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Case Report
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Parelaphostrongylus tenuis Cerebrospinal Nematodiasis in a Horse with Cervical Scoliosis and Meningomyelitis

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There are reports of horses with acute onset acquired cervical scoliosis and cutaneous analgesia. The underlying dorsal gray column myelitis that produces these neurologic signs has been only presumptively attributed to migration of *Parelaphostrongylus tenuis* within the spinal cord. Despite previous confirmation brain by polymerase chain reaction testing, of *P. tenuis* within the brain of horses by polymerase chain reaction testing, genetic testing has failed to definitively identify the presence of this parasite in cases of equine myelitis. This case report provides molecular confirmation via polymerase chain reaction of *P. tenuis* within the cervical spinal cord of a horse with scoliosis and cutaneous analgesia.

Key words: Meningeal worm; Parasite; Parelaphostrongylus.

Parelaphostrongylus tenuis is a neurotropic nematode that causes severe inflammation during aberrant migration within the central nervous system of camelids,[1] small ruminants,[2,3] and rarely cattle.[4,5] Eleven cases of presumptive *P. tenuis* nematodiasis have been reported in equidae.[6–9] Eight of those cases displayed acquired unilateral cervicothoracic analgesia and cervical scoliosis.[6,8] Polymerase chain reaction has confirmed verminous equine encephalitis with *P. tenuis*[10] but has failed to confirm infection in cases of acquired scoliosis. This case report describes confirmation of *P. tenuis* by polymerase chain reaction testing in a horse with acquired unilateral cervical analgesia and cervical scoliosis with histopathological lesions consistent with nematodiasis.

A 5-month-old Thoroughbred filly was examined on the farm after sudden development of c-shaped lateral cervical scoliosis (right side convex) first noticed hours earlier. The filly was lethargic and had a pot belly, poor body condition (3/9), and a dull haircoat. Normal sensation was present on the left (concave) side of the cervical region, but complete analgesia was present on the right (convex) side. Vital signs were within normal limits. No cranial nerve deficits were detected. Flunixin meglumine[a] (1.1 mg/kg IV) and dexamethasone[b] (0.1 mg/kg IV) were administered without improvement. Euthanasia was elected due to presumed poor prognosis.

Immediately postmortem cerebrospinal fluid was collected from the cerebellomedullary cistern. The fluid was grossly clear and colorless. Fluid analysis revealed increases in erythrocytes (475/μL) and albuminocytological dissociation (total nucleated cell count 2/μL; ref range <5/μL and total protein 162 mg/dL; ref range ≤80 mg/dL) consistent with central nervous system inflammation. Cytological analysis revealed 30 cells on a cytospin slide comprised of 19 macrophages, 8 lymphocytes, and 3 neutrophils. Neither microorganisms nor atypical cells were identified.

The cervical vertebral column from C1 to C5 and associated musculature was removed and shipped to the University of Pennsylvania New Bolton Center for histopathology and sample collection for *P. tenuis* PCR testing. Lesions consistent with parasitic migration (multifocal random necrotizing eosinophilic to hemorrhagic meningomyelitis) were discovered. A focally extensive area of hemorrhage within the white and gray matter in the right dorsolateral segment of C4–C5 obscured the dorsal horn of the gray matter (Fig 1).

Eleven segments of cervical spinal cord as well as cervical spinal nerves were examined histologically with emphasis on the C4–C5 spinal segment. Many segments contained multifocal, large, random but well-demarcated hemorrhagic and malacic foci and less severely affected regions contained discrete 300–500 um diameter foci of malacia containing and surrounded by inflammatory infiltrates of eosinophils, macrophages, lymphocytes, plasma cells, multinucleated giant cells, and fewer neutrophils with similar infiltrates in the meninges and cuffing the leptomeningeal vessels. Immunohistochemistry of the spinal cord for *Sarcocystis neurona*, a causative agent of equine protozoal encephalomyelitis, was negative. The abnormal spinal cord section of C4–C5 was submitted for PCR testing targeting the second internal transcribed spacer region of the rRNA of *P. tenuis* as previously described.[10] The extracted DNA was PCR positive, and the resultant 116-bp sequence

