“Migration to Críation”

Allison K. Eardley

Mississippi State University

College of Veterinary Medicine

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Advisor:

Dr. Gretchen Grissett, DVM, MS, DACVIM (LA)

Associate Professor

Introduction:

Parelaphostrongylus tenuis is a nematode commonly found in the central nervous system of its definitive host, white-tailed deer (*Odocoileus virginianus*), in Eastern North America, lending it the common name meningeal/brain worm.[9] Unlike the definitive host, *P. tenuis* often causes neurological problems in aberrant or dead-end hosts such as llamas (*Lama glama*), alpacas (*Vicugna pacos*), elks (or red deer; *Cervus elaphus*), moose (*Alces alces*), as well as numerous other deer species and cloven-hoofed livestock. Through an examination of current literature and past reports, this case report outlines the advanced clinical signs, diagnostic strategy, prognosis, pathophysiology, and treatment options for *P. tenuis* infection in camelids.

History & Presentation:

Baraka is an approximately 10-year-old pregnant female llama that presented to Mississippi State University College of Veterinary Medicine's Food Animal Service on March 13, 2021, for being acutely down in the pelvic limbs. A few days prior to presentation, Baraka was ataxic. She began to lose control of her pelvic limbs and was found recumbent on March 11, 2021. On March 12, 2021, she was treated with fenbendazole by her primary care veterinarian but showed no improvement. Baraka was estimated to be around 330-340 days pregnant at the time of presentation.

Upon presentation, Baraka was bright, alert, and responsive. Her vitals were within normal limits with a temperature of 101.2 degrees Fahrenheit (range 99.5-102.0), a pulse of 52 beats per minute (range 60-80) and a respiratory rate of 36 breaths per minute (range 10-30). She weighed approximately 119.3 kilograms with a body condition score of 4/9. Cardiopulmonary auscultation revealed no crackles, wheezes, or irregular heart sounds. Mucus membranes were

pink and moist with a capillary refill time of less than 2 seconds. On neurologic exam, she was mentally appropriate with intact cranial nerves. She was non-ambulatory tetraparetic. Proprioceptive placement was unable to be examined. Her flexor-withdrawal reflexes were absent in all four limbs and segmental reflexes were intact. Her neuroanatomical localization was multifocal.

Diagnostic Approach & Differential diagnoses:

In most cases, antemortem diagnosis of aberrant *P. tenuis* migration is often a diagnosis of exclusion based on clinical signs. A presumptive diagnosis is based upon the presence of asymmetric neurologic deficits, history of exposure to areas inhabited by white-tailed deer, and eosinophilic pleocytosis on cerebrospinal fluid analysis. Cerebrospinal fluid analysis may show eosinophilic pleocytosis, but absence of this on CSF analysis does not rule out a meningeal worm infection.[7] However, CSF eosinophilic pleocytosis in llamas has been most consistently reported in cases of clinical parelaphosstrongylosis.[2,7] Definitive diagnosis of meningeal worm infection is made at necropsy[1] and confirmed by microscopic demonstration of the larvae within the brain or spinal cord.[10]

After obtaining a detailed history, a thorough physical exam and neurologic exam are the appropriate next steps as these can help with accurate neuro-localization of the lesion, to rule out other causes of neurologic deficits (bacterial, fungal, viral, nutritional, neoplasia, etc.), and to gauge the severity of the presumptive parasitic infection. As far as differential diagnosis of neurologic disease in camelids is concerned, *P. tenuis* tends to be the only agent on the list while in the field.[5] Despite this tendency in llamas, other differentials should be considered since most cases of *P. tenuis* are diagnoses of exclusion. Other differentials to consider include degenerative

myeloencephalopathy, discospondylitis, intervertebral disc disease, heat stress, vertebral body malformation/malalignments, and extradural mass lesions.[3]

