CASE REPORT

An Outbreak of Herpesvirus Myeloencephalitis in Vaccinated Horses

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Summary

In the foaling season of 1977, five vaccinated horses in a Standardbred breeding stable were affected with herpesvirus myeloencephalitis. Respiratory and abortigenic forms also occurred in other individuals on the premises. Equine herpesvirus type 1 was isolated from the brain of one case of myeloencephalitis and from lungs of two aborted fetuses. Twelve of 16 horses demonstrated fourfold or greater increases in titres to equine herpesvirus type 1.

Résumé

Une éruption de myélo-encéphalite à herpèsvirus, chez des chevaux vaccinés

Au cours de la période de poulinage de 1977, cinq des chevaux d'un haras de Standardbred, préalablement faccinés contre la rhino-peumonite équine, souffrirent d'une myélo-encéphalite attribuable à l'herpèsvirus équin du type 1. D'autres sujets de ce haras manifestèrent des troubles respiratoires ou des avortements attribuables à ce virus que les auteurs isolèrent du cerveau d'un des chevaux atteints de myélo-encéphalite et des poumons de deux avortons. La recherche d'anticorps spécifiques à l'herpèsvirus équin du type 1, dans le sérum de 16 des chevaux de ce haras, en révéla un titre égal ou supérieur à 1:128, chez 12 d'entre eux.

Introduction

Respiratory disease in the young and abortions in pregnant mares are the common manifestations of equine herpesvirus type 1 (EHV-1) infection. In 1966, EHV-1 was isolated at necropsy from nervous tissue of one of seven horses clinically affected with ataxia in Norwegian studs (10).

In 1971, Danish workers reviewed recent occurrences of the nervous disease associated with EHV-1 and further commented "cases of apparently enzootically occurring ataxia and paraplegia in horses have been noticed in Denmark for more than 100 years" (1). In 1971 and 1977 American workers experimentally induced varying degrees of paralysis in pregnant mares given EHV-1 subcutaneously (6, 7). In 1975, Thorsen and Little in Canada isolated EHV-1 from spinal cord tissue of a paralyzed mare (11). In 1976, Charlton *et al* (2) recorded an outbreak in a Canadian premise in which three mares developed severe clinical signs and virus was subsequently isolated from the brain tissues of two of these mares.

This case report concerns an outbreak of equine herpesvirus infection in a stable of Standardbred horses. Nervous signs occurred in five vaccinated horses. Three other vaccinated mares aborted or lost their foals soon after birth. Respiratory disease was observed in both adult and yearling animals.

History and Clinical Findings

This Standardbred breeding farm housed 21 horses of various ages. Over the period February to July, 1976 all mares and stallions were vaccinated with a modified-live rhinopneumonitis vaccine[1] by intramuscular injection. Mares were vaccinated two weeks before transport to another farm for breeding and four to eight weeks following their return. Three yearlings, a pet pony, a saddle-horse and a boarding mare were not vaccinated.

In December of 1976 upper respiratory tract disease occurred in two foals (foal a and foal d) and in the boarding mare, mare B (Table I).

On December 24 mare A, a six year old mare, returned to the farm after a week's absence for breeding. On December 31 she developed stiffness of the hindquarters and ataxia progressing to recumbency within 12 hours. Initial examination at this time revealed dysuria, and this was relieved by catheterization. She was able to remain standing with assistance for short periods and was therefore put in a sling. During the first five days that she was kept in the sling, her condition was stable with slight improvement daily. She was maintained on intravenous fluid containing amino acids, dextrose and vitamins, and on an intramuscular preparation containing benzathine penicillin G, penicillin G procaine, dihydrostreptomycin sulfate and prednisolone acetate.[2] During the last two days her condition deteriorated and she was subsequently euthanatized on January 6.

On January 1, 1977 another mature mare, mare C, was bumping into walls but remained standing. Over the next few days this mare made an uneventful and apparently complete recovery.

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[1]Rhinomune, Norden Laboratories, Lincoln, Nebraska.

[2]Derafort injectable ®, Ayerst Laboratories, Montreal, Quebec.

