CASE REPORT

A Case of Severe Transient Sinus Bradycardia in Herpes Simplex Infection

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ABSTRACT

Herpes simplex virus remains the commonest organism of sporadic encephalitis. Common presentations in herpes simplex encephalitis are seizures and behavioural changes apart from fever, lethargy and headache. Cardiac manifestations, nonetheless, are uncommon in herpes simplex infection. We presented an 8-year-old boy with clinical meningoencephalitis and bradycardia. The initial impression was typhoid meningitis due to severe bradycardia. He was managed in paediatric intensive care unit with transcutaneous cardiac pacemaker and infusion of low dose noradrenaline until the bradycardia resolved. A diagnosis of herpes simplex encephalitis was made based on clinical and specific right temporal and focal radiological findings including right insular ribbon involvement, focal changes over temporal and frontal electroencephalographic (EEG) inference and positive HSV IgM serological confirmation.

Keywords: Herpes simplex, HSV infection, Herpes infection, Sinus bradycardia, Arrhythmia

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INTRODUCTION

Type 1 herpes simplex virus (HSV) encephalitis, commonly presented with symptoms and signs include headache, fever, altered conscious level, focal neurological signs, seizures and aphasia. Polymerase chain reaction (PCR) detection of HSV DNA in the cerebrospinal fluid (CSF) is the gold standard investigation. It has high percentage of sensitivity and specificity; however, virus distribution may not be uniform leading to false negative results.

In addition to neurological complications, HSV infection was known to cause cardiac arrhythmias (1). Syncopal attacks and ictal asystole have been mentioned in few cases attributed to HSV encephalitis. This case is an evidence that HSV infection should be considered in view of signs of meningoencephalitis and significant bradycardia.

CASE REPORT

A Malay boy, aged 8, presented with a week history of persistent fever, headache and lethargy that had not improved despite a course of antibiotic. At home, he became fretful, refused to talk and slept most of the time. He was treated as clinical meningoencephalitis in view of high-grade fever, neck stiffness, altered behaviour and commenced on intravenous ceftriaxone as well as acyclovir. Initial laboratory investigations showed leucocytosis with total white count of 26.7×10^9/L (predominantly neutrophil 85%) and C-reactive protein of 103 mg/L.

Lumbar puncture was initially abandoned as he developed episode of relative bradycardia with pulse around 60 bpm. Apprehended about impending cerebral oedema, the lumbar puncture was cancelled. A computed tomography (CT) brain was arranged and showed subtle meningeal enhancement at the right parieto-temporal and pontine regions and lesion of right insular ribbon as shown in Figure 1. He was commenced on intravenous dexamethasone for bacterial meningitis as impression was typhoid or legionella meningoencephalitis due to altered behaviour, neck stiffness and bradycardia.

On day 2 of admission, he deteriorated further with severe bradycardia down to 40 bpm with normal blood pressure. Figure 2 showed a series of electrocardiograms (ECG) showed sinus bradycardia with normal PR interval 0.12-0.16s and normal QTc 0.4-0.42s with normal creatine kinase and creatine kinase-MB. His

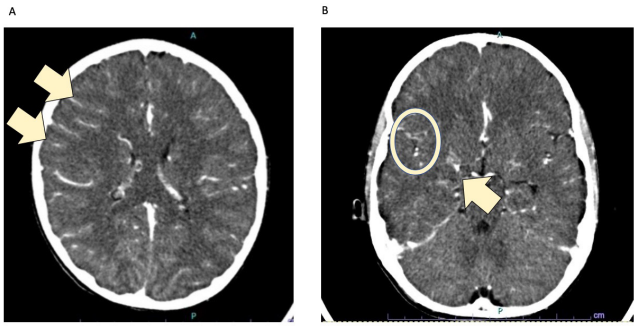

Figure 1: Axial view CT Brain with contrast showed (arrows) subtle meningeal enhancement at the right parieto-temporal regions (A) and pontine region (B) with no sign of raised intracranial pressure or oedema or cerebral abscess and subtle lesion over right insular ribbon (circle in B).

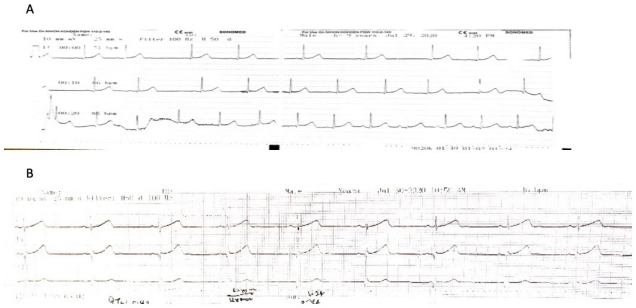

Figure 2: ECG showing progressing sinus bradycardia. (A) is an ECG on day 2 of admission showing sinus arrhythmia with heart rate 60 bpm, normal axis for age, PR interval 0.17ms and QTc interval 0.44ms. (B) is an ECG on day 3 of admission showing sinus rhythm with heart rate 50 bpm, QTc interval 0.4 ms and PR interval 0.12ms.

echocardiography findings were grossly normal, good ventricular function and no pericardial effusion thus ruling out myocarditis. Therefore, he was transferred to paediatric intensive care unit (PICU) for placement of low setting (5mA current) transcutaneous cardiac pacemaker alongside low dose noradrenaline infusion as per Advanced Cardiac Life Support (ACLS) algorithm.