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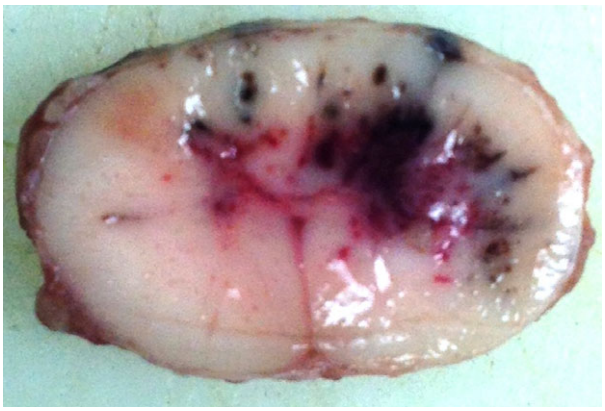

Fig 1. Spinal cord lesion at C4–C5 extending approximately 2 cm cranially from which samples tested positive on PCR for *P. tenuis*. Note the extensive hemorrhage within the white and gray matter in the right dorsolateral segment of C4–C5 obscuring the dorsal horn of the gray matter.

was 100% identical to *P. tenuis* in GenBank (accession number GU122925).

Discussion

In the previously reported cases of presumptive *P. tenuis* nematodiasis, cervical scoliosis and analgesia were attributed to continuous dorsal gray column lesions, whereas general proprioceptive (GP) ataxia and upper motor neuron (UMN) paresis were associated with surrounding white matter involvement.[6,8] In non-equine aberrant hosts, *P. tenuis* lesions tend to involve the spinal cord white matter even when camelids display similar cervical scoliosis.[11] The apparent predilection for the dorsal gray matter lesions in the horse cannot be fully explained although positive tropism via neurotransmitters abundant in this area of the spinal cord has been proposed.[6] This case displayed both clinical (analgesia, scoliosis, GP ataxia/UMN paresis) and histopathological signs (dorsal gray column and lateral white matter lesions) consistent with equine verminous myelitis.[6] The C4 spinal cord lesion site is also identical to the region in which a larva of the *Metastrongyloidea* (presumed to be *P. tenuis*) was previously identified.[6]

Antemortem diagnosis of verminous myelitis is often challenging as acute onset of asymmetric spinal cord disease can result from neoplasia, trauma, or infection with bacteria, viruses, fungi, or protozoa.[12] Parasites that have been identified in the brain or spinal cord of horses include rhabditid nematodes (*Halicephalobus gingivalis)*, strongyloid nematodes (*Strongylus vulgaris, S. Equinus, Angiostrongylus cantonensis, P. tenuis),* spiruroid nematodes (*Draschia megastoma),* filarid nematodes *(Setaria spp.)*, and warble fly larvae *(hypoderma spp.)*.[7,10,12,13] Concurrent cerebrospinal fluid xanthochromia, pleocytosis, and increase in total protein occur inconsistently and are neither sensitive nor specific for nematodiasis.[12] Although eosinophilic pleocytosis supports a diagnosis of parasitic infection, eosinophils are not always found in the CSF of horses with verminous encephalitis as might be expected.[14–16] Marked malacia and inflammation result from a combination of mechanical damage due to migration as well as host immune response forming characteristic parasitic migration tracts that may be visible only microscopically on postmortem examination.[12,17]

Routine laboratory testing including CBC, biochemistry profile, and urinalysis was not performed due to its limited utility to differentiate between causes of nematodiasis. *H. gingivalis* is only occasionally detected in urine due to renal infestation or in biopsies of granulomas of skin or head (not present in this case);[18] larva, however, have rarely been detected in routine cerebrospinal fluid analysis.[19] Additional signs of infestation with the soil dwelling saprophyte (uveitis, sinusitis, osteomyelitis, and mastitis)[18] were not detected. Hypoderma can cause skin warbles, and in horses can cause signs of encephalitis more commonly than signs of myelitis due to predilection for the brain (15/16 cases) based on apogeotropism, for example, the more vertical position of the head and neck.[20] The filly in this report had no contact with cattle or fields previously inhabited by cattle, a common predisposing variable.[20] *Strongylus vulgaris* has been associated with two separate clinical syndromes, acute severe forebrain disease, evidenced by blindness, circling, dementia, and dysphagia, due to parasite-induced embolic showers[14,21] and a more chronic syndrome due to larval migration through the spinal cord and brain, which could not be excluded as a cause of the filly's clinical signs.

