Equine encephalitis caused by snowshoe hare (California serogroup) virus

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Snowshoe hare virus (SSH), a mosquito-transmitted bunyavirus of the California (CAL) serogroup, has been documented in all provinces of Canada as well as in the Yukon and Northwest Territories (1). Serological studies have revealed CAL serogroup antibodies in horses in several provinces with exposure rates varying from 12.3–41.1% in hemagglutination inhibition and 8.3–50.0% in neutralization surveys (1,2).

Despite this high seroprevalence, there has been only one report in animals of seroconversion to SSH associated with clinical disease (3). We herein confirm a second clinical infection and seroconversion to SSH; we present the first recorded case in western Canada and describe the progression of the disease.

In August 1987, an eleven-month-old Quarter Horse filly was referred to the Western College of Veterinary Medicine (WCVM), Saskatoon, Saskatchewan because of a neurological problem. The current owners had purchased the filly by auction two months previously. Prior to the sale, the horse had apparently been vaccinated and dewormed. The filly shared a pasture with six other mature horses, all of which were healthy. The horses were fed a diet of brome and alfalfa hay. Water was provided from a slough, which had not dried up as usual this year. The horses' pasture had also remained moist for most of the season.

The filly had been healthy until the morning of the day prior to presentation, when the owners had noticed that she was "wobbly". By the evening the horse's condition had deteriorated. She had fallen several times and, although she could always rise on her own, she spent an increasing amount of time lying down. She appeared to be "nodding off" when left to stand quietly. When offered water she overreached and hit her muzzle on the pail (hyperkinesia). The horse had not improved after 36 h and was referred to the WCVM.

On presentation the filly weighed 338 kg, and was in poor to moderate condition. Clinical abnormalities were confined to the nervous system. The horse was tense and anxious. When left to stand quietly she would frequently lower her head, closing her eyes, as if going to sleep, but would startle spontaneously out of this state. At the same time and continuously, various muscle groups would twitch spontaneously and randomly. The muscles of the head and neck seemed the most affected. The horse could masticate and swallow normally at this stage. There was generalized hyperesthesia, which was most prominent on the head and neck. Her gait was hypermetric; when encouraged to speed up, she would become generally very tense and refuse to proceed. While turning in tight circles she would repeatedly step on her front feet, and the hindlimbs would circumduct and pivot. Pulling her tail to one side as she walked made her sway readily; attempting this while standing demonstrated good muscular strength. Hopping reflexes on both forelimbs and hindlimbs were delayed. Raising the horse's head did not impair balance; turning the horse's head from side to side often produced a wide-based stance.

The significant results of the initial diagnostic tests were as follows: mild leukocytosis (12.4×10^9/L), with a mild regenerative left shift of 8.2×10^9/L segmented neutrophils and 0.5×10^9/L band neutrophils, PCV 0.36 L/L. The CSF contained RBC 0.86×10^9/L, WBC 7×10^6/L, which were primarily lymphocytes, some of which were of a large granular type. The CSF protein was 0.6 g/L (normal < 0.4 g/L), the glucose was 3.6 mmol/L (normal), and the CK was 12 U/L (normal < 10 U/L).

The assessment of the horse was that she was suffering from multifocal or diffuse lesions of the central nervous system, involving one or several of the following sites: both cerebral and cerebellar cortices, the brain stem, thalamus and cranial nerve nuclei, and possibly the spinal cord. The clinicopathological findings indicated nonsupprative inflammation of the CNS with neuronal necrosis, consistent with viral encephalitis (5).

Preliminary therapy consisted of antibiotics (22,000 IU/kg procaine penicillin IM bid, Ethacillin, rogar/STB, Pointe Claire, Quebec) and tetanus antitoxin (5,000 IU IV, Equine Antitoxin, Colorado Serum Company, Fort Williams, Colorado), after all samples had been collected. In view of the potential diagnosis of rabies, it was decided not to obscure clinical signs by the administration of corticosteroids.

