perivascular pattern. The disseminated and focal forms are most common, but an ocular form of GME can occur. In disseminated GME, white matter of cerebrum, caudal brain stem, cerebellum, and cervical spinal cord are involved most commonly. Focal lesions are most common in the pontomedullary region and cerebral white matter and often have accompanying disseminated lesions.^{2, 36} Adult female purebred dogs develop GME most often, but dogs of any age, breed, and sex can be affected. Disseminated GME is usually acute in onset and progression compared with a slower onset and progression in the

focal form. Clinical signs of GME are variable, but ataxia and cervical discomfort are most common with spinal cord involvement. Vestibular dysfunction, blindness, seizures, and behavior change can occur with GME-induced encephalitis.³¹ Pyrexia, conjunctivitis, and respiratory and gastrointestinal abnormalities can precede the neurologic dysfunctions in some dogs. The cause of GME is unknown. Evidence to suggest an infectious or immune-mediated origin has been found, but a definitive cause awaits further investigation.^{34, 36}

Common differential diagnoses for GME-induced meningomyelitis include degenerative disc disease, cervical malformation/malarticulation, neoplasia, discospondylitis, trauma and other causes of meningomyelitis. A definitive antemortem test for focal spinal cord GME is not available. Dogs with disseminated GME can have a predominately neutrophilic leukocytosis in blood; however, with either form, the most reliable means of establishing an antemortem diagnosis is CSF analysis. A pleocytosis ranging from 6 to 600 WBC/mm³ can be noticed in CSF. Neutrophils predominate in acute or chronic-active disorders, whereas a mononuclear response, largely lymphocytes, monocytes, and occasionally plasma cells, is more common in chronic GME. Total CSF protein is elevated commonly (40 to 400 mg/dL).^{2, 31} BBB disturbance with marked elevation in gamma globulin values is noticed on CSF electrophoresis of dogs with acute GME. Most dogs with chronic GME have evidence on CSF electrophoresis of diminished BBB disturbance compared with dogs with acute GME; however, gamma globulin values remain elevated.³¹

Prednisone (1 to 2 mg/kg/day) can resolve or improve the clinical signs associated with meningomyelitis; however, the course is progressive in most dogs even with treatment.²⁹ The glucocorticoid dose can be lowered, with the ultimate goal of alternate-day therapy, after the clinical signs stabilize. A rapid decline or abrupt discontinuation of the glucocorticoid dose results in rapid clinical deterioration. The prognosis for permanent recovery is poor.^{2, 29}

Steroid-Responsive Suppurative Meningomyelitis

A suppurative meningitis responsive to glucocorticoid treatment has been reported.²⁵ Most cases involve young, large dogs but no breed or sex predilection is recognized. Except for a leukocytosis in blood, the CNS appears to be the only organ system affected. An immunopathogenesis is suspected based on the absence of an identifiable cause and the response to glucocorticoid therapy. Neurologic deficits are rare except in advanced cases. High fever; paraspinal discomfort; a stiff, short-strided gait; and reluctance to walk are the most common clinical signs.

This condition is considered by many veterinarians to be the most likely diagnosis in young, large dogs with signs of meningomyelitis.^{7, 25, 27} Additional considerations have been discussed (see under "Differ-

ential Diagnoses’’). A definitive antemortem test for suppurative meningitis is not available. A neutrophilic pleocytosis and elevated total protein is noticed in CSF; however, results of blood and CSF cultures are negative.²⁵

Prednisone (2 to 4 mg/kg/day orally) is initially administered. Following a favorable response, the treatment regimen is modified over 1 to 2 months to an alternate-day therapy and reduced dose. Therapy should continue for 4 to 6 months. Clinical signs resolve during treatment, and in most dogs medication can be discontinued. Clinical signs can recur in some dogs if the glucocorticoid is discontinued or reduced too rapidly. If this occurs, the initial dose of prednisone is readministered, and after a favorable response the glucocorticoid dosage is reduced more slowly. The prognosis for full recovery is excellent.²⁵

A more advanced meningitis with myelitis and encephalitis has been recognized in Beagles, German Shorthaired Pointers, Bernese Mountain Dogs, and sporadically in other breeds.^{14, 16, 23, 24} Affected dogs are generally between 3 and 18 months of age and initially demonstrate the cardinal signs of meningitis. As the myelitis ensues, gait and reflex abnormalities indicative of the affected spinal cord segment develop. Blindness and seizures can occur with encephalitis.

