Neurologic diseases in New World camelids
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INTRODUCTION

Neurologic disease in New World camelids (NWCs) is common, but the available literature regarding these diseases is fairly scarce given the relatively new introduction of camelids into the veterinary community. As NWC practice expands and more research is conducted to better understand these unique animals and their diseases, our ability to diagnose and treat neurologic conditions will likely improve. That said, the following neurologic conditions in NWC are the most common and therefore the most well-studied, and will be discussed in further detail: Meningeal worm (*Parelaphostrongylus tenuis*), polioencephalomalacia, listeriosis, otitis media/interna, viral encephalitis, and heat stress. As in other species, neurologic disease in NWC may manifest in a variety of ways and may mimic musculoskeletal and metabolic conditions. A systematic approach to evaluation of neurologic NWCs is critical to determine neuroanatomic localization and to obtain an accurate diagnosis.

MENINGEAL WORM

Cerebrospinal nematodiasis caused by the nematode *Parelaphostrongylus tenuis* (*P. tenuis*) is commonly referred to as “meningeal worm.” It is a common cause of neurologic disease in NWCs in the Midwest and Eastern United States, where there are a large number of white-tailed deer (*Odocoileus virginianus*), which are the definitive host for *P. tenuis*. When NWC ingest infected gastropods (the intermediate host), the third stage larvae of *P. tenuis* (L3) migrates from the gastrointestinal tract to the spinal cord and typically causes clinical signs within two months. Once in the spinal cord, L3 mature into L4 and L5 (adults), and destroy white matter tracts (axons) in the process. Although uncommon, aberrant migration can damage spinal cord grey matter (neurons) and the brain.

Clinical signs of meningeal worm are variable, but typically include a wide-based hind limb stance and hind limb ataxia that may progress to recumbency. Most affected NWCs maintain a normal attitude, appetite and mentation. Atypical cases that involve parasite migration to the brain can lead to depression, head pressing, cranial nerve signs, seizures, or circling.

Antemortem diagnosis of meningeal worm is based on compatible clinical signs and CSF analysis. Collection of CSF in NWCs with meningeal worm from the lumbosacral space is more sensitive for elevations in protein and total nucleated cell count (TNCC) compared to the atlantooccipital space, and is easier to perform. Increased CSF eosinophil count is a consistent finding in affected NWCs and may be accompanied by increased protein and TNCC. A recent study found that observation of > 17% eosinophils among all nucleated cells in CSF had a sensitivity of 85% and a specificity of 92% for *P. tenuis* infection when using necropsy as a gold standard. In addition, > 1.4 eosinophils/μl of CSF had a sensitivity of 85% and a specificity of 96% for diagnosis of meningeal worm. Occasionally, NWCs with meningeal worm will have a peripheral eosinophilia, but this is not a consistent finding.

Treatment of meningeal worm includes fenbendazole at 50 mg/kg PO once daily for 5 days, non-steroidal anti-inflammatory drugs such as flunixin meglumine at 1.1 mg/kg IV every 12 - 24 hours, Vitamin E as an anti-oxidant and supportive care such as fluid therapy and nutritional support. Recumbent animals should be kept in deeply bedded stalls and encouraged to stand several times throughout the day. If they are unable to stand, passive range of motion and massage can be done, and a sling or float tank may be required. Animals that improve typically do so within a few days of starting treatment and may require several weeks to normalize, although some animals show residual neurologic signs due to neuron loss and CNS fibrosis despite effective anthelmintic therapy. Recumbent animals are less likely to recover fully, and neurologic deficits that are present 6 months after treatment are likely to remain.
A definitive diagnosis of meningeal worm can only be obtained postmortem. Parasite migration lesions are typically more extensive in the cervical spinal cord but can also be found in the thoracic and lumbar regions.\textsuperscript{2,3,6} Histologically, migration tracts are associated with asymmetric foci of rarefaction and neuroparenchymal necrosis with eosinophilic, lymphoplasmacytic or granulomatous inflammation.\textsuperscript{4}