TABLE I

CHRONOLOGICAL EVENTS AND SEROLOGY RESULTS OF THE EQUINE HERPESVIRUS OUTBREAK

Identity	Illness	Herpesvirus Titres[a] Acute	Convalescent
Mare A	Dec. 31 — Ataxia Jan. 6 — Destroyed	N/A[b]	N/A
Foal a	Dec. 24 — U.R.D.[c]	24	>128
Mare B	Boarding Mare — U.R.D.	64	N/A
Mare C	Jan. 1 — Ataxia — Recovered	N/A	>128
Foal c		<8	96
Mare D	Jan. 3 — Ataxia — Hospitalized to Jan. 6 at O.V.C. — Recovered	16	>128
Foal d	Chronic U.R.D.	0	>128
Stallion E	Jan. 6 — Ataxia — Recovered	32	>128
Mare F	Jan. 13 — Ataxia — Destroyed	16	N/A
Mare G	Jan. 13 — 12 hr. old foal died	64	>128
Mare H	Jan. 29 — Aborted	48	>128
Mare J	Jan. 30 — Aborted	48	64

[a]Titres — Acute Jan. 6 and convalescent Feb. 7.
[b]N/A — Not available.
[c]U.R.D. — Upper respiratory tract disease.

On January 3 mare D, a five year old mare with a yearling foal that had repetitive episodes of upper respiratory tract disease since the summer, developed acute ataxia. She was promptly sent to the Department of Clinical Studies, Ontario Veterinary College, Guelph. On admission, she was extremely ataxic and the right hindleg was paretic. There was an extreme nystagmus to the right of both eyes causing a constant blinking and moving of the head to the right with each ocular movement. A slight head tilt to the left was noted. There was extreme proprioceptive loss resulting in falls and difficulty correcting knuckling of the fetlocks. The clinical diagnosis was asymmetrical cerebellar deficits with asymmetrical myelitis. The following day the mare had improved markedly and by mid-afternoon could move about fully, apparently without apprehension. No treatment was given other than nursing care and on January 6, 1977 she was released.

On January 6 stallion E became incoordinated and although he recovered rapidly, all breeding contracts were cancelled for three months. On January 13 mare F, a 17 year old mare, that suddenly became recumbent was destroyed. Mare G foaled on January 13 and her term foal died at 12 hours of age. On January 29 and 30 mare H and mare J both aborted at seven months gestation. On April 19, another mare on the premise had a normal full term foal.

Gross Lesions

Mares A and F were submitted for necropsy. Mare G's foal and the fetuses of mare H and J were also examined.

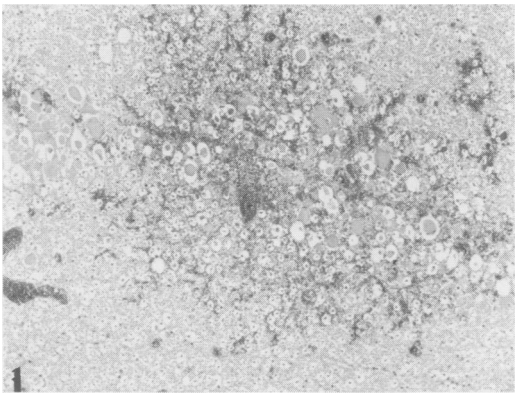
Mare A was in good condition at necropsy but had numerous pressure point abrasions on the body. A few litres of brownish fluid containing fibrin strands were present in the abdominal cavity and there were firm adhesions of serosal surfaces. A 1-2 cm perforation was present at the apex of the urinary bladder and the entire serosal surface was dull and dark red. Marked meningeal congestion and blotchy hemorrhages were on the surfaces of the spinal cord.

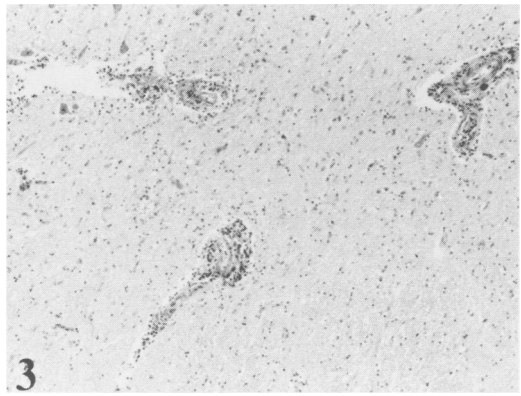
Mare F had grossly apparent hemorrhagic lesions in the grey columns, the ventral aspect of the arachnoid space and to a lesser extent in white matter of the spinal cord. Gross lesions were not observed in other organs.