CSF findings are similar to dogs with suppurative meningitis except for more elevated values. An extensive suppurative leptomeningitis with severe arteritis and fibrinoid necrosis of vessel walls has been reported at necropsy. The degree of myelitis and encephalitis may be related to the duration of the untreated disease course.²³ Treatment with prednisone, as described for suppurative meningitis, is indicated; however, most affected Beagles and some dogs of other breeds do not respond to medication and must be euthanized despite aggressive therapy. Overall the prognosis is guarded to poor for dogs affected severely.

RICKETTSIAL INFECTIONS

A meningoencephalomyelitis can occur in dogs subsequent to infection by *Rickettsia rickettsia* and *Ehrlichia canis*, causing Rocky Mountain spotted fever (RMSF) and ehrlichiosis, respectively. Ticks serve as the reservoir and vector for both diseases. There is no sex, breed, or age predilection. In the acute phase, both diseases produce an immune-mediated vasculitis in multiple organs involving capillaries, venules, small veins, and arterioles with attendant inflammation and necrosis.^{12, 39} Neurologic abnormalities, including hyperesthesia, cervical rigidity, ataxia, paresis-to-paralysis, vestibular dysfunction, and seizures have been reported to occur in approximately 30% of dogs affected with either disease. Nonneurologic signs include fever, depression, anorexia, and lymphadenopathy. Petechial hemorrhages or other signs of hemorrhagic diathesis are uncommon in both diseases but have been reported more frequently in ehrlichiosis.¹²

Anemia, thrombocytopenia, and hypoalbuminemia occur commonly in both diseases, whereas leukopenia and hyperglobulinemia are more common in ehrlichiosis, and leukocytosis is more common in RMSF.¹² A mild to moderate elevation in CSF protein and WBCs indicates CNS involvement. Neutrophils and lymphocytes are reported to be the most common cell types in CSF of dogs affected with RMSF and ehrlichiosis, respectively; however, this observation was based on a small number of cases.¹² Serologic testing is the mainstay of diagnosis. A single positive IgG titer is sufficient to diagnose ehrlichiosis, whereas a fourfold or greater rise in titer is needed to confirm RMSF.¹² In both diseases, serum titers rise rapidly despite concurrent antibiotic therapy. The diagnosis of RMSF may also be confirmed on skin biopsy specimens by direct immunofluorescent testing.⁴

Tetracycline (22 mg/kg orally every 8 hours) is effective in most cases of acute RMSF and ehrlichiosis. Doxycycline (5 mg/kg orally every 12 hours) and chloramphenicol (15 mg/kg orally every 8 hours) achieve higher concentrations in the CSF and may also be useful in cases with CNS involvement. Most affected dogs improve within 24 to 48 hours of starting treatment and have a good prognosis for recovery.¹¹ Recovery is predicated on the return to normal of clinical and hematologic abnormalities with concurrent declines in antibody titers. Antibody titers decrease in infected dogs typically after 6 to 10 months. Severely affected animals will have a slow recovery, and some animals will have permanent neurologic disabilities. Immune-mediated sequelae may cause neurologic dysfunction in some affected dogs⁵; therefore the administration of immunosuppressive drugs (prednisone, 1 mg/kg slowly tapering to 0.5 mg/kg orally once daily for 2 to 15 months) in conjunction with tetracycline therapy has been suggested. Veterinarians are reminded that immunosuppressive therapy in rickettsial infections is controversial, and the administration of immunosuppressive drugs may worsen the clinical condition.