**POLIOENCEPHALOMALACIA**

Although typically considered a disease of ruminants, polioencephalomalacia (polio) can also cause neurologic disease in NWCs. Like in ruminants, polio is thought to be due to thiamine deficiency and/or sulfur toxicity.\textsuperscript{11,12} Thiamine deficiency can result from excessive carbohydrate consumption because overgrowth of bacteria such as \textit{Clostridium sporogenes} and \textit{Bacillus thiaminolyticus} produce thiaminase, which breaks down thiamine and renders it unavailable to the animal. Plants such as bracken fern and horsetail also produce thiaminase, and overdosing of amprolium (coccidiostat) can inhibit active transport of thiamine and cause polio.\textsuperscript{7} The pathogenesis of sulfur toxicity likely involves bacterial metabolism of sulfur in C1 to hydrogen sulfide, which inhibits cytochrome oxidase and interrupts electron transport, leading to disruption of aerobic metabolism.\textsuperscript{13-15} Clinical signs of polio in NWCs include altered mentation, blindness, ataxia, circling, muscle fasciculations, opisthotonus, recumbency and seizures.\textsuperscript{12,16} Blood work is typically normal, although acidosis associated with carbohydrate overload or amprolium toxicity has been observed.\textsuperscript{7} CSF analysis is typically unremarkable. Treatment includes thiamine hydrochloride at 10 – 15 mg/kg intravenously or subcutaneously every 4 - 6 hours for several days, or until clinical signs improve.\textsuperscript{11} If given intravenously, thiamine should be diluted in isotonic fluids and given slowly to avoid adverse reactions. Response to treatment with thiamine can also aid in diagnosis. Supportive care including fluid and nutritional support are important. Prognosis for survival of polio in NWCs appears to be worse than in ruminants, with the majority of all reported cases resulting in death.\textsuperscript{11,12,16,17}

Necropsy findings include diffuse swelling and focal necrosis of the cerebral cortex. A distinct line of demarcation between necrotic and normal appearing cerebral cortical gray matter may be observed.\textsuperscript{12,16} Histopathology typically reveals laminar cortical necrosis, edema, congestion and perivascular hemorrhage.\textsuperscript{11,16}

**LISTERIOSIS**

Infection of the brain and meninges with \textit{Listeria monocytogenes} can occur in NWCs, although it does not occur as commonly as in small ruminants. Reported cases have involved crias from 7 days to 3 months of age that presented with acute onset neurologic signs.\textsuperscript{18,19} Most NWCs present with unilateral signs such as circling, leaning to one side, horizontal nystagmus and ataxia, but may also present with depression, recumbency, and seizures.\textsuperscript{7,18,19} Antemortem diagnosis relies on compatible clinical signs and supportive clinicopathological findings. Routine blood work may show mature neutrophilia and hyperfibrinogenemia, and CSF analysis may reveal increased protein and increased TNCC with intracellular bacteria present in neutrophils.\textsuperscript{18,19} An affected neonatal cria was found to be blood and CSF culture-positive for \textit{L. monocytogenes}.\textsuperscript{19} Treatment includes antimicrobials targeted at \textit{L. monocytogenes}, including oxytetracycline at 20 mg/kg IV once daily for 5 – 7 days, or high-dose potassium penicillin at 80,000 IU/kg IV every 6 hours for 5 – 7 days.\textsuperscript{7} Prognosis in NWCs is guarded as most cases fail to respond to treatment.\textsuperscript{7,18,19} Necropsy findings may include diffuse encephalitis or meningoencephalitis characterized by microabscesses consisting of neutrophils and glial cells.\textsuperscript{18}

**OTITIS MEDIA/INTERNEA**

Otitis media/interna can occur secondary to otitis externa or can be due to ascending bacterial infection via the Eustachian tubes. Studies regarding otitis in NWCs are lacking, but spinous ear ticks (\textit{Otobius megnini}) have been associated with cases in Texas, and \textit{Propionibacterium sp.} has been isolated from the ear canal of an affected animal.\textsuperscript{7,20} Other bacteria that have been isolated from otitis cases include \textit{Arcanobacter pyogenes},
Clinical signs of otitis externa include head shaking, head tilt, ear pruritis, and otic discharge, while otitis media/interna can result in facial nerve paralysis and vestibular signs. Signs of facial nerve paralysis include ear droop, lip droop, ptosis, lack of palpebral reflex, lack of menace response and corneal ulceration secondary to exposure keratitis and decreased lacrimation. Animals with vestibular signs may show nystagmus, ataxia, head tilt and circling.