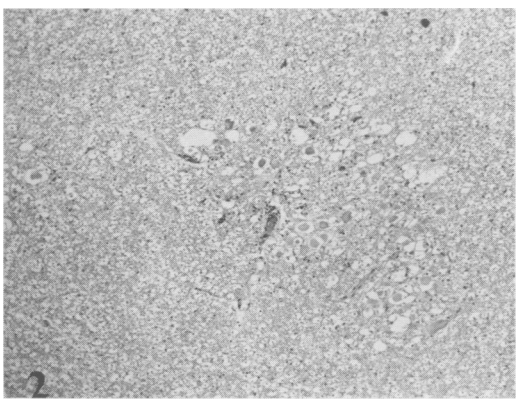
Microscopic Lesions

Histological lesions were present in brain and in spinal cord of mare A. Areas of cerebral cortex, thalamus and medulla had perivascular infiltrates that were predominantly mononuclear and adjoining parenchyma was malacic (Figure 3). Few vessels had medial hyalinization and neutrophilic infiltrates. A moderate mononuclear cell reaction was present between neurons of the Gasserian ganglion. All levels of spinal cord had lesions, although lumbosacral lesions were most marked. Typically, leptomeningeal vessels were inflamed and the inflammation continued into nervous tissue as the vessels penetrated into the spinal cord. Degenerative changes in the tunica media, mononuclear cell cuffs in the adventitia and few thrombosed vessels were noted. Focal areas of malacia with prominent swollen axones particularly in lateral funiculi of white matter typically adjoined affected vessels (Figure 2).

Mare F had necrotic and occasionally thrombosed arterioles in cerebral cortex, caudate nucleus, internal capsule, mid-brain, medulla and leptomeninges. Areas of malacia were often associated with affected arterioles. Perivascular mononuclear cell cuffing was common around these vessels. Gasserian ganglioneuritis was







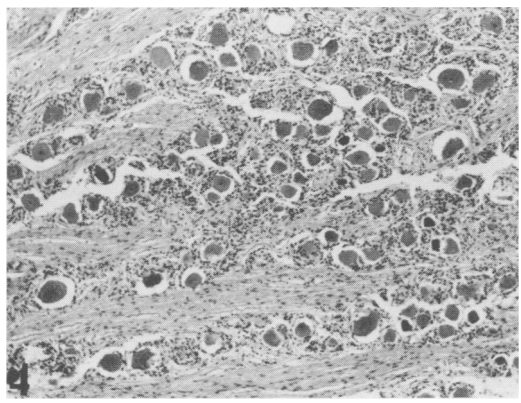


FIGURE 1. Lateral funiculus of thoracic spinal cord of mare F. Note severe acute hemorrhage, periaxonal vacuolation and swollen axons in this mare destroyed within 12 hours of becoming recumbent.

FIGURE 2. Lateral funiculus of cervical spinal cord of mare A. Note swollen axons and spongiform change. This mare was maintained for seven days following onset of signs.

FIGURE 3. Brain stem of mare A. Marked perivascular cuffs of mononuclear cells. Perivascular clear spaces are artifactual.

FIGURE 4. Gasserian ganglion of mare A. Marked mononuclear cell reaction between neurons. H & E stain. Original magnification X40.

characterized by hemorrhages and infiltrations of large numbers of lymphoid cells between neurons (Figure 4). The most outstanding lesion was the extensive hemorrhages in the dorsal and ventral grey columns, the ventral portions of the leptomeninges and the white funiculi of the spinal cord (Figure 1). Necrotic leptomeningeal and spinal arteries and arterioles with mononuclear cell cuffs were also evident. The lungs had discrete, moderate peribronchiolar and perivascular lymphoid cell cuffs.

Virology and Serology

Equine herpesvirus type 1 was isolated from the spinal cord of mare A, but was not recovered from tissues of mare F. In addition, isolates were also made from lung of mare G's foal and mare H's fetus.