BACTERIAL INFECTIONS

Bacteria infect the meninges of the CNS typically through hematogenous spread following systemic infections (particularly heart, lungs, liver, and bone) or direct spread from sinuses, ears, penetrating skull fractures, and iatrogenic contamination (e.g. spinal needles).^{3, 21} Affected animals are typically adult, but no breed or sex predilection is noticed. The clinical signs are predicated on the initial site of infection and the clinical course. Evidence of brain stem and cerebral involvement is most common because of the typical routes of infection (i.e., sinuses, ears, skull fractures); however, the cardinal signs of spinal meningitis may occur alone or in conjunction with higher CNS involvement. Evidence of a meningoencephalomyelitis is noticed if the infection spreads to involve the CNS parenchyma.

Staphylococcus aureus, *Staphylococcus epidermidis*, *Pasteurella multocida*,

and *Pasteurella* species cause bacterial infection of the CNS most commonly; however, infection by other organisms is possible although the overall prevalence of CNS bacterial infection in small domestic animals is low.^{11, 21} Polymicrobial infection of the CNS in dogs and cats by anaerobic bacteria (including *Bacteroides*, *Fusobacterium*, *Peptostreptococcus*, and *Eubacterium*) has been reported recently.⁸

Nonneurologic signs may include evidence of organ system involvement remote from the CNS: specifically dyspnea, coughing, and lassitude with cardiopulmonary involvement; head shaking and ear scratching with ear involvement; naso-ocular discharge and sneezing with sinus involvement; and anorexia, vomiting, and jaundice with hepatic involvement. Fever, shock, hypotension, and disseminated intravascular coagulation may occur.²³

Diagnostic tests to confirm involvement of organ systems remote from the CNS are ordered based on the results of the history and physical examination. In all cases of suspected bacterial meningoencephalomyelitis, the minimum database should include results of complete blood count, serum biochemistry, urinalysis, electrocardiogram, thoracic radiographs, and bacterial cultures of blood and urine. Ophthalmic and otic examinations, skull radiographs (including x-ray computed tomography or magnetic resonance imaging), abdominal radiographs, and ultrasonography of the abdomen and thorax may help identify a specific infection site.

CSF analysis and culture are required to confirm bacterial infection of the CNS. Increased protein and a pleocytic neutrophilia are noticed typically on CSF analysis. The incidence of positive cultures of bacteria from CSF is much lower in dogs compared with humans.^{11, 23} The cause of this disparity is unknown but may be related to the small volume of CSF typically available from dogs for culture. In all cases, aerobic and anaerobic cultures of CSF should be performed.

Treatment is based on results of CSF culture and sensitivity. Therapeutic strategies include administration of high concentrations of an antibacterial drug that is known to cross the BBB and CSF-brain barrier and to which the organism is susceptible. The drugs of choice to treat CNS bacterial infections are chloramphenicol, sulfonamides, trimethoprim, and cephalosporins. In the presence of inflammation, ampicillin and penicillin also reach adequate concentrations in the CNS. A bactericidal drug that can enter the CNS and to which the organism is susceptible should be used whenever possible. Although chloramphenicol readily penetrates the BBB, the use of this bacteriostatic drug may lead to relapses.^{11, 23} Because chloramphenicol can inhibit the hepatic metabolism of phenobarbital and diphenylhydantoin, resulting in toxic serum levels of these anticonvulsants, the concurrent use of these drugs is done with caution.²³

Therapy may begin before culture results are available. Intravenous therapy is recommended to maintain high serum drug concentrations. *Staphylococcus* is presumed, and ampicillin (5 to 10 mg/kg intravenously every 6 hours) is administered unless Gram's stain indicates a gram-negative organism. High doses of ampicillin, sulfonamides, chloram-

phenicol, or intrathecal gentamicin appear to be effective for the treatment of gram-negative bacterial infections of the CNS.²³ Moxalactam and cefotaxime are also effective against gram-negative bacteria, but the costs of these newer cephalosporins may be prohibitive in larger dogs. The use of glucocorticoids in animals with bacterial infection of the CNS is controversial, and treatment with osmotic agents for any attendant CNS edema is recommended.