CBC and serum biochemical analysis are typically normal in NWCs with otitis. Approximately half of the otitis cases in a retrospective study had elevated CSF protein concentration. Skull radiographs are useful if there are bony lesions, such as destruction of the tympanic bulla or temporomandibular joint arthritis. Computed tomography is often necessary to detect extensive soft tissue damage, such as tympanic bulla abscessation. Non-surgical treatment consists of broad spectrum systemic and topical antimicrobials, but surgical treatment is often required for otitis media/interna. A CT scan is often required prior to surgical intervention in order to assess the severity of tissue involvement. Subtotal ear canal ablation and lateral bulla osteotomy has been successful in treating otitis media in an 11-week old alpaca.

VIRAL ENCEPHALITIS

Viral encephalitides such as Eastern Equine Encephalitis (EEE), West Nile virus (WNV), equine herpesvirus-1 (EHV-1) and rabies have been reported in NWCs.

EEE

Eastern Equine Encephalitis virus is a member of the Togaviridae family (Alphavirus genus) and typically causes disease in horses and occasionally humans. An enzootic lifecycle in birds is maintained by the Culiseta sp. mosquito, although other mosquito species includes Aedes sp. and Ochlerotatus sp. can spread the virus to non-avian hosts. Like horses, NWCs represent a dead-end host and develop disease during the late summer to early fall. A retrospective analysis that surveyed several veterinary hospitals in the United States described 9 NWCs with EEE, all of which were from the East coast. Interestingly, 7 of 9 animals were under 1 year of age, and 4 of 9 were under 10 weeks of age. Clinical signs in these NWCs included fever, lethargy, ataxia, altered mentation, seizures, recumbency, vestibular signs, torticollis or opisthotonus, and cranial nerve deficits. CBC and serum biochemical analyses were unremarkable. Treatments consisted of intravenous fluid therapy, flunixin meglumine, corticosteroids, antimicrobials, fenbendazole, thiamine and Vitamin E supplementation. The mortality rate in this group was 89%, with a mean time to death of 2 days. EEE was confirmed by virus detection using IHC and PCR in CNS tissue. Necropsy findings included encephalitis with lymphocytic and neutrophilic inflammation. Neuronal necrosis and edema were present, and intracytoplasmic alphavirus inclusions were observed within neurons and glial cells.

The immunologic response of healthy alpacas to the bivalent killed EEE virus vaccine (Intervet, Inc., Millsboro, DE) was evaluated in 2009. Animals under 2 years of age achieved EEE antibody titers similar to that in horses, although 2 booster vaccinations were required. Therefore, it is recommended to vaccinate NWCs against EEE in endemic areas such as the East coast and Southeastern United States.

WNV

To date, there have been 6 reported cases of WNV in alpacas. WNV is a member of the Flaviviridae family (Flavivirus genus) and typically causes disease in horses and humans. Similar to EEE, birds are the natural reservoir and the disease is transmitted by mosquitoes (Culex sp.). Horses and NWCs are dead-end hosts and typically develop disease in late summer and early fall. Clinical signs in NWCs include fever, depression, altered mentation, hyperesthesia, torticollis, head tremors, ataxia, and recumbency. CBC and serum biochemical analyses are often normal, but CSF analysis may reveal increased protein and increased TNCC. Like with EEE, there is no specific treatment for WNV. The prognosis is poor despite supportive care. Necropsy findings typically reveal no gross lesions. Histopathology often reveals lesions similar to those in horses with WNV, including encephalomyelitis characterized by lymphocytic inflammation, multifocal axon
loss, and neuronal necrosis. Neutrophils are not typically seen, and lesions may be most severe in the brainstem and cervical spinal cord. A killed equine WNV vaccine (West Nile Innovator, Fort Dodge Animal Health, Fort Dodge, IA) was evaluated in alpacas and llamas. All animals received 3 vaccinations at 3-week intervals, with the vast majority demonstrating seropositivity within 3 weeks of the second vaccine. No adverse reactions were seen in these animals, and the antibody titers persisted for up to 40 weeks. Although the antibody titer required to protect NWCs against WNV is unknown, the equine WNV vaccine appears to offer humoral protection.

