EPM: Update on Diagnosis, Treatment, and Prevention

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Equine protozoal myeloencephalitis (EPM) is a neurologic disease of horses found throughout North, Central, and South America. It's a tricky disease to definitively diagnose and treat and, thus, has been an area of much research.

At the International Conference on Equine Infectious Diseases Practitioner's Day, held Oct. 21 in Lexington, Ky., Dan Howe, PhD, a molecular parasitologist at the University of Kentucky Gluck Equine Research Center, provided veterinarians and horse owners with an update on current EPM diagnosis, treatment, prevention, and research.

EPM Overview

Howe began with an overview of the primary causative organism's (*Sarcocystis neurona)* lifecycle. He explained that this parasite is fairly host-specific, and its major characteristic are the hallmark cysts called sarcocysts that form in intermediate host animals' (e.g., skunk, raccoon cat, armadillo) muscle tissues.

When one of these infected animals is killed, it might get consumed by a scavenging opossum, *S. neurona*'s definitive host, in which the parasite reproduces in the intestines. When the opossum defecates in a horse's feed or water source, those same parasites can then infect the horse and sometimes invade the central nervous system.

Risk factors for EPM in horses not only include presence of opossum populations but also any factors that might cause a horse stress and, thus, impair his immune system, Howe said. *S. neurona* infection, however, does not necessarily equate to disease, he added, explaining that veterinarians and researchers see a high seroprevalence indicating exposure to the parasite (30-50%) but a low disease incidence (less than 1%) in the horse population.

"Factors influencing this might include immune competence and/or inoculum size (number of parasites the horse ingests)," Howe said.

Basic Research

Basic EPM research is needed to help understand parasite infection, Howe said. Currently, a whole genome sequencing project is in progress on EPM strain SN3, which hesaid should be a resource for discovery and characterization of *Sarcocystis* antigens and virulence factors.

Howe said that one recent EPM research development has been the discovery of SnSAGs, which are proteins covering the surface of *S. neurona* parasites that elicit a robust immune response in horses. This is significant because it presents candidates for EPM vaccine development, he noted.

Diagnosis

Veterinarians diagnose horses with EPM based on history, clinical signs, a neurologic exam, and serologic (blood) or polymerase chain reaction (PCR) tests. Howe noted, however, that PCR tests are being used less frequently due to false negative results, and that serologic tests such as indirect immunofluorescence antibody test (IFAT) and enzyme-linked immunosorbent assay (ELISA) tests, might be superior choices.

"However, it must be remembered that the presence of antibodies in blood indicates infection, but not disease," said Howe.

Cerebrospinal fluid (CSF) testing to detect antibodies produced in the central nervous system (CNS) is a better approach, but it is confounded by normal passive transfer of antibodies from the blood across the blood-brain barrier. "To test for CNS-produced antibodies, we need an assay that can quantify, which is why the Western blot results for CSF could be misleading," he added.

Howe said the SnSAG2, 4/3 ELISAs measure antigen-specific antibodies and are simple and straightforward, removing the risk of operator error. But again, these tests used on blood samples alone are not sufficient for disease detection.

Howe went on to describe a recent multi-investigator study evaluating 128 cases diagnosed by postmortem examination. The horses were divided into four categories based on whether they had EPM, cervical vertebral myelopathy (Wobbler syndrome), another neurologic disease, or were normal.

The researchers tested paired serum and CSF samples with the SnSAG2, 4/3 ELISA to determine the most accurate method for serologic diagnosis of EPM. They concluded that serum titers alone are poor indicators of disease but that higher CSF titers are associated with EPM. They also determined that SnSAG2, 4/3 serum to CSF ratios yielded excellent diagnostic accuracy.

Treatment

U.S. Food and Drug Administration-approved anticoccidial drugs for treating EPM in horses include a pyrimethamine/sulfadiazine combination (marketed as ReBalance, ponazuril (marketed as Marquis), and diclazuril (marketed as Protazil). Howe's one word of cautionis that, while effective, pyrimethamine/sulfadiazine can result in bone marrow suppression and anemia in some horses.

The best treatment, however, is prevention. Howe suggested avoiding the transmission source--opossums--as best as possible. Another potential prevention method is prophylactic use of an anticoccidial drug, which Howe said could be safe and somewhat effective. He cautioned, however, that more studies are needed to determine proper dosing. He also said a preventive vaccine could be feasible, but this is a long-term proposition.

Take-Home Message

"Basic EPM research is ongoing and will help lay the foundation for future studies that can lead to development of clinical applications," Howe concluded.

He emphasized that new EPM diagnostics are available (e.g., SnSAG2 , 4/3 ratios) and noted a need for additional treatment options and preventive prospects.

Disclaimer: Seek the advice of a qualified veterinarian before proceeding with any diagnosis, treatment, or therapy.