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Equine herpesvirus myeloencephalopathy: an update on EHV-1

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Introduction

Equine herpes virus 1 (EHV-1) is a common pathogen of the horse that can induce mild respiratory distress, abortion, neonatal death and neurological disease. EHV-1 is a member of the Alphaherpesvirinae with a 150 kbp double-stranded DNA genome, consisting in 80 open reading frames (ORFs). EHV-1 establishes a life-long infection in a high percentage of animals following exposure to virus and outbreaks of neurologic disease are thought to be initiated by viral reactivation of neuropathogenic strain of EHV-1 or by virus spread after a recent history abortion or respiratory disease in affected horse population. The neurological signs in equine herpes virus myeloencephalopathy (EHM) range from temporary ataxia, paresis and urinary incontinence to complete paralysis and death. Infections that cause severe neurological dysfunction may only involve either one or two horses or be associated with larger outbreaks. Neurological syndromes have also been observed in various environments open to horses: breeding farms, riding schools, race tracks and more recently veterinary hospital. Furthermore, while several breeds and age groups seem to be at a lower risk of developing EHM, other factors, including EHV-1 strains, host immunity, and still unknown parameters could also explain that experimental EHV-1 infections were frequently partially successful. Studies clearly showed the influence of age on expression of the disease, since horses > 20 years were more subjected to high titre viraemia and development of neurologic disease than younger adult horses.

Neurovirulent and non neurovirulent strains

While the prevalence of EHV-1 abortion in most horse breeding countries has been decreasing, reports of EHV-1 neurological disease have been increasingly common in recent years in the USA and some studies were also reported in Europe. The interest for EHM was emphasized by increase research effort. Recent studies from Nugent et al in 2006, that have linked a specific mutation (A2254 → G2254) in the amino acid sequence (N752→D752) of the EHV-1 polymerase gene (ORF 30) with an increased neurological disease constituted undeniably a turning point in this area research. The key role of this mutation was confirmed by two reverse genetics experiments respectively realized in neurovirulent strain (Ab4) and in nonneurovirulent strain (NY03) of equid herpes virus type 1 (Goodman et al., 2007; Van de Walle et al., 2009). The identification of this unique single mutation polymorphism in ORF 30 allowed the development of real-time PCR assays to discriminate between non-neuropathogenic and neuropathogenic strains of the virus (Single Nucleotid Polymorphism PCR). Most of the recent studies characterized strains isolated in America and Europe and demonstrated that the G2254 genotype (associated to neurovirulent strain) could be observed in non neuropathotype samples (after abortion or respiratory disease) and the A2254 genotype (associated to non neurovirulent strain) in neuropathotype samples (after EHM).
Diagnosis

Laboratory diagnosis of EHM is currently based on at least one of the following criteria: detection of EHV-1 in nasal swabs or blood by PCR, virus isolation, serological testing (virus neutralisation) and post-mortem examination but since 2009 a consensus exist for the detection by PCR from two samples types: nasal swab and blood (EDTA tube).

Description of 2 recent outbreaks in France

In a riding school

One of the last epidemic disease reported in North of France, in a riding school, is one of the most important described during the last decade in Europe if one considers case fatality as criterion for quantifying severity of the outbreak. Indeed, 7 horses among 66 exhibited neurological disease, among which 5 were euthanized. In comparison, previous data from outbreaks in Belgium and Netherlands respectively revealed 10/41 neurologically affected horses among which 6 were euthanized and 20/41 neurologically affected horses, among which 1 was euthanized and another one died within the first three days. A particularity of this outbreak was that it concern only one premise in the North of France. One key point was certainly the early suspicion of EHV-1 infection at 0d, leading to enhanced sanitary measures even before the confirmation by laboratory analyses. As such, this procedure may have avoided the development of clusters of silent EHV-1.

Since no nasal discharge or cough was detected during this episode, daily recording of temperature was found to be an effective warning sign as previously described. Fever was indeed systematically present within two days before the severe neurological signs were noted. In our study, half of the horses that developed neurological disease were vaccinated, as was one of the two horses which recovered. Even if a recent report suggested that vaccinated horses could have some clinical protection against severe symptoms of EHV-1, there are still at present no data to definitely support the view that vaccination is of real benefit against EHM (Lunn et al., 2009).

In a studfarm

More recently, an episode was reported in a thoroughbred studfarm were 169 horses (60 mares, 44 foals and 65 yearlings) were stabled. The outbreak commenced with two cases of myeloencephalitis which presents within a 24 hour period. A neuropathogenic strain of the virus was identified. Six groups were constituted depending of the origin and status of the horses. One week later several foals presented clinical signs and fever and nasal discharge.

Nasal swabs and blood (EDTA tube) were collected from all horses and analyzed. The screening revealed positives cases in 3/6 groups. A non neuropathogenic strain of the virus was identified. The status of each foal was investigated each week during 42 days. The viral load varies from 200 to $10^7$ viral particles/ml in nasal swabs. The kinetic of decrease of the positive sample allows managing the animals in each group and between the different groups. A total of four cases of EHV-1 related abortion occurred over the 4-6 months following the initial cases. Various tissue samples from horse and foetuses were taken at necropsy, genital swabs taken on aborted mares and all were analyzed by molecular biology techniques. One neuropathogenic strain and 3 non neuropathogenic were then identified on foetuses.
This outbreak associated with EHV-1 on a breeding farm in Normandy described the three forms of the disease (EHM, respiratory and abortion) over a short period.

The definitive source of contamination remains unknown for the two outbreaks. Hypotheses could be proposed, including a reactivation of latent EHV-1 from the two suspected horses who had presenting fever and low-grade manifestations in the riding school and possible introduction of a positive horse from abroad in the studfarm.

**The take home message**

However, until there is a more complete understanding of all risk factors associated with EHM appropriate prevention and control measures should be taken during any type of EHV-1 outbreak regardless of A/G2254 genotype (Lunn et al., 2009; Pronost et al., 2010).

**References**