**EHV-1**

An outbreak of EHV-1 in NWCs was first reported in 1988, during which 21 alpacas and 1 llama developed acute vitritis, optic neuritis and retinitis. In addition, 4 of these animals developed depression, nystagmus, heat tilt and paralysis. A few years later, experimental intranasal inoculation of 3 llamas with EHV-1 that was isolated from the brain of a neurologic alpaca resulted in neurologic disease in all animals. Clinical signs developed 6–8 days following EHV-1 infection and included head pressing, blindness, opisthotonus, ataxia, muscle fasciculations and head tremors. Necropsy findings in these animals included meningoencephalitis and multifocal cerebral vasculitis with cerebral and retinal edema. Necrotizing retinitis with intranuclear inclusion bodies was seen in 1 animal. Thus, it is thought that EHV-1 gains access to the brain and retinas through intranasal transmission, which may occur subsequent to viremia or via direct access by way of the olfactory tract. Routine vaccination using available equine EHV-1 vaccines is not recommended due to the low disease prevalence in NWCs. Limiting access of NWCs to horses is recommended to decrease possible transmission.

**Rabies**

Like other mammalian species, NWCs are highly susceptible to rabies virus. Wildlife serve as the natural reservoir for rabies virus, with the skunk, coyote, bat, raccoon and fox most often implicated in the United States. The first reported case of rabies in a NWC in the United States was in a llama in Oklahoma in 1989, with several reports subsequently documented. Early clinical signs of rabies in NWCs include lameness, ataxia and posterior paralysis which can progress to an aggressive or paralytic form. In the aggressive stage, animals may bite at inanimate objects, self-mutilate or demonstrate changes in vocalization. Paralytic rabies can manifest as severe depression, hypersalivation, facial paralysis, pharyngeal paralysis and recumbency. Disease progression is rapid with most animals dying within 1–4 days after the onset of clinical signs. Diagnosis of rabies is postmortem using IHC, fluorescent antibody testing or PCR. Vaccination with a killed rabies vaccine is recommended in endemic areas.

**HEAT STRESS**

NWCs have adapted to a broad range of different climatic conditions, but are particularly suited for cooler climates. Thus, hyperthermia can cause problems in hot, humid environments that are very different from their original habitat of the high plains of South America. In unshorn animals, heat is radiated only through the thermal windows (ventral abdomen, axilla and medial thighs), which make up just 20% of the skin surface. Heat stress is a common condition in the summer months in the Southwest, Midwest, South and Southeastern United States. Depending on the severity and chronicity of hyperthermia, any cell type or tissue can be damaged, but neurons tend to be highly sensitive. Clinical signs of heat stress include elevated rectal temperature (> 105°F), dehydration, respiratory distress, tachycardia and ataxia. Heat stress often manifests as weakness in the forelimbs that can then progress to recumbency. A CBC may reveal botryoidal neutrophils, which refers to fragmented neutrophil cytoplasm secondary to thermal damage. Serum biochemical analysis may reveal elevations in muscle enzyme activity (CK and AST) due to muscle cell injury.

Diagnosis of heat stress is based on clinical signs and ambient temperature/heat index. Since there is no definitive antemortem test for heat stress, diagnostic tests for meningeal worm should be considered. Treatment of heat stress involves cooling by using a cold hose and ice packs in the axillary and inguinal regions. The
animal should be sheared if this has not been done. Fluid therapy should be administered with caution, given the risk of pulmonary edema secondary to heat-induced lung damage. Additional supportive care may include non-steroidal anti-inflammatory treatment, corticosteroids, Vitamin E supplementation, and nutritional support. If meningeal worm is a differential, fenbendazole treatment should be initiated (see above).

For prevention of heat stress, whole-body shearing of NWCs in hot and humid summer months is recommended, given that shearing assists heat dissipation which results in a cooler surface body and rectal temperature. Access to sprinklers, wading pools and fans can also decrease incidence of heat stress.

SUMMARY

Several neurologic conditions affect NWCs and often present a diagnostic challenge given the variable and often non-specific nature of neurologic signs. Neurologic diseases that are shared by ruminants and NWCs include polio, listeriosis and otitis, while horses and NWCs can be affected by EEE, WNV and EHV-1. Because of their unique integumentary system, NWCs are uniquely susceptible to heat stress. A complete neurologic examination in addition to routine blood work +/- lumbosacral CSF analysis should be baseline diagnostic procedures for NWCs that present with neurologic disease. Although not discussed in detail here, trauma and neoplasia should always be considered potential causes of neurologic disease in NWCs.
REFERENCES


