



The Return of the Viral Helhest: Presentation of a Western Equine Encephalitis Case Report

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Abstract

Western equine encephalitis is a central nervous system disease caused by the Alphavirus virus of the Togaviridae family, transmitted by the Aedes Albifasciatus vector. We describe the case of a previously healthy 30-year-old male patient, resident in an urban area of the province of Buenos Aires, with a work history of contact with horses, who was hospitalized and diagnosed with meningoencephalitis. Due to the sluggish course of his condition that none of the most common microorganisms were isolated, an Elisa IgM antibody test was requested in cerebrospinal fluid, which was positive for western equine encephalitis virus. Although it is essential to take into account the low epidemiological incidence of the disease, and in this case, with a high mortality rate; that, despite carrying out supportive treatment, the neurological sequelae that were triggered prevented a favorable evolution in the patient.

Introduction

A Helhest in Scandinavian mythology refers to a three-legged horse of the goddess of the underworld Hela, who used it to announce illnesses, accidents and especially deaths. Western equine encephalitis is a central nervous system condition caused by the Alphavirus virus of the Togaviridae family transmitted by the Aedes Albifasciatus vector. According to the WHO, the current epidemiological situation in Argentina through the announcement of the National Service for Food Health and Quality (SENASA), reports equines infected with the virus. In November 2023, the Ministry of Health activated the epidemiological alert to detect possible cases in humans. So far, more than 572 suspected cases have been reported, of which more than 108 have been confirmed in the country, with a fatality rate ranging between 3 and 15%, mainly in older males [1]. The disease in humans is registered again in the country after more than two decades, since the last detections were in 1983 and 1996.

Case Report

We present the case of a 30-year-old man, with a work history of contact with horses, who consults for fever and dyspnea for 48 hours. On-call he presents rapid neurological progression with deterioration of the level of consciousness that requires IOT/AVM, for

which he is admitted to a closed unit; a CT scan of the brain is performed with signs of cerebral edema, HIV Negative, CSF with proteinorrachia 76, Glucorraquia 57, Leukocytes 182 with predominance of polymorphonuclear 97%. Therefore, it was diagnosed as probable CNS infection.

During his stay in the ICU, the neurological examination stands out; The appearance of bilateral spontaneous horizontal nystagmus, disproportionate motor deficit, with signs of pyramidal release: (hypertonia, spasticity and hyperreflexia) (Figure 1). The initial tests (basic analysis and cultures for common microorganisms) are normal; EEG with slow rhythm without discharges. The MRI of the brain shows hyper intensity in T2 and Flair in the basal ganglia, midbrain and pons (Figure 2).

In the presence of an active epidemiological surveillance circular by the Argentine Ministry of Health for equine encephalitis, an IgM Elisa test is requested on cerebrospinal fluid, which is positive. With these data, the timely diagnosis for western equine encephalitis is reached; which as a consequence leads to severe motor and ventilator sequelae, with total dependence for daily life activities. Treatment is carried out with hemodynamic, ventilator support, anticonvulsants and anti-cerebral edema measures. However, he presents a torpid evolution that leads to death in April 2024.

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Keywords

Western Equine Encephalitis, Alphavirus, Incidence, Sequelae, Mortality.

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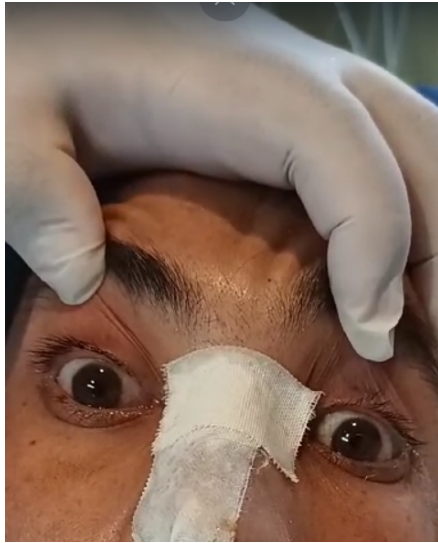


