Japanese Encephalitis presenting with cerebral venous sinus thrombosis: a case report

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SUMMARY

A 17-year-old man from Sarawak presented with acute encephalitis syndrome. Serologic testing revealed raised Japanese Encephalitis (JE) IgM antibody titre in which first serum JE was negative followed by positive second serum JE IgM one week later. Magnetic resonance imaging (MRI) and Magnetic resonance venogram (MRV) showed cerebral venous sinus thrombosis (CVST) which is a rare presentation of JE. Early identification of CVST is important as anticoagulation needs to be started to reduce adverse neurological sequelae and improve prognosis.

INTRODUCTION

Japanese Encephalitis (JE) is a form of viral encephalitis endemic in certain parts of the world including South East Asia and western pacific regions. It is a vaccine preventable disease. The JE vaccine has been part of the immunisation programme in Sarawak state in Malaysia since 2002. This report describes a case of Japanese Encephalitis presenting with cerebral venous sinus thrombosis in Sarawak. This type of presentation is rare and was first reported by Min Jia et al., in BMC neurology 2012[1] and Mokkappan S et al., in BMJ case report 2015.[2] This will be the third case report in the world and first in Malaysia with certain important differing features.

CASE DESCRIPTION

A 17-year-old man presented with fever for four days, neck pain and reduced consciousness for two days. He lives in a rural area beside a river. There was no history of travel to pig rearing farms but he had contact with domestic animals such as chicken and ducks. He had patent ductus arteriosus which was ligated at 1-year-old. He did not receive JE vaccination before. Upon arrival to hospital, he developed two episodes of generalised tonic clonic seizures which were aborted with intravenous (IV) diazepam. His Glasgow coma scale (GCS) was E4V1M5: 10/15 with bilateral pupils measuring three millimetres and reactive to light. Neurological examination revealed neck stiffness with reduced movements over his right lower limb compared to his left lower limb. Reflexes were brisk and there was increased tone over his right lower limb. Right plantar reflex was equivocal but up-going on the left side. There was gaze preference towards his right side. His temperature was 38.7-40°C. No clinical evidence of vasculitis. Investigation results revealed normal white blood cell count with thrombocytopenia and haemoconcentration. Renal function was mildly impaired in keeping with dehydration (urea: 7.8mmol/L, creatinine: 131µmol/L). Coagulation profile was normal. Serology for dengue, HIV, hepatitis C, syphilis and antinuclear antibody were negative. Lumbar puncture on admission revealed opening pressure of 12.5cmH20, 1 lymphocyte on cell count, normal protein and glucose ratio with negative cerebrospinal fluid (CSF) and blood cultures. Initial cerebrospinal fluid JE and serum JE were negative. Echocardiogram showed normal heart with no evidence of thrombus. Computed tomography (CT) brain on admission showed leptomeningeal enhancement with an ill-defined left thalamic hypodensity suggestive of infarction.

Magnetic resonance imaging (MRI) brain done two days after admission revealed T2 and FLAIR hyperintensity over bilateral middle cerebral artery (MCA) territory involving the insula, frontoparietal cortex, bilateral thalamus, bilateral head of caudate and lentiform nuclei and left side of midbrain (Figure 2). Restricted diffusion over these regions was seen on diffusion-weighted imaging (DWI) sequence. There was no blooming effect on gradient recalled echo (GRE) sequences or post-gadolinium (GAD) enhancement. On magnetic resonance venogram (MRV) sequence, there was an abrupt tapering over middle and distal part of superior sagittal sinus extending into the bilateral proximal transverse sinuses suggestive of venous thrombosis (Figure 1). These features were suggestive of multifocal infarct involving bilateral MCA territory, basal ganglia, bilateral thalamus and left midbrain with superior sagittal and transverse sinuses thrombosis.

He was intubated on admission and was started on IV acyclovir, IV ceftriaxone and IV dexamethasone. IV phenytoin loading and maintenance doses were given to control his seizures. Initially aspirin were started and subsequently changed to low molecular weight heparin once the diagnosis of cerebral venous sinus thrombosis (CVST) was made on day-4 of admission. His serum JE IgM was repeated a week later which showed seroconversion to positive titres.

During hospitalisation, he developed multiple complications including nosocomial pneumonia, urinary tract infection, sacral sore and upper gastrointestinal bleeding secondary to prepyloric ulcer. Tracheostomy was done for prolonged intubation. He was able to open eyes spontaneously. There were horizontal and rotatory nystagmus over both eyes. He could not obey commands and developed spastic quadriplegia with wasting of muscles. Despite prolonged hospitalisation and support, his neurological recovery was minimal with his best achieved GCS was E4VTM3.