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TABLE 1
Arboviral serology of a filly with encephalitis[a]

	Hemagglutination inhibition			Complement fixation			Serum neutralization		
Day[b]	2	11	56	2	11	56	2	11	56
Antigen									
EEE	—	—	—						
WEE	40	40	20						
POW	—	—	—						
SLE	—	—	—						
CV	—	640	320				—	—	—
SSH	10	320	160	—	—	—	20	320	320
JC	—	320	160	—	—	—	—	—	—

EEE = eastern equine encephalitis, WEE = western equine encephalitis, POW = Powassan, SLE = St. Louis encephalitis, CV = Cache Valley, SSH = snowshoe hare, JC = Jamestown Canyon

– = < 1:10 in hemagglutination inhibition and neutralization tests and < 1:4 in complement fixation test

[a]Results are expressed as the reciprocal of the serum dilution
[b]Refers to days after onset of signs

Twelve hours after admission, the horse had become slightly more depressed, with exacerbation of all clinical signs, including a marked intention tremor of the head as she prehended food and water, and dysphagia due to paresis of the anterior portion of her tongue. She also developed projectile diarrhea.

Approximately 60 h after onset of original signs, the horse became recumbent and had a single generalized seizure with tonic-clonic muscle tremors and opisthotonus. The seizure lasted for 2–3 min, after which the horse sat up quietly in sternal recumbency for about 20 min then rose on its own. No therapy was given. The severity of clinical signs continued unchanged until the fourth day of illness, after which she began to recover.

On the sixth day of illness she no longer twitched spontaneously, but was still generally hyperesthetic when touched or in response to loud sudden noises (clapping, banging doors). An EEG at this stage was characterized by periodic episodes of generalized synchronous slow high-amplitude wave activity (Figure 1). The duration of these episodes was for an average of only 3–4 s every 2–3 min and is consistent with diffuse encephalitis and generalized seizure activity. By day 13 the filly weighed 358 kg and was discharged with a good prognosis. A definitive serological diagnosis of SSH was made by SN (Table 1). Serology was negative for antibodies to *Toxoplasma*, equine herpesvirus-1, and equine viral arterites virus.