Figure 1. Involuntary, rapid, repetitive, bilateral horizontal movement of the eyes. (Bilateral Spontaneous Horizontal Nystagmus)

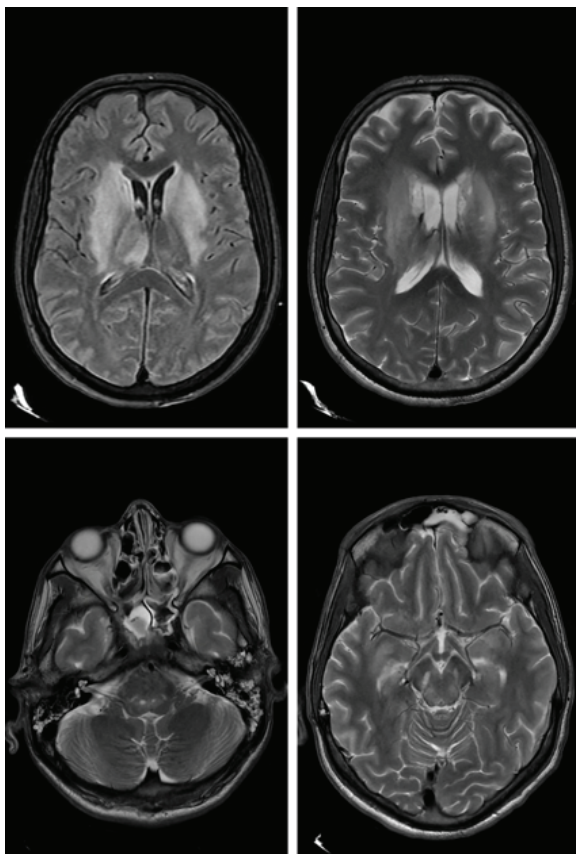


Figure 2. T2 and Flair brain MRI shows subcortical hyper intensities at the level of the thalamus, internal capsule, basal ganglia and brain stem (midbrain and pons)

Discussion

PubMed, MEDLINE, and the Cochrane Library were searched, restricted to English-language publications from January 2016 to September 2024.

It was first isolated in 1930 (Meyer et al., 1931, marking the initial identification of the western equine encephalitis virus) in the San Joaquin Valley in California, however, the virus was only isolated from the human brain in 1938 [2]; in Argentina, the WEE virus was first isolated in horses in 1933. Since then, major equine epizootics have been recorded in the temperate zones of the north and center of the country [3]. The virus is present in much of the Americas, with virological or serological evidence of circulation in western Canada, the United States, Mexico, and regions of South America, such as Ecuador, Brazil, Uruguay, and Argentina [4]. In November 2023, the Ministry of Health activated the epidemiological alert to detect possible cases in humans. To date, >572 suspected cases have been reported, of which >108 have been confirmed in the country, with a fatality rate ranging from 3 to 15%, mainly in older males [1].

Western equine encephalitis (WEE) is a zoonotic disease caused by an RNA virus of the Alphavirus genus [5]. The transmission cycle is enzootic and epizootic with episodic increases where humans and equines are the final host [1]. The immunopathogenesis of the disease occurs in the early moments of infection, most alphaviruses are first encountered by resident macrophages or dendritic cells, infected macrophages secrete proinflammatory cytokines that recruit CD4 and CD8 T cells, they avoid the innate immune response by recruiting to the site of infection. Subsequently infected macrophages infiltrate the brain, chemoattractant molecules are upregulated in the brain, which disrupt the blood-brain barrier and recruit additional immune cells to the brain, secretion of proinflammatory cytokines triggers viral encephalitis [6]. Clinical signs are not pathognomonic, but may include fever, headache, myalgia, asthenia, and malaise. The incubation period is 2 to 10 days, most cases are asymptomatic or present as mild, nonspecific symptoms that resolve spontaneously in 7 to 10 days [1]. A certain number of cases usually present neurological symptoms with neck stiffness, sensory impairment, seizures, spasticity, and coma. Imaging findings are nonspecific and may be multiple, usually showing inflammatory changes in the thalamus or basal ganglia. In our patient, all of the above was observed, in addition to involvement at the brain stem level. The literature usually describes the presence of lymphocytic pleocytosis and hyper proteinuria in cerebrospinal fluid.