Single case reports of asymmetric brain disease and cauda equina syndrome in the United States have been attributed to *Draschia megastoma*[16] and *Setaria labiatopapillosa*[15] respectively. A close relative of the latter, *Setaria digitata*, is the cause of "Kumri," a fairly common syndrome of spinal ataxia due to nematodiasis in Central and Southeast Asia.[22] The lone case of equine meningoencephalomyelitis due to *A. cantonensis* in the United States occurred in a miniature horse with fever and signs of brainstem, cerebellum, and spinal cord dysfunction.[17] An increasing prevalence of infection of the definitive host, *Rattus Norvegicus*' population in New Orleans offered a possible explanation for exposure to the protostrongylid previously only reported in Asia.[17]

Within the Metastrongyloidea, only Angiostrongylidae and Protostrongylidae families display neurotropism and infect the central nervous system (CNS).[7] Of the 7 genera within the family Protostrongylidae, only *P. tenuis* and *Elaphostrongylus* can infect host CNS, and the latter has never been reported in North America.[23] In North America, *Parelaphostrongylus tenuis* is an endemic parasite of white-tailed deer (*Odocoileus virginianus)*. A prevalence of 86% in that species might actually underestimate the true widespread nature of this nematode based on current methods of testing gastropod intermediate hosts.[24]

No effective commercial antemortem test for equine *P. tenuis* myelitis exists. When interpreted in the context of physical examination findings and history, advanced imaging has the potential to suggest the presence of nematodiasis, but molecular confirmation is

needed for an accurate diagnosis. Recent use of MRI has been able to aid diagnosis of human nematodiasis due to *A. cantonensis,*[25] a nematode closely related to *P. tenuis*.[17] The large size of the equine neck, however, precludes the routine use of MRI in equine cervical diagnostic testing. The positive PCR result for *P. tenuis* is the first definitive identification of the protostrongylid worm in an equine spinal cord and only the second definitive identification of *P. tenuis* in the equine central nervous system.[10] In a previously reported and confirmed *P. tenuis* verminous encephalitis case, multiple larvae, eggs, and both a male and female adult Metastrongylid were identified phenotypically.[7]

Immune response and clearance of the aberrant parasite before necropsy or formalin fixation of the tissue before PCR testing were possibly responsible for the inability to confirm *P. tenuis* in previous cases, which had a more chronic course of infection than this case. In a recent study evaluating sensitivity of PCR for detection of *P. tenuis* DNA in formalin-fixed neural tissues from 38 goats, camelids or wild ungulates with characteristic histologic lesions of *P. tenuis*, only 19 cases were PCR positive.[26] *P. tenuis* DNA can therefore be detected with PCR from formalin-fixed, paraffin-embedded tissue even if a nematode is not visible in the sample. Absence of the nematode at time of sample collection, small size of sample tested, and extended time of tissue in formalin fixation were potential reasons for negative results. In this case prompt euthanasia might have preserved the *P. tenuis* DNA before a full immune response could eliminate it.

Cases of *P. tenuis* nematodiasis in horses range in age from 6 months to 3 years[6,8] and cases in cattle range in age from 3 to 7 months.[4,5] No clear explanation exists why juvenile animals seem to be overrepresented; but the prognosis for horses remains worse. No horse has ever recovered from *P. tenuis*-associated CNS infection despite successful use of the combination treatment of moxidectin, fenbendazole, and dexamethasone in calves with meningitis.[5] One horse is alive after 10 years, but severe scoliosis persists (personal communication AJ). The chronicity and locally extensive nature of gray column lesions in horses with scoliosis may preclude recovery after clinical signs occur; therefore, white-tailed deer and gastropods should be kept away from equine pastures. *P. tenuis* myelitis should be considered for any horse with scoliosis and unilateral analgesia.

Footnotes

[a] FLUNIXIJECT (flunixin meglumine) Injectable Solution Henry Schein Animal Health Dublin, OH 43017

[b] DEXAJECT® Henry Schein® Animal Health Dublin, OH

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Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Fig S1. Aerial view of the filly with cervical scoliosis.
Fig S2. Cervical scoliosis with right-sided convexity.