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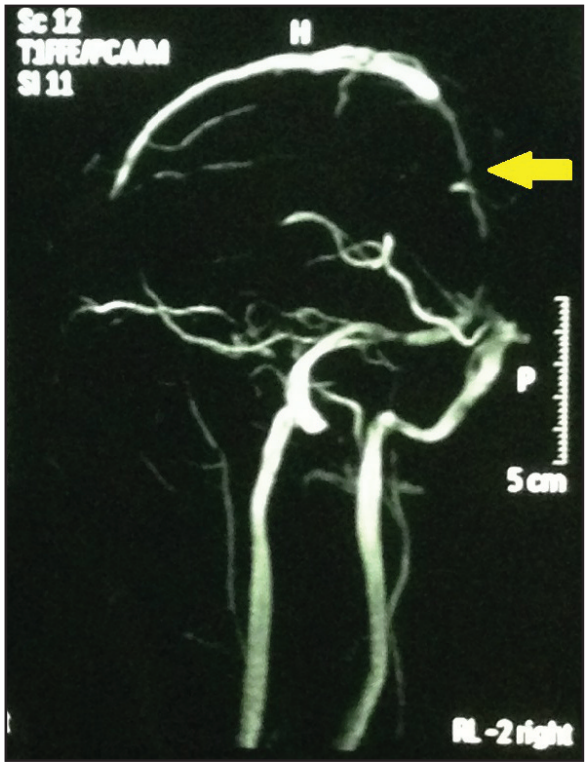

Fig. 1: Magnetic resonance venogram showed abrupt tapering over the middle and distal part of superior sagittal sinus extending into bilateral proximal transverse sinuses.

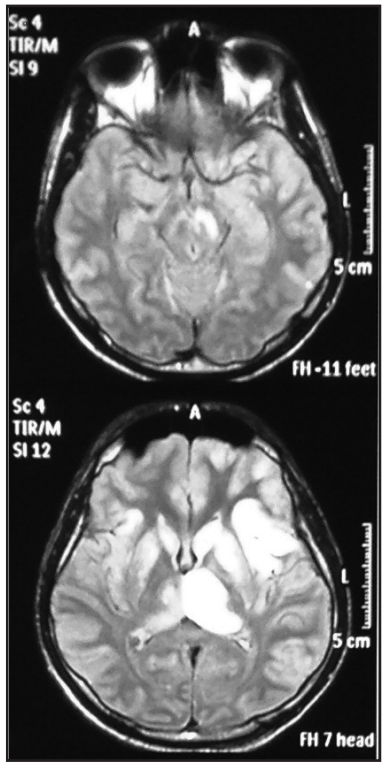

Fig. 2: MRI FLAIR sequence showed hyperintensity over bilateral MCA territories involving insula and frontoparietal cortex including bilateral thalamus, bilateral head of caudate nuclei, bilateral lentiform nuclei and left side of midbrain.

DISCUSSION

Japanese Encephalitis is a vector borne disease caused by JE virus which is a flavivirus. It is transmitted to humans through infected Culex mosquitoes.[3] The disease can be asymptomatic or manifest mild to severe neurological disease characterised by high grade fever, headache, neck stiffness, disorientation, spastic paralysis, seizures, coma, and death.[3] The case-fatality rate is as high as 30% and up to 20-30% of those who survive suffer permanent intellectual, behavioural or neurological problems such as paralysis, recurrent seizures or the inability to speak.[3]

In CVST, CSF pressure elevation is usually due to venous congestion and impaired absorption of the CSF via arachnoid villi mainly located in sagittal sinus leading to cerebral oedema with mass effect. For this patient, his normal CSF pressure is possibly due to an early thrombosis and the infarcted areas has not resulted in cerebral oedema yet. In fact, repeated CT brain on day-5 of admission did reveal features of increased intracranial pressure as evidenced by basal cistern effacement.

Diagnosis is confirmed by serologic evidence of raised antibody titre from cerebrospinal fluid or serum. In neuroimaging, thalamus is the most commonly affected structure which can be bilateral with or without haemorrhage.[4,5] Other structures that can be involved include cerebral cortex, basal ganglia, midbrain, pons, spinal cord, and cerebellum.[4] In this case, his MRI and MRV revealed involvement of bilateral thalami, left midbrain and cortical infarct secondary to CVST (superior sagittal and transverse sinus thrombosis). In Min Jia et al. case report, his patient had bilateral occipital lobes, temporal lobes and thalamic swelling, marked leptomeningeal enhancement, bilateral sigmoid sinuses and left lateral sinus thrombosis.[1] In the case report by Mokkappan S et al., his patient had bilateral thalami and head of caudate nuclei bleeding with thrombosis of bilateral transverse, right sigmoid and straight sinuses.[2]

While dehydration is a known aetiology for CVST, CVST accounts for only 0.5% of all stroke while dehydration is a common occurrence in the emergency department. The patient in this case had mild dehydration. Other factors are possibly in play for this patient to develop CVST. JE may cause a prothrombotic state to the cerebral venous system in which the mechanism is still not fully understood.

At the moment, there is no antiviral treatment for JE. Treatment is mainly supportive. However, the presence of CVST requires anticoagulation.

CONCLUSION

In a patient who presented with acute encephalitis in an endemic area, JE needs to be considered and serologic testing should be done from CSF and serum samples and then repeated at least a week later to demonstrate a rise in

antibody titre. Early identification of CVST is important as treatment involves anticoagulation to reduce adverse neurological sequelae and improve prognosis.

DECLARATION OF INTEREST

None.

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