Acute recumbency associated with *Anaplasma phagocytophilum* infection in a horse

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An 11-year-old Hanoverian-cross gelding weighing 549 kg (1,208 lb) was referred to the Tufts University School of Veterinary Medicine Hospital for Large Animals (TUSVM) in late fall for evaluation and treatment of acute onset ataxia and recumbency. Vaccination history was incomplete, but the horse had been vaccinated against rabies (killed virus vaccine) 6 months previously. The horse had been imported from Canada 3 months earlier and had recently been moved to a barn in Massachusetts. No other horses at the barn had any neurologic or respiratory tract disease; there was no evidence to suggest that the horse had ingested or been exposed to any medication or neurotoxins. A prepurchase examination performed 1 month earlier had not revealed any abnormalities in neurologic function. Infestation with ticks had occurred recently in this and other horses at the same location; however, the ticks had been removed prior to evaluation of the horse in late fall for evaluation.

Findings of physical examination were unremarkable except for mild facial abrasions, edema of the distal portions of both hind limbs, and recumbency. The horse was afebrile at admission and able to move all 4 limbs. To enable safe transfer from the trailer to the stall, the horse was premedicated with xylazine (5.5 mg/kg [2.5 mg/lb], IV) and anesthesia was induced with ketamine (2.2 mg/kg [1 mg/lb], IV) and diazepam (0.11 mg/kg [0.05 mg/lb], IV). For maintenance of anesthesia, the horse was administered a solution of 5% dextrose in water (1 L) with 2 g of ketamine and 500 mg of xylazine via IV infusion to effect; anesthesia was maintained throughout the transfer to the stall, collection of CSF, and placement of the horse in a sling. An atlanto-occipital puncture was performed to obtain a CSF sample, and an aliquot of CSF was submitted for cytologic evaluation. Additional samples were submitted for diagnosis of equine protozoal myeloencephalitis via a western blotting technique, assessment of antibodies against equine herpes virus-1, and quantification of IgM against West Nile virus and eastern equine encephalitis virus via ELISA. During this period of anesthesia, the horse was placed in a body sling; with the horse in ventral decubitus, recovery from anesthesia occurred without complications. The horse was alert, oriented, and had some interest in eating hay; cranial nerve examination revealed no deficiencies, and there was good tone and weak but purposeful movement in all limbs. The anal reflex and tail tone appeared normal, and cutaneous sensation was present in all areas that could be assessed. Edema was present to a moderate degree in both hind limbs and mildly in the left forelimb. No attempt was made to elicit spinal reflexes. Blood samples for a CBC, blood gas analysis, and serum biochemical analyses were collected at this time. Nonspecific treatment for edema of the CNS was instituted and included a single bolus of mannitol (20% solution; 1 g/kg, IV), methylprednisolone sodium succinate (1 mg/kg, IV, once), and flunixin meglumine (1 mg/kg, IV, q 12 h). Hydration was maintained for the first 24 hours of hospitalization with a 10-L bolus of lactated Ringer’s solution administered IV, followed by a constant rate infusion of the same solution at a rate of 1.3 L/h.
The CSF was clear and colorless; cytologic examination revealed 2 RBCs/µL and no nucleated cells. Total protein concentration of the CSF was 34 mg/dL (reference range, 20 to 110 mg/dL). Abnormalities identified via a CBC included mild anemia (5.77 × 10⁶ RBCs/µL; reference range, 6.5 to 12.8 × 10⁶ RBCs/µL) and marked lymphopenia (472 cells/µL; reference range, 1,590 to 5,180 cells/µL). The horse was thrombocytopenic; cytologic examination of a blood smear revealed 2 to 4 platelets/hpf, correlating with a platelet concentration of approximately 20,000 to 90,000 platelets/µL (reference range, 83,000 to 271,000 platelets/µL). Large numbers of neutrophils contained gray cytoplasmic inclusions consistent with Anaplasma phagocytophilum (formerly Ehrlichia equi) infection. Results of serum biochemical analyses were largely unremarkable with the exception of high creatine kinase activity (1,790 U/L; reference range, 80 to 446 U/L) and unconjugated (direct) bilirubin concentration (5.90 mg/dL; reference range, 0.20 to 3.00 mg/dL). The serum ionized calcium concentration was 1.42mmol/L (reference range, 1.20 to 1.47mmol/L), and results of blood gas analysis indicated adequate ventilation and oxygenation.

After evaluation of the laboratory data, treatment for infection with A phagocytophilum was initiated. The horse received oxytetracycline hydrochloride (10 mg/kg [4.5 mg/lb] administered IV in 500 mL of physiologic saline [0.9% NaCl] solution over a period of 15 minutes, q 12 h). Ponazuril (15% paste) was administered orally (5 mg/kg [2.27 mg/lb], q 24 h) pending results of the western blot analysis performed to rule out equine protozoal myeloencephalitis. When the horse was fully awake, it was hoisted in the sling and had the ability to bear some weight, although severe ataxia and conscious proprioceptive deficits were easily appreciable (eg, knuckling and atypical foot placement). Muscle tone seemed moderately weak on assessment via a gentle tail pull. That night, 2 brief episodes of mild seizure-like behavior were observed, which resolved before treatment could be initiated. The horse continued to receive oxytetracycline and ponazuril as described until the third day of hospitalization: because results of the western blot analysis did not support a diagnosis of equine protozoal myeloencephalitis, administration of ponazuril was discontinued. Neurologic function improved rapidly, and at 48 hours after initiation of treatment, the patient was removed from the sling and was able to ambulate with moderate proprioceptive deficits (including crossing of fore- and hind limbs, hind limb circumduction, and truncal sway). Mentation and cranial nerve function remained throughout the period of hospitalization, and no further episodes of fever were detected.