The etiological search is carried out through serology (IgM), viral identification by PCR in cerebrospinal fluid or brain tissue sample, as long as cultures for common microorganisms have been ruled out [1]. The treatment fundamentally focuses on patient care, alleviating symptoms and improving quality of life; In our patient, pharmacological measures were managed with levetiracetam for ictal seizures. A regimen was started with an initial dose of 3000 mg/day and for spasticity, baclofen was started with an initial dose of 30 mg/day with a maintenance dose of 60 mg/day with escalation to diazepam at an initial dose of 10 mg/day. Since no pharmacological response was obtained, therefore, management with IV morphine was started.

According to review articles, it has been documented that Alphavirus infection can cause serious neurological sequelae, such as neuropsychological changes and intellectual disabilities. They are most frequently described in children, but can affect individuals of any age group. The recent increase in viral clinical cases and associated neurological deficits have reminded us that viral infections can cause long-term detrimental effects. Western equine encephalitis is considered the second deadliest of the three major alpha-encephalic viruses, with a mortality rate of

3-7%, so it is not surprising that case studies describe that up to 30% of survivors develop neurological sequelae, the most common being intellectual disability, emotional instability, behavioral changes, and spastic paresis, among others [3]. In the case of the patient, he presented a marked ventilator sequel, due to an alteration of pCO₂ retention, despite the fact that ventilator rehabilitation was carried out, it was never possible to wean him from mechanical ventilation, which is why he died from ventilator-associated pneumonia. Respiratory control is a complex process that involves the interaction of multiple areas of the brain, including the medulla oblongata, the pons nuclei, the cerebral cortex, and the brainstem nuclei. This neural network coordinates the activity of the respiratory muscles to maintain a constant supply of oxygen and eliminate carbon dioxide from the body, continuously adapting to metabolic demands and environmental conditions. The basal ganglia are a set of gray matter nuclei located at the base of the brain. Although they have traditionally been associated primarily with the coordination of movement and motor control, they also play an important role in the regulation of breathing, albeit indirectly, by being involved in the planning and execution of movements, they can also indirectly influence breathing through the regulation of the muscular activity associated with it. In addition, they are interconnected with areas of the brain that participate in the control of breathing, such as the brain stem, which facilitates their influence on this process. Consequently, although the basal ganglia do not directly control breathing, their influence on the regulation of muscular activity can indirectly affect respiratory function by influencing the muscles involved such as the diaphragm and intercostal muscles. In summary, patients affected by equine encephalitis may require prolonged MRA due to severe neurological complications affecting respiratory function, level of consciousness and the ability to protect the airway. Treatment of these complications is essential to improve the patient's prognosis and recovery.

The aftermath of the Texas WEE outbreak in 1971 also determined the cost of infection per person at \$320,000 USD more than 20 years later, the economic burden associated with patients suffering long-term sequelae is too high, total hospital costs during the first week of infection were approximately \$21,000 USD [3].

It is essential to highlight that prevention is key in the management of equine encephalitis. Mosquito control measures, horse vaccination, and in some cases antiviral prophylaxis are important to prevent the disease in humans and animals. In addition, early and aggressive treatment of neurological complications can help improve the prognosis in affected cases [1].

Conclusion

It is essential to have institutions and health personnel trained for passive epidemiological surveillance and timely detection of infectious diseases, to avoid underdiagnoses; due to the low incidence of the disease itself. The diagnosis of this entity should be considered in the context of negative results for common microorganisms and an epidemiological link with infected horses. An adequate and timely primary prevention intervention would reduce the economic consequences that could result in disastrous total hospital costs for someone who suffers long-term sequelae.

Conflicts of Interest

All authors declare that they have no conflicts of interest.

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