Although meningeal worm infection in camelids most commonly presents with neurologic deficits localizing to the spinal cord, clinical signs are generally non-specific and may affect brain as well. A variety of symptoms indicate intracranial disease, such as ataxia, abnormal mentation (dementia, stupor, coma), visual abnormalities, circling, falling or rolling, weakness, delayed postural reactions, incoordination, head tilt, altered neck and head position, nystagmus, strabismus, and seizures. Among camelids exhibiting these signs, neoplasia, trauma, hydrocephalus, among other congenital defects, cerebral abscessation, listeriosis, otitis interna, and polioencephalomalacia can be diagnosed. Neurologic symptoms can arise from electrolyte imbalances such as hypocalcemia, hypomagnesemia, hypoglycemia, and ketosis, in addition to dietary deficiencies such as copper, vitamin A, vitamin E, selenium, calcium, magnesium, potassium, and phosphorus.[1] Similarly, toxicoses such as poisoning from lead, poisonous plants, and salt poisoning should be taken into consideration. In all neurologic cases, Rabies encephalitis should be considered. To make a presumptive diagnosis of meningeal worm infection, these differential diagnoses must be ruled out.[1]

Pathophysiology:

The white-tailed deer serves as the definitive or natural host, meaning that worms can reproduce and lay eggs within the animal, and infected deer shed larvae in their feces. The infective larval stage is considered the third larval stage (L3), which is developed inside the intermediate host (gastropods). Infected snails or slugs are digested and the L3 are released into the abomasum. Within 10 days, the L3 migrates to the spinal cord via the spinal nerves.[4] As the

larvae aged 30 days and shed two molts, they move cranially through the subdural space and leave the spinal cord. *P. tenuis* adults inhabit the subdural spaces or the surrounding venous sinuses of the brain.[4] The eggs of adult worms are laid in the meninges of white-tailed deer. They are then circulated through the body's venous system and travel to the lungs where they hatch into first-stage larvae (L1). Infected deer cough up, swallow, and pass the L1 in their feces.[4] The larvae invade or are ingested by terrestrial gastropods, such as snails or slugs. Over a period of 3-4 weeks, snails and slugs serve as intermediate hosts where first stage larvae grow into infective third stage larvae (L3).[4] Infected white-tailed deer transmit the parasite to gastropods which can then be ingested and cause disease in captive livestock, including domestic sheep and goats, llamas, alpacas, camels, and rarely domestic cattle or horses. Moose, mule deer, black-tailed deer, elk, caribou/reindeer, pronghorns, and big-horned sheep are also susceptible. However, worms don't usually mature to reproductive adults in these aberrant or "dead-end" hosts, and these hosts don't shed larvae in their feces. Instead, worms may migrate through the brain and spinal cord and cause severe neurological disease and death. Dead-end hosts become infected by ingesting terrestrial snails and slugs infected with L3. The larvae penetrate the gastrointestinal wall and travel up lateral spinal nerves to the spinal cord and/or brain causing damage as they migrate. Once infected, clinical disease begins 45-53 days later.[9] Disease pathogenesis involves physical trauma and inflammation of the CNS as well as potentially toxic products released by the parasite.[5] Symptoms vary according to larval density and migration patterns and include ataxia, hyporeflexia, hypermetria, proprioceptive deficits, weakness, recumbency, inability to change positions, base-wide stance, exercise intolerance, weight and muscle loss, head or body tilting, circling, torticollis or opisthotonos, circling, blindness, paresis or paralysis, urinary

incontinence, seizures, and diaphragmatic paralysis and dyspnea. Progressive posterior paralysis is the single most common presentation, but almost any CNS sign can be observed.[3]

Treatment & Management Options:

The treatment of meningeal worm infection is most successful when started early in the disease process. Many treatment regimens have been tried, but the ones that involve fenbendazole (50 mg/kg, PO, q24 for 5 days), ivermectin (0.3 mg/kg, SQ, once), steroids (dexamethasone 0.1 mg/kg, IV/IM/SQ, q24 for 3 days; prednisolone sodium succinate 0.5-1 mg/kg, IV/IM/SQ, q12 for 3 days) or NSAIDs (flunixin meglumine 1 mg/kg, IV/IM/SQ, q12 for 5 days) have been the most successful. Females should not receive dexamethasone when they are pregnant since it could cause an abortion. Prednisolone sodium succinate, for no more than 3 days, may have a reduced risk of abortion compared to dexamethasone because it lacks a carbon-16 substitute. The blood-placental barrier may not be crossed by corticosteroids that lack the carbon-16 substitution; therefore, large amounts of corticosteroids will probably need to be administered for prolonged periods to terminate a pregnancy.[6] A combination of anti-inflammatory drugs is essential to reduce inflammation associated with migrating larvae and secondary inflammation caused by their death. Ivermectin is most effective against larval stages prior to their entrance into the spinal cord since it does not readily cross the blood-brain barrier. However, damage to nervous system tissues during larval migration may alter the blood-brain barrier. Nevertheless, ivermectin therapy should still be initiated even when CNS signs are visible to eliminate any persistent larvae in the gastrointestinal tract.