By the sixth day of hospitalization, there were no neurologic deficits detectable when the horse walked or trotted. After 7 days, IV administration of oxytetracycline was discontinued and cytologic examination of a blood smear did not reveal any A phagocytophilum inclusion bodies within neutrophils. Results of serologic testing for West Nile virus-specific IgM and eastern equine encephalitis virus-specific IgM were negative; analysis of the CSF sample revealed no antibodies against equine herpes virus-1 at a 1:4 dilution. The referring veterinarian had frozen a sample of serum that was obtained before oxytetracycline treatment and had collected another sample after treatment for assessment of A phagocytophilum-specific antibody titers. In the initial (acute) serum sample, no antibodies against A phagocytophilum were detected, whereas antibodies against the organism were detected in the serum sample obtained 1 month later (convalescent) to a 1:100 dilution. The horse remained hospitalized for 12 days overall, and a follow-up report at 2 months after discharge indicated that the horse made a complete recovery.

Equine granulocytic ehrlichiosis was first described in horses in 1969 and has since been described in horses on both coasts of the United States (including the geographic area from which the horse of this report originated) as well as in South America and multiple European countries. Originally named E quii, the organism has been determined to be very nearly genetically identical to E phagocytophilum (the agent that causes tick-borne fever of ruminants in Europe) and the causative agent of human granulocytic ehrlichiosis. Furthermore, the genome of this species was at least 98.2% homologous with any Anaplasma species. To resolve these inconsistencies, a change in nomenclature to A phagocytophilum was implemented in 2001 and now encompasses the agent of all 3 disease manifestations. In the interests of consistency with the new nomenclature, the clinical syndrome caused by infection with A phagocytophilum will be referred to as equine granulocytic anaplasmosis in this report.

Anaplasma phagocytophilum is transmitted by the adult stage of different species of Ixodes ticks. In the eastern United States, I scapularis has been implicated in the transmission of infection, whereas I pacificus is the vector on the West coast. In Germany (and probably the rest of Europe), the organism is transmitted by I ricinus. There is a wide variety of clinical signs of equine granulocytic anaplasmosis, including fever, anorexia, icterus, ataxia, edema, petechiae, and orchitis. Characteristic hematologic changes associated with the disease in horses include mild anemia, progressive thrombocytopenia, hyperbilirubinemia, and profound lymphopenia (< 1,000 cells/µL) in the early stages of infection. However, most infected horses probably do not have clinical signs because as many as 50% of clinically normal horses in some areas of California have antibodies against A phagocytophilum.

In horses that become recumbent, differential diagnoses include viral encephalitides, equine herpes virus-1 infection, botulism, tetanus, rabies, meningitis, neoplasia, intoxication, aberrant parasitic migration, CNS or musculoskeletal trauma, and various metabolic diseases or derangements. However, although ataxia is a commonly described clinical sign associated with equine granulocytic anaplasmosis, the diagnosis has not been previously associated with involuntary recumbency. In the horse of this report, clinical signs of A phagocytophilum infection were evident, including anemia, edema, fever, icterus, lymphopenia, thrombocytopenia, an increasing serum immunoglobulin titer, and cytoplasmic inclusion bodies within the peripheral neutrophil.
population. A rapid improvement in clinical signs that is correlated with the initiation of treatment with oxytetracycline has been extensively described in other cases of equine granulocytic anaplasmosis. In addition to the reports of ataxia in horses, neurologic signs have been reported in humans infected with *A phagocytophilum* and *E chaffeensis* and dogs infected with *E canis.* Most of the alternative diagnoses considered in the horse of this report were ruled out either through diagnostic testing (ie, equine herpes virus-1 and eastern equine encephalitis virus infections, West Nile viral encephalitis, equine protozoal myeloencephalitis, and inflammatory conditions of the meninges) or clinical examination and disease progression (ie, rabies, botulism, neoplasia, parasitic migration, and musculoskeletal disease).

The pathogenesis of recumbency secondary to *A phagocytophilum* infection is speculative but suggests a neurologic etiology. Generalized vasculitis is a common clinical feature of infection and was evident in the horse of this report as edema of the lower portions of limbs. A similar diffuse or cervical myelovasculitis would be consistent with most of the neurologic signs observed. The brief seizure-like activity observed in the horse of this report may have been secondary to recovery from anesthesia or indicative of a focal area of cerebral vasculitis. Analysis of a CSF sample did not reveal hyperproteinemia or high mononuclear cell concentration and therefore did not provide evidence of inflammation. However, these findings did not rule out vasculitis in the CNS because the lesions may have been distal to the region of CSF collection or not contiguous with the ventricles or spinal canal. The consistency with which ataxia is described in horses infected with *A phagocytophilum* is suggestive that neurologic dysfunction is part of the clinical characteristics of disease. Clinicians should be aware of equine granulocytic anaplasmosis as a differential diagnosis in recumbent horses that have fever, edema, or characteristic hematologic changes such as anemia, lymphopenia, thrombocytopenia, or cytoplasmic inclusions bodies within neutrophils.

References


