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Double Trouble with Herpes Simplex Virus 1 Encephalitis

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Abstract
Herpes Simplex virus (HSV) is the most common cause of fatal sporadic necrotising viral encephalitis. The incidence is two cases per million people per year. They are associated with high mortality and morbidity without proper treatment. We report a case 46 years old with clinical features suggestive acute encephalitis. Despite various modalities of investigations for diagnosis of HSV are available, it posed a challenge. On the other hand two of the rare complication of HSV infection, myoclonic epilepsy and rhabdomyolysis occurred in this patient despite prompt initiation of the treatment.
Keywords: *Herpes Simplex virus, Encephalitis, myoclonus, rhabdomyolysis, status epilepticcus, acute kidney injury.*

Introduction

Herpes simplex virus (HSV) type 1 being most common cause of sporadic fatal encephalitis worldwide, often characterised by the clinical syndrome of rapid onset of fever, headache, altered level of consciousness, seizures and focal neurological signs. Prevalence is more common among children and adolescents.

Besides reactivation, direct immediate CNS invasion occurs via the trigeminal nerve or olfactory tract. Pathogenesis of CNS damage has both direct viral-mediated and indirect immune mediated mechanisms. This is supported by the altered presentation of HSV encephalitis in immunocompromised patients whom disease progression is slow. Majority of the patients, necrosis occurs in the temporal lobe with clinical neurological deficits consistent with areas affected.

Various movement disorders have been reported in post HSV encephalitis based on the area affected. Chorea, ballism, Choreoathetosis and myoclonus were reported as movement disorders in patients of post HSV encephalitis. Myoclonus is a complex hyperkinetic movement disorder characterised by sudden, brief, involuntary jerks of a single or group of muscles.

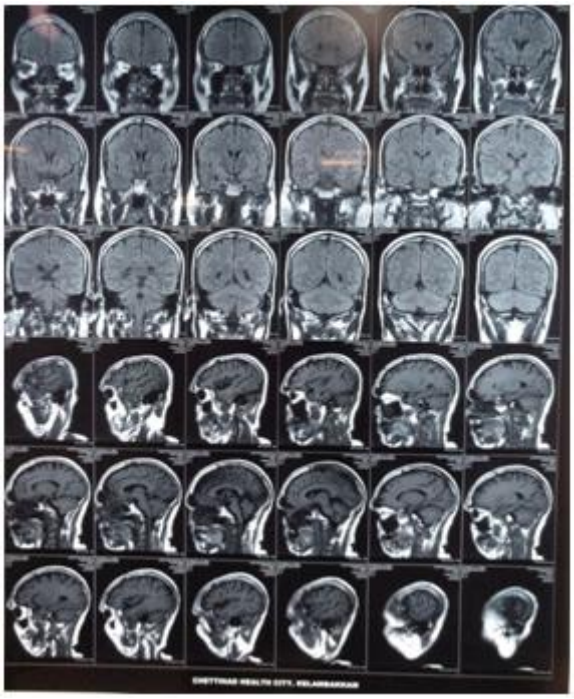
Case Report

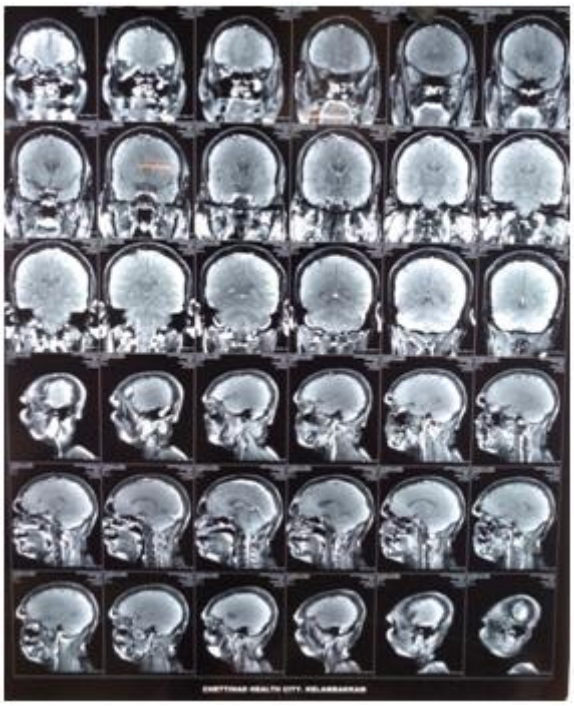
46 years old male with no co-morbid conditions presented with Complaints of fever for past 4 days, high grade, intermittent, associated with chills and rigors. Patient had an episode of vomiting a day before admission, associated with aggressive behaviour and had a single episode of seizures involving all the limbs, up-rolling of eyeballs, tongue bite and drooling of saliva. Patient had no history of trauma, urinary or faecal incontinence, bleeding manifestations, rash,

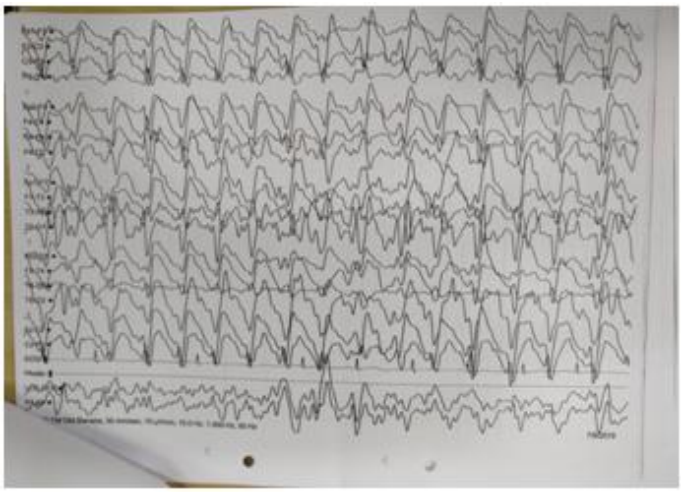
jaundice, neck stiffness. Patient has a history of alcohol consumption takes 2-3 drinks in month, with last intake three weeks back. No history of native medicine intake, drug allergy or any past medical illness.