Recovery requires not only drug therapy, but also supportive care and physical therapy. When llamas are unable to stand, slings are useful to support them, and physical therapy is

helpful for strengthening their muscles. The use of hydroflotation therapy has also been observed in cases of prolonged recumbency.

Even though it may be severely debilitating and potentially fatal, meningeal worm infections can be avoided. Infection can be reduced considerably with routine deworming every 4-6 weeks, avoiding cohabitation with white-tailed deer, and maintaining a clean and dry environment unfavorable to snails and slugs. In herd health management, judicious anthelminthic therapy warrants concern for developing resistance. Resistance is unlikely to become a problem in the meningeal worm because these infections do not become patent.[8] Though this seems logical, there is much debate on this topic when it comes to other parasites that effect llamas and are susceptible to ivermectin.

Expected Outcome & Prognosis:

Based on the severity of clinical signs, prognosis of each individual case will vary. For example, a llama that has difficulty standing has a poor prognosis (10-20%), whereas one that is able to stand unaided have a fair to good prognosis (75-85%).[1] Llamas that survive clinical disease do not appear to develop patent infections and pose little risk to other animals.[8] Llamas that have permanent neurologic deficits can still be productive members of their herd, either as breeding stock or as companion animals.

Case Outcome:

Baraka received ivermectin (1cc/70lb, SQ, q24, once), meloxicam (1 mg/kg, PO, q24 every other day for 3 days), gabapentin (5 mg/kg, PO, q24), and fenbendazole (50 mg/kg, PO, q24 for 5 days). Her abdomen was ultrasounded at least twice daily to check for a viable fetal

heartbeat. She received passive-range-of-motion on all four limbs at least three times a day. Hydroflotation was initiated as well but was unsuccessful. She had a developed a bed sore on the lateral aspect of her left hock that was being medically managed with topical silver sulfadiazine four times a day. Despite aggressive management with SSD cream and frequent bandaging, the wound did not heal. On April 11, 2021, Baraka delivered a healthy female cría named Isabella. Whole blood was collected from Baraka in case Isabella needed a plasma transfusion. After parturition, Baraka was placed in a sling and encouraged to walk. Although she took small steps in at least three limbs, for her to regain strength in those muscles, she was going to need months of physical therapy and supportive care. Unfortunately, Baraka was considered to have a poor to guarded prognosis. She was non-ambulatory, and she had not improved since presentation (roughly 4 weeks). With little to no improvement with physical therapy, owners elected for humane euthanasia, and she was submitted for necropsy. Gross examination of the brain and spinal cord was unremarkable. The microscopic lesions appreciated in the thoracic and thoracolumbar spinal cord were diagnostic for verminous infection with *P. tenuis.* Multiple cross sections of the nematode parasite were observed within thoracic spinal cord and parasitic tracts were appreciated in the thoracolumbar segments.

Discussion:

Clinical medicine is illustrated throughout this case, as well as the collaborative nature of diagnosis and treatment. The key in this case lies in early detection and aggressive treatment. While this case had a poor to guarded prognosis, most often early detection with initiation of treatment results in a good prognosis with a 75-85% chance of recovery. A fence is not sufficient to keep deer out, and chemicals to kill snails leave persistent residues in the environment that are

harmful and are of limited efficacy. Most of the prevention against meningeal worm larval infection aims to kill the larvae while they are migrating, but before they enter the spinal cord. In the high-risk periods of the year, deworming must be performed every 4 to 6 weeks. The most efficacious anthelmintics for protection against meningeal worm have been ivermectin (1 cc of 1% ivermectin per 100 pounds body weight, injected under the skin, every 4 to 6 weeks) or fenbendazole (4.5 cc of 10 % fenbendazole per 100 pounds body weight, given orally, once daily for 3 to 5 days).[1]

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