Acute and convalescent serum samples were collected on January 6 and February 7 and titrated in a serum neutralization test for equine herpesvirus type 1. Seroconversions of fourfold or greater occurred in 12 of 16 for which acute and convalescent samples were available. Four of these 12 remained clinically healthy. Results on clinically ill horses and offspring are tabulated (Table I.). Both acute and convalescent samples were available for only two of the five horses that were clinically affected with nervous disease. Mare D had a conversion from 20 to greater than 128. Stallion E seroconverted from 32 to greater than 128. Foals a, c and d all seroconverted.

Discussion

As described in previous reports, this outbreak of herpesvirus myeloencephalitis in horses also had features of respiratory and genital tract disease occurring concurrently in other horses on the premises (1, 10). Little and Thorsen (8) report respiratory disease to progress to nervous disease; most others do not report signs of clinical disease preceding the nervous disease (1, 2, 10). None of the five horses affected with nervous disorders in the present outbreak had apparent respiratory or genital tract disease.

The nervous disease is of low morbidity and variable severity and affected horses often recover (2, 3, 8). Five of 21 were affected in the present outbreak and of these five, three recovered and two were euthanized. Both in experimental and in naturally occurring cases pregnancy appeared to be a prerequisite for disease (6, 7, 8, 10). Our cases and those reported by Dinter and Klingeborn (3) demonstrate that the disease also occurs in barren mares and stallions. A history of respiratory tract disease (particularly in young stock), abortions in the last trimester and the occurrence of nervous disease in a number of other horses on the premises should suggest herpesvirus myeloencephalitis as the cause of the nervous disease.

Vasculitis with secondary hypoxic degeneration in adjacent neural tissue appears to be the prominent histopathological change in both natural and experimental cases (2, 6, 7, 8). Vascular changes are generally more prominent in the spinal cord than in the brain and white matter lesions of the spinal cord are more prominent than grey matter lesions (6). Mare F was destroyed the day she became recumbent and the spinal cord lesions in this mare were acutely hemorrhagic. Mare A was maintained for seven days in a slig and the spinal cord lesions were malacic and perivascular cuffs more prominent. Neither mare had neuronophagia or other evidence of primary infection of nervous tissue itself. Vasculitis has been documented in endometrium, lungs and uveal vessels in experimentally produced herpesvirus myeloencephalitis indicating a diffuse vascular disease with most prominent involvement of nervous tissue.

Jackson *et al* (7) speculate that the pathogenesis of this disease involves direct passage of the virus from the blood leukocytes into endothelial cells. This, they say, explains both the occurrence of the disease in the presence of serum neutralizing antibody and the primary vascular nature of the disease. They further suggest that this property of EHV-1 of causing disease by primarily affecting vessels and not nervous parenchyma makes it unique among the herpesvirus infections of the different animal species. There is one other herpesvirus disease that has similar pathogenesis. Malignant catarrhal fever, a viral disease of the bovine and certain wild ruminants, is a vascular orientated disease with parallels to myeloencephalitis of the horse. Malignant catarrhal fever of the wildebeest of Africa is known to be caused by a herpesvirus (9).

Acute and convalescent serum samples were available for two of the five affected. A fourfold or greater increase of serum neutralizing antibody to EHV-1 occurred in these two. Five of six horses that had respiratory or genital disease also seroconverted to the same degree. Similar seroconversions and high titres five days or more after onset of disease have been documented in both field cases and experimental cases (1, 6, 7, 10). These results support the view expressed by Dinter and Klingeborn (3) that the nervous disease occurs because of reinfection or possibly recurrent infection of seropositive horses. Equine herpesvirus-1 has been isolated from nervous tissues of only four other horses in addition to one of our cases (2, 9, 10). It has been suggested that inactivation by high levels of circulating antibody at the time of preparation of tissue for culture may be the reason for so few isolations (6).

Vaccination was ineffective in preventing this outbreak of disease. Cases of abortion due to EHV-1 in vaccinated mares were widespread in Ontario during the 1977 foaling season (5). Respiratory disease in vaccinated young stock and abortion in vaccinated mares in Maryland have been documented (4). Our initial concern was that the attenuated vaccine virus caused the disease. The length of time that passed between vaccinations and clinical disease in our outbreak pointed to the vaccine being ineffective rather than the direct cause of the disease. The apparent efficacy of the vaccine in previous foaling seasons in Ontario suggests either a change in the field virus infecting horses or in the vaccine virus *per se*.

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