Equine Herpesvirus 1 Myeloencephalopathy

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KEYWORDS

• Equine herpesvirus 1 • Equine herpesvirus myeloencephalopathy • Etiology
• Epidemiology • Pathogenesis • Clinical signs • Diagnosis • Treatment

KEY POINTS

- EHV-1 is ubiquitous in horses worldwide and greater than 80% of horses are estimated to be latently infected with the virus. Because of this the elimination of the virus from the population is unlikely, and efforts need to focus on prevention and treatment of clinical diseases associated with EHV-1.
- Clinical disease manifestations of EHV-1 include respiratory disease, late-term abortion, neonatal foal death, chorioretinopathy, and EHM.
- Sudden onset of signs including ataxia, paresis, and urinary incontinence; involvement of multiple horses on the premises; and a recent history of fever, abortion, or viral respiratory disease in the affected horse or herdmates are typical features of EHM outbreaks, although there is considerable variation between outbreaks with respect to epidemiologic and clinical findings.
- The mechanism underlying CNS endothelial infection is unknown, as are the risk factors that determine its occurrence. Although viral factors are certain to be important, host and environmental factors also play a critical role.
- An antemortem diagnosis of EHM is supported by ruling out other neurologic conditions; demonstrating xanthochromia and an elevated cerebrospinal fluid protein concentration; and identifying or isolating EHV-1 from the respiratory tract, buffy coat, or CSF.
- The equine ocular fundus is physiologically and anatomically similar to that of the CNS, but the eye's unique anatomic features permits observation of the chorioretinal vasculature in vivo and may allow for using the eye as a surrogate to study aspects of EHM pathogenesis.
- The treatment of EHM is challenging and directed toward supportive nursing and nutritional care and reducing CNS inflammation.
- Immunity following infection or vaccination offers limited protection in particular in regards to EHM. This lack of induction of protective immunity to EHV-1 is likely caused by immunomodulatory properties of the virus. Early recognition of suspected cases and the close monitoring of high-risk horses represent the most reliable measures at preventing outbreaks of EHM.

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INTRODUCTION

Equine herpesvirus 1 (EHV-1) myeloencephalopathy (EHM), although a relatively uncommon manifestation of EHV-1 infection, can cause devastating losses on individual farms, boarding stables, veterinary hospitals, and show and racing venues. Although outbreaks of EHM have been recognized for centuries in domestic horse populations, many aspects of this disease remain poorly characterized. In recent years, an improved understanding of EHM has emerged from experimental studies and from data collected during field outbreaks at riding schools, racetracks, horse shows, and veterinary hospitals throughout North America and Europe. These outbreaks have highlighted the contagious nature of EHV-1 and have prompted a reevaluation of diagnostic procedures, treatment modalities, preventative measures, and biosecurity protocols for this disease. This article focuses on the recent data related to the cause, epidemiology, pathogenesis, immunity, diagnosis, treatment, and prevention of EHV-1 infection with emphasis on EHM.

ETIOLOGY

EHV-1 is an important, ubiquitous equine viral pathogen that exerts its major impact by inducing abortion storms or sporadic abortions in pregnant mares, early neonatal death in foals, respiratory disease in young horses, and myeloencephalopathy.[1] Although EHM is a sporadic and relatively uncommon manifestation of EHV-1 infection, it can cause devastating losses and severely impact the equine industry, as exemplified by recent outbreaks at riding schools, racetracks, horse shows, and veterinary hospitals throughout North America and Europe.[2–4]

EHV-1 and EHV-4 are α-herpesviruses and are distinguishable from EHV-2, EHV-3, and EHV-5 by biologic properties and virus neutralization tests, and from each other by restriction endonuclease fingerprinting of DNA, DNA sequences, and several immunologic tests based on monoclonal antibodies to each virus.[1,5,6] EHV-1 and EHV-4 are closely related but genetically and antigenically different and associated with distinct disease profiles.

EHV-1 is a DNA virus that possesses linear double-stranded genomes composed of a unique long region, joined to a unique short region that is flanked by an identical pair of inverted repeat regions, the terminal repeat and the internal repeat regions.[7] The EHV-1 genome is 150 kilobases in size and encodes for 76 open reading frames or genes. Expression of these genes within infected cells is tightly ordered into a highly controlled cascade.[8] One complete replication cycle takes approximately 20 hours during which well-ordered sequential events occur, including attachment to the host cell membrane, membrane fusion and penetration, translocation of viral DNA to the nucleus, viral DNA replication and protein synthesis, assembly of the capsid, envelopment, and lysis of the cell with release of progeny virions.

Virulence markers distinguishing EHV-1 strains that induce EHM and/or abortion have recently been determined. The most important discovery may be the association with a single nucleotide polymorphism at position 2254 in the DNA polymerase gene (ORF 30) and the occurrence of EHM.[9] Analysis of more than 100 EHV-1 outbreaks with various clinical presentations demonstrated that variability of a single amino acid residue at position 752 of the DNA polymerase was found to be strongly associated with the occurrence of EHM, with EHV-1 strains associated with neurologic outbreaks involving a D_{752} genotype, whereas most nonneurologic outbreaks involved a N_{752} genotype.[9,10] The observation that EHV-1 viruses of the D_{752} genotype have a greater potential to induce EHM was recently supported by an experimental study using recombinant viruses with differing polymerase sequences.[11] The N_{752} mutant virus