Case Report

Herpes Simplex Virus-2 Encephalitis Complicated with Multiple Cranial Neuritis and Dysautonomia

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Introduction: Herpes simplex encephalitis (HSE) is mainly caused by herpes simplex virus-1 infection (HSV-1). Herpes simplex virus-2 (HSV-2) infection is rare except in neonates or the immune-compromised. Cranial neuritis is rarely reported in association with HSE. This case study in an eleven-month-old followed by a literature review on cranial neuritis in HSE in children is presented due to the rarity of both situations. Case Report: An eleven-month-old otherwise healthy infant presented with encephalitis due to HSV-2 infection which was complicated with dysautonomia manifesting as blood pressure fluctuations and tachycardia, and cranial neuritis manifesting as unilateral ptosis and palatal palsy. The clinical presentation of brain stem encephalitis was confirmed by the Magnetic Resonance Imaging findings of hyperintense foci and contrast enhancement in the medulla oblongata. Following treatment with acyclovir, he made a complete recovery. He did not have any clinical or laboratorial evidence suggestive of immune deficiency. Conclusion: HSV-2 infection can occur beyond the neonatal age group even in the absence of immune compromise. The brainstem encephalitis manifesting as cranial neuritis and autonomic dysfunction made a complete recovery.

Keywords: Brainstem encephalitis, cranial neuritis, herpes simplex virus encephalitis

Introduction

Encephalitis is mostly caused by viral etiologies and herpes simplex virus (HSV) is considered to be responsible for 20% of all infective encephalitis.[1] Herpes simplex viral encephalitis (HSE) is notorious due to the unfavorable neurological outcome and death, reported in about 30% of affected patients.[2] It is mainly caused by herpes simplex virus-1 (HSV-1) infection, accounting for 90% of infections.[3] HSE related to herpes simplex virus-2 (HSV-2) is rare and is often limited to neonates or to the immunocompromised.[3] HSV-2 is generally considered to cause a milder illness.

HSE is notorious to affect the frontal and temporal lobes,[4] responsible for the common clinical features of behavioural and personality changes, cognitive impairment, aphasia, seizures, and motor weakness. It is likely that the virus spreads to these areas via neural pathways, for example, the temporal lobe through spread along the olfactory pathway and the temporal and frontal lobes via spread from the trigeminal ganglia where the virus is known to lie dormant for long durations.[4] Rarely, brainstem involvement is reported. The pathogenesis is related to infection or inflammation or associated infarction causing dysfunction of cranial nuclei/nerves and or the vasomotor centre. Autonomic dysfunction is considered to be related to this effect on the vasomotor centre. Reports of cranial neuritis secondary to HSE...
caused by HSV-2 infection are limited to a single case report in a neonate.\cite{5}

**Case History**

An eleven-month-old previously healthy infant admitted with persistent drowsiness and seizures. He had three days of fever, one episode of loose stool, and vomiting before admission. There was no exposure to any toxin, drug overdose, recent travel or significant past history to consider renal, liver, or metabolic disorder. Examination revealed a Glasgow coma scale of 12/15 with no obvious cranial nerve palsies or focal weakness. The limited fundoscopy detected no papilledema. There were no skin rashes or signs supportive of meningeval infection.

Although his vital parameters were within the normal range on admission, within a few hours the blood pressure dropped causing features of peripheral circulatory dysfunction. This responded to a single fluid bolus of 0.9% sodium chloride. His vital parameters remained stable for the next 12h. Thereafter a progressive elevation of blood pressure to above the 99th centile for age and length was noted. The elevated pressures persisted for more than 24h. His heart rate increased to 110–130 bpm in sleep in the absence of temperature or seizures. His pupils were equally reactive. Abnormal posturing or temperature fluctuation were not experienced.

His drowsiness persisted with an unchanged coma scale over the first 72h. On the third day of admission, he was noted to have unilateral ptosis. He also had palatal weakness manifesting as spontaneous drooling and cough induced by sucking. Examination revealed deviation of the eye to the left with normal pupillary response and reduction of movements of the palate on the left side. The rest of the cranial nerve examination was normal. Upper and lower limbs were neurologically normal. The palatal palsy required insertion of a nasogastric tube for safe feeding and regular suction and oral glycopyrolate to avoid the accumulation of secretions.