His infective screening including blood culture, leptospirosis, dengue and chikungunya, mycoplasma, parvovirus and cytomegalovirus were all negative. However, the microbiology test for HSV IgM serology came back positive at day 12 of admission. We finally proceeded with lumbar puncture at day 14 of admission. An EEG was also performed as shown in Figure 3 showing bi-frontal slowing with intermittent discharges over right temporal area..

The CSF revealed normal result with no organisms were seen on gram stain or cultured. CSF for viral PCR was requested and revealed no detected virus. Considering the clinical progress, CT brain findings that confined to right temporal region and insular ribbon, and EEG with focal abnormalities to the right temporal and frontal regions, the final diagnosis was revised to HSV encephalitis. It

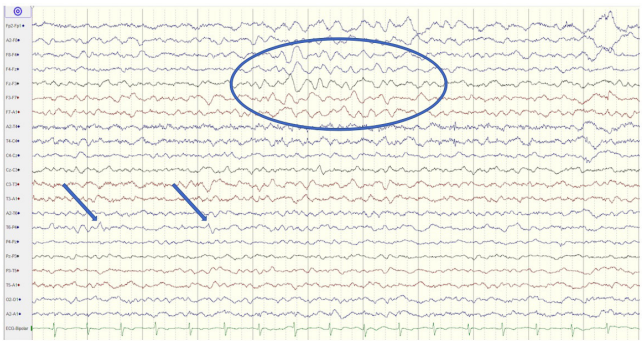

Figure 3: The awake EEG showed a transverse view montage of the patient with disturbed background activity with marked slowing over bilateral frontal regions (circle) and intermittent discharges in right temporal areas (arrows).

was unfortunate that we were unable to perform an MRI brain to ascertain the meningoencephalitis due to maintenance issue.

Over the completion of ceftriaxone for 14 days, 6 days of dexamethasone and acyclovir for 21 days, the patient showed significant improvement as he was discharged without any complication.

DISCUSSION

HSV spawn up to 40% causes of sporadic encephalitis cases. It subsists the only viral encephalitis with an effective anecdote to date. In 2017, a study published in the United States showed a data of hospitalisation was 10.3 ± 2.2 cases per millions in neonates and 2.4 ± 0.3 cases per millions in children (2). Meanwhile, case fatality rate in neonates and children was 6.9% and 1.2% respectively (2).

HSV encephalitis commonly presented depending on the location of the affected lesion. Classically, HSV encephalitis confines asymmetrically to temporal lobes and therefore symptoms such as fever, headache and impaired consciousness or behavioural alterations are typical (3). Meanwhile, fronto-temporal lesion types encompassing symptoms such as aphasia, seizures and occasionally coma.

The limbic nervous system is also an area that HSV seems preferentially targeted (4). The limbic system involves in memory, cognition, behaviour and autonomic nervous system (4). It is where the subcortical structures meet the cerebral cortex. Comprehensively, HSV encephalitis may disrupt the autonomic nervous system that complicated the heart rhythm, and, in this case, it caused transient severe bradycardia.

Bradycardia is elusively associated with Gram-negative and intracellular bacterium such as *S. typhi, L. pneumoniae* and *Chlamydia sp*. This phenomenon could be explained firstly, an autonomic nervous system mechanism via vagally mediated pathogen-induced

bradycardia and secondly complex immune system involving endotoxins and cascade of immunological responses. In this case, the only positive microbiological analysis was HSV IgM serology which retrospectively suggested the clinical picture despite the raise of total white blood cells, which led the managing team to treat him as bacterial meningitis or possible typhoid infection. HSV IgM is however is not confirmatory and about 10% could be false positive due to cross-infection (5).

Sinus node arrest and asystole associated with HSV encephalitis have been reported (3). Interestingly, in temporal lobe epilepsy, there have been association with cardiac arrhythmias. HSV encephalitis commonly affect temporal lobe unilaterally, following the nasal passage, hence in this cases, based on the CT and EEG findings a centrally mediated autonomic disturbance is sensible to explain the bradycardia phenomenon (2). Furthermore, right insular ribbon changes also known to cause autonomic disturbance as well.

In this patient, we placed a transcutaneous cardiac pacemaker and low dose of noradrenaline infusion as per ACLS algorithm. Despite taking around four days to resolve the cardiac manifestation, there was no prerequisite indication to convert the pacemaker to a permanent form. This proved the transient nature of his bradycardia. Hence, it was appropriate to continue antibiotic and antiviral management in leading to full resolution of the cardiac arrhythmias.

CONCLUSION

HSV infection can be complicated with central autonomic disturbance leading to cardiac arrhythmias, particularly bradycardia. In such cases, when cardiac causes have been ruled out, typical EEG changes in addition to temporal and insular ribbon lesions in neuroimaging, HSV should be a primary suspect to be the culprit of autonomic disturbances.

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