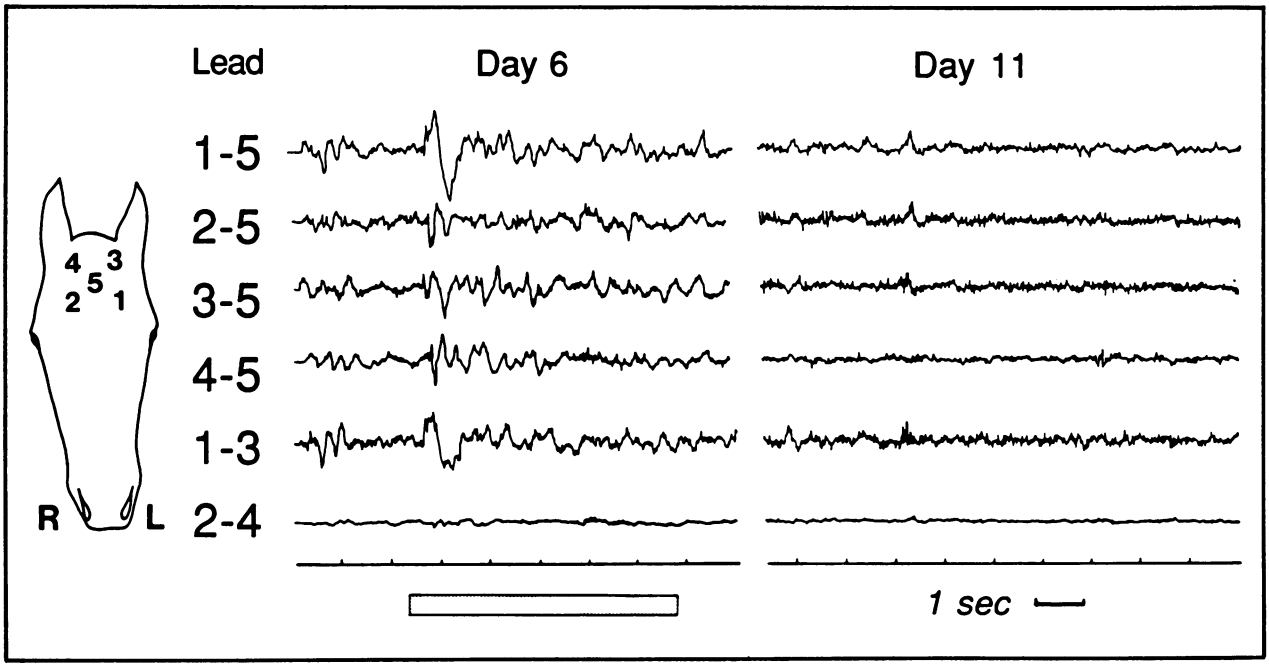

Figure 1. Electroencephalogram of filly on days 6 and 11 with clinical snowshoe hare encephalitis. Periodic high-amplitude slow wave activity (bar) on day 6 is abnormal. The EEG confirms clinical recovery on day 11.

California serogroup viruses have been shown to infect a wide range of wild and domestic animal species in Canada (1), however, their role as etiological agents of disease in animals has only rarely been suggested. CAL serogroup viruses have been isolated from fifteen species of *Aedes* mosquitoes in Canada as well as from *Culiseta inornata* and *Culex* spp. mosquitoes (1,8,9). Yuill *et al* (6) studied population dynamics and antibody rates to a CAL serogroup virus in the snowshoe hare (*Lepus americanus*) and provided evidence that mortality was higher among hares with CAL serogroup antibodies than those without. Keane *et al* (7) demonstrated CAL serogroup antibodies in two cats with clinical signs consistent with arbovirus infections, however, only single serum samples were tested. Lynch *et al* (3) demonstrated seroconversion to SSH virus in a yearling Hunter stallion with encephalitis, but the authors were cautious in their interpretation, as it was unclear whether the clinical signs in this horse were due to SSH virus or other factors. The current report provides conclusive evidence that SSH virus is capable of causing symptomatic infection of horses.

Snowshoe hare virus should be considered during mosquito season as a possible etiological agent of encephalitis in symptomatic horses

The signs of arboviral infection appear to vary with the host species, the dose of the virus, the age of the host, its nutritional status and season. In humans, children appear to be more susceptible to symptomatic infection (encephalitis, flu-like symptoms) due to CAL serogroup viruses (1), whereas adults usually remain asymptomatic. Both our case and the only other reported equine case of SSH encephalitis (3) were in yearling horses. It is possible that young horses are at higher risk.

In humans, poor nutritional status has been implicated as a predisposing factor for the development of nervous signs after an arboviral infection (10). This horse was in below average condition, and one may speculate that this was an additional risk factor for not only a significant infection, but also for the development of the encephalitic form of the disease.

Transmission of arboviruses is by mosquitoes. The other reported case of SSH encephalitis occurred in July (3); the horse in this report was presented in August. This probably reflects a seasonal trend, coinciding with peak populations of mosquitoes. There was a relatively high density of mosquitoes in southern Saskatchewan in 1987 and it is interesting that the pasture where the horses were kept had been unusually moist that year.

Hemagglutination inhibition seroconversion in this filly was demonstrated to three antigens — SSH and JC, which are related CAL serogroup antigens, and to CV. Previously, Artsob *et al* (11) have shown HI cross reactions in horses between SSH and a bunyavirus that was subsequently identified as CV by SN. A serum neutralization test is therefore necessary to identify the causative agent; in this case SSH was the responsible agent.

The lack of complement-fixing antibodies in this horse parallels observations commonly seen in humans infected with CAL serogroup viruses, wherein a poor or nonexistent complement fixation response often occurs (1).

Rabies, equine herpesvirus type 1, western equine encephalitis and eastern equine encephalitis are the most common viral causes of equine neurological disease in Canada (12). Snowshoe hare virus should also be considered during mosquito season as a possible etiological agent of encephalitis in symptomatic horses.

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