Initial haematology showed 11.3*10^3 u/L total white cell count with <5.0 mg/L c-reactive protein. His renal and liver functions and electrolytes were normal (SGPT 14U/L, SGOT 33U/L, BU 14U/L, Serum creatinine 36 μmol/L Serum Sodium 136 mmol/L, and potassium 4.3 mmol/L). The chest X-ray was clear. Lumbar puncture detected normal cerebrospinal fluid (CSF) pressure; 22/cumm lymphocytes, 1/cumm polymorphs, sugar of 3.9 mmol/L, and protein of 30mg/dL. CSF viral PCR panel was positive for HSV-2. The electroencephalogram showed diffuse slowing. Magnetic Resonance Imaging showed white matter high signal intensities in posterior parietal and occipital regions and hyperintensity foci with contrast enhancement in the bilateral medulla oblongata. His mother was positive for HSV-2 antibodies, but his father was negative. The baby’s screen for immune deficiency was negative.

He was commenced on appropriate doses of intravenous anti-bacterials, high dose acyclovir, prophylactic anticonvulsants, and oseltamivir during the initial phase but subsequently limited to intravenous acyclovir for 21 days. Elevated blood pressure required single dose of Amlodipine after which the blood pressure remained stabilized. Palatal dysfunction was managed with nasogastric tube feeding. Fibreoptic evaluation was deferred due to autonomic dysfunction.

There was a progressive improvement of the level of consciousness and disappearance of ptosis and stabilisation of blood pressure by end of the first week of treatment. Recovery of palatal dysfunction was slow with an independent self-feeding state achieved only by end of three weeks. Two-month post-discharge review confirmed complete recovery and normal developmental outcome.

**Discussion**

HSE accounts for 10–15% of all encephalitis in the United States but a recent study from Sri Lanka in 99 cases of suspected encephalitis in adults and children, detected no cases of HSV.\cite{6} In spite of its reputation for serious mortality and morbidity, 20% of HSE are known to present with mild disease or atypical course of illness. Host factors are clearly critical in its determinant and several specific genetic host factors such as impaired cellular interferon (IFN) responses and Toll-like receptor 3 (TLR3)-IFN type 1 and 3 pathway defects have been implicated for this variability.\cite{7}

Studies limited to HSE in children are rare. HSV-1 infection is responsible for clear majority of cases. Exceptional case of HSV-2 infection is limited to the neonatal period or rare adolescent who is sexually active. HSV-2 central nervous system (CNS) infection is often mild.

Commonly reported complications of HSE are related to localization of the cerebral involvement, often in temporal and frontal lobes, which can be unilateral or bilateral. The localization to these specific brain regions may occur as a consequence of spread along particular neural pathways, possibly via olfactory pathways to the temporal lobes or from trigeminal ganglia, where the virus is described to be latent. Bulbar dysfunction
in HSE is reported rarely. It is reported mainly in those with opercular syndrome which manifest with dysarthria, facial diplegia, and swallowing difficulties, most making a remarkable recovery over time. The pathology in most is related to unilateral or bilateral cortical dysfunction in the insular region.

The cause of bulbar dysfunction and ptosis in our patient were related to cranial neuritis. The pathogenesis may be related to the virus spreading along nerve trunks by retrograde axonal transport to cranial or spinal sensory ganglia. The most frequently reported is vagal nerve neuritis often manifesting as vocal cord palsy due to recurrent laryngeal nerve involvement.[8] Some other reports include sixth cranial nerve and third cranial nerve[9] neuritis. Our literature search on cranial neuritis following HSE in children found only four cases in the English language. These include one case of HSV-2 in a 16-day-old neonate with brainstem involvement with facial diplegia and absence of gag reflex due to involvement of seventh, ninth, and tenth cranial nerves,[5] a six-year-old with HSE with the involvement of unilateral facial nerve and absent gag reflex due to possible ninth and or tenth nerve neuritis,[10] two ten-year-olds with HSE complicated with multiple cranial neuritis. Cranial nerves II, III, and VII were affected in the second.[11,12] In all these cases, the cranial neuritis was reported to have improved over a few weeks duration as seen in our patient.

**Conclusion**

HSV-2 rarely affects children beyond the neonatal age group and can be a cause of brainstem encephalitis. The associated cranial neuritis improved over a short period of time.

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**Conflicts of interest**

There are no conflicts of interest.

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