On examination, patient was conscious, not oriented to time, place or person, febrile, restless. GCS - E3V4M5. No pallor, icterus, cyanosis, clubbing or pedal oedema. No signs suggestive of external trauma. Pulse rate was 112 beats per minute regular in rhythm, blood pressure was 112/76 mmhg in right arm on supine position, respiratory rate was 22 per minute abdominothoracic and was maintaining 98% saturation in room air, temperature - 102 degree fahrenheit. Cardiovascular and respiratory system and per abdomen examination were clinically normal. Neurological examination revealed altered sensorium, bilateral pupils were equal 4mm in diameter and reacting to light, patient was moving all four limbs equally, bilateral plantar was equivocal, kernig's and brudzinski's test were negative,No abnormal movements.

Patient had features suggestive of acute encephalitis and routine investigations were sent. Complete blood count revealed raised leucocytosis with neutrophil predominance, raised urea and creatinine levels, liver function test and serum electrolytes were within normal limits. Urine routine examination showed positive for blood and negative for albumin, ketone, sugar, Red Blood Cell (RBC) and cast. Arterial Blood Gas (ABG) suggestive of high anion gap metabolic acidosis with mild elevation of lactate. ECG showed sinus tachycardia, chest Xray revealed normal study. Procalcitonin was negative. Serology for HIV, Hepatitis B and Hepatitis C were negative.



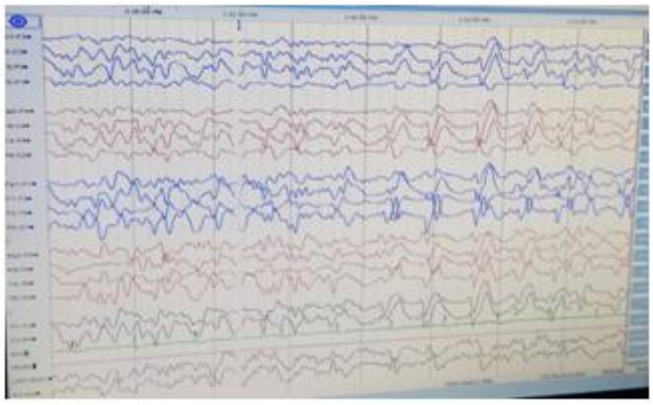




Patient was started on empirical therapy and hydration done. Magnetic resonance imaging (MRI) of brain revealed normal study with no features suggestive of oedema, lumbar puncture yielded clear cerebrospinal fluid (CSF) with lymphocyte predominance, normal sugar, mildly elevated protein and high chloride levels suggestive of viral aetiology, ADA - 1.43. Gram stain, AFB stain, KOH mount of CSF sample were negative. CSF culture, blood culture, urine culture showed no growth. On day 3 of admission raised renal parameters persisted, hyperkalemia, ABG showed high anion gap metabolic acidosis with elevated lactate and urine blood positive with absent RBC, followed by which Creatinine Kinase (CK) total was sent came to be 28,153. Renal parameters and serum potassium became within normal limits after forced alkaline diuresis and hydration, meanwhile CK declined. Contrast enhanced MRI was done revealed normal study.

Viral PCR was done with CSF sample and HSV 1 PCR was detected. Patient was on antiviral therapy and anti-epileptic management, despite that patient developed myoclonic jerks of bilateral lower limb on day 5 of admission. Patient was started on benzodiazepines and sodium valproate. Later involved all the limbs and trunk and epileptic myoclonus became status epilepsy. EEG was performed with diffuse epileptic foci with predominance over bilateral frontal and temporal regions. Epileptic myoclonus became late refractory, patient was started on a loading dose followed by infusion of phenobaribitone at 4mg per kg per hour followed by which epilepsy resolved clinically.

EEG was repeated with minimal epileptic spikes over the left frontal and temporal regions which later completely resolved. Phenobarbitone infusion stopped and switched to bolus doses in adjuvent with other anti-epileptics Antiviral therapy was given for 21 days supplemented with anti-epileptics. Patient recovered with no residual neurological deficit. Patient reviewed after 6 months with no further seizures episodes and on regular follow up.



Discussion

HSV type 1 encephalitis being sporadic presentation has devastating course with significant morbidity and mortality, despite availability of antiviral therapy. Course of the acute HSV type 1 encephalitis has been associated with many complications. Survivors have significant neuropsychiatric and neurobehavioral problems. Mortality rate is high as 20-30% despite antiviral therapy. It accounts about 10-20% of the annually reported viral encephalitis cases in united states and rose to 31.5% in India.

In this case, patient presented with characteristic clinical syndrome of acute viral encephalitis, MRI brain which has high sensitivity for viral encephalitis revealed normal study. But CSF picture was of viral aetiology that prompted for proceeding for gold standard test, viral PCR that detected HSV type 1. Patients with suspected HSV encephalitis ought to receive empirical therapy, since delays of treatment have led to significant neurological sequelae.

Seizures being the most common presentation of HSV encephalitis is predominantly focal seizures followed by generalised clonic tonic seizure type with