Treatment response is based on resolution of clinical signs and a negative CSF culture. Oral antibiotics may be administered after the animal has demonstrated adequate response to intravenous therapy. Treatment should continue for 2 to 4 weeks beyond clinical improvement. The prognosis varies with the duration and severity of the bacterial infection.^{11, 23} Most patients will respond well to the appropriate management.¹¹

SYSTEMIC FUNGAL INFECTIONS

Several species of fungi can produce CNS mycosis (see Table 1). Infectious fungi have a worldwide distribution with some demonstrating endemicity. In the United States, histoplasmosis is endemic in the Central Mississippi River Valley, the Ohio River Valley, and areas along the Appalachian Mountains³⁰; blastomycosis is endemic in the Mississippi, Missouri, and Ohio River Basins²⁶; and coccidioidomycosis is endemic in the Lower Sonoran life zone of the southwest.²² Most fungi that infect domestic animals are saprophytic soil organisms. The routes of infection are typically by inhalation or ingestion. Most fungi are opportunistic organisms, and animals with fungal infections are usually immunosuppressed (e.g., young animals, concurrent infections, or immunosuppressive drug therapy²³). Affected animals have systemic involvement, typically involving the lungs, intestines, lymph nodes, bone, heart, liver, skin, and eyes. Dissemination to the CNS is by hematogenous or lymphatic routes usually; however, infection may also reach the CNS by direct route (e.g., from nasal chambers, middle or inner ear). *Cryptococcus neoformans* and to a lesser extent *Blastomyces dermatitidis* have a predilection for CNS tissues and account for the majority of CNS fungal infections in small domestic animals.¹¹

The mycotic agents produce a disseminated granulomatous meningoencephalomyelitis. Animals with meningomyelitis have clinical neurologic signs that range from cervical discomfort to paralysis depending on the severity of the mycotic infection; however, more commonly vestibular dysfunction and seizures accompany the meningomyelitis, indicating multifocal CNS involvement. Occasionally the clinical signs indicate a more focal disease process. Animals with fungal disease are often systemically ill with evidence of fever, weight loss, diarrhea, anorexia, and lethargy or depression. In addition, animals with cryptococcosis often have a naso-ocular discharge, sneezing, peripheral lymphadenopathy, and multiple skin lesions of the head, whereas

animals with blastomycosis have ocular problems, inspiratory dyspnea or chronic cough, peripheral lymphadenopathy, and multiple skin lesions.²⁶

The strategies and diagnostic tests used to confirm mycosis of organ systems remote from the CNS are similar to those described for bacterial infections except for immunodiagnostic testing. Complement-fixation test, gel diffusion precipitin test, tube agglutination test, and fluorescent immunoassay are used to detect antibody to specific fungi in various body fluids. The latex agglutination test is used to detect fungal antigen in various body fluids, whereas the fluorescent-antibody test is used to identify fungal organisms in tissues and cultures. A titer in serum of greater than 1:8 or a rising titer on one or a combination of these tests would be diagnostic of systemic mycosis.¹⁸ Cytologic examination of body fluids or affected tissues can also confirm systemic mycosis.^{6, 23}

The definitive diagnosis of CNS mycotic infection is based principally on analysis of CSF. CSF protein is elevated, and a predominately neutrophilic pleocytosis is noticed typically. Fungal organisms in CSF are observed in approximately 60% of animals with CNS cryptococcosis,²³ whereas *Blastomyces dermatidis* and *Coccidioides immitis* are rarely noticed in CSF. In animals with CNS mycosis but without demonstrable fungal organisms in CSF, fungal culture and immunodiagnostic testing of the CSF can be performed. A provisional antemortem diagnosis of CNS mycosis can be determined by demonstrating fungal organisms in extraneural tissue or by positive serum titers in animals with clinical neurologic dysfunction but no evidence of mycosis in CSF.

The prognosis for animals with CNS mycosis is poor. Drugs used to treat systemic mycosis in extraneural tissues achieve inadequate concentrations in the CNS to be effective. Only one report of successful treatment for CNS mycosis in small pet animals has been reported.⁶ Amphotericin B (0.25 to 0.4 mg/kg intravenously in 500 mL 5% dextrose 1 to 3 times weekly for 21 days; dose and frequency were varied to maintain serum urea nitrogen, creatinine, and potassium concentrations in the normal range), 5-fluorocytosine (30 mg/kg orally every 6 hours for 42 days), and ketoconazole (20 mg/kg orally every 12 hours for 350 days) were administered to a 4-year-old Lhasa Apso diagnosed with cryptococcal meningoencephalitis. The dog had no detectable evidence of recurrence of cryptococcosis 5 years after cessation of therapy. End of treatment strategy was based on clinical response and normal results on repeated CSF analyses and serologic testing.

PROTOZOAL INFECTIONS

Toxoplasma gondii and *Neospora caninum* are cyst-forming coccidia. Dogs or cats may become infected with *T. gondii* by ingesting either the oocysts (found in feces of domestic cats or other *Felidae*) or tissue cyst (found in tissue of infected animals).⁹ Although morphologically similar to *T. gondii*, the life cycle of the newly recognized *N. caninum* is still unknown.¹⁰

T. gondii is a widely distributed protozoan that infects many species of animals; however, infection in most animals is inapparent. Clinical manifestations are similar for both organisms. Young animals are at risk to develop an acute, progressive phase that has a high mortality rate and may be related to an incompetent immune system.²³ Concurrent infections and immunosuppressive drug therapies may be associated with toxoplasmosis and neosporidiosis in adult animals. Both diseases can produce a disseminated meningoencephalomyelitis characterized by ataxia to paralysis, polymyositis, vestibular dysfunction, and seizures.^{10, 15} Animals with meningomyelitis may have paraspinal discomfort, muscle rigidity, and decreased vertebral mobility similar to other diseases producing meningomyelitis; however, unique features of these two diseases are pelvic limb hyperextension, decreased spinal cord reflexes, and muscle pain and atrophy.^{10, 15} Affected animals are typically less than 4 months of age with a chronic course. In these young animals, results of electromyography of axial and appendicular muscles are abnormal and can confirm a neuromuscular component of the disease. Clinical signs indicating multifocal CNS involvement, including cranial nerve dysfunction, occur more commonly in adult dogs.

Animals with CNS toxoplasmosis and neosporidiosis typically do not show evidence of systemic illness, despite the pantropic nature of both organisms. Affected animals will have hepatitis, pneumonia, myocarditis, and ocular lesions occasionally. Selection of appropriate diagnostic tests to confirm involvement of extraneural organ systems is based on results of the history and physical examination.

Antemortem confirmation of CNS toxoplasmosis and neosporidiosis can be difficult. Positive results on immunotesting of serum or CSF will help confirm the diagnosis. Immunotesting for both organisms is required because of the similarity in clinical features and lack of cross reactivity between the two organisms (i.e., a negative titer for toxoplasmosis does not rule out neosporidiosis, and vice versa).²³ A fourfold rise in IgG titer in two serum samples taken 2 weeks apart or a single elevated IgM titer is supportive of a diagnosis. The diagnosis of either disease should not be based on the results of a single IgG titer because of possible false-positive and false-negative results. Identification of the organism in tissue samples is direct evidence of infection. Skeletal muscle, as indicated by results of electromyography, should be examined for the antemortem confirmation of either diseases.

The prognosis for recovery in animals with CNS toxoplasmosis or neosporidiosis is poor.^{9, 10, 15} Sulfadiazine (31 mg/kg orally every 12 hours) and trimethoprim (6 mg/kg orally every 12 hours) are administered for 4 weeks. These drugs are considered useful in preventing development of intracellular tachyzoites; however, treatment is considered noneffective once neurologic signs have developed. Clindamycin (13.5 mg/kg orally every 8 hours) was effective in treating polymyositis attributed to *T. gondii*¹³; however, once developed, resolution of pelvic limb hyperextension is unlikely, regardless of treatment.

SUMMARY

Animals with meningomyelitis have clinical neurologic signs that typically range from paraspinal discomfort to tetraplegia; however, most affected animals also show evidence of multifocal CNS involvement with brain stem and cerebral cortical structures being affected most commonly. The cause, duration, and host response to the disease process will determine the clinical signs in individual animals. Confirmation of a specific causative agent is difficult, but CSF analysis and immunotesting of serum and CSF yield the most rewarding diagnostic results. Successful treatment is based on formulation of an appropriate and aggressive therapeutic regimen. In some diseases, no effective treatment is available, and some animals may develop permanent neurologic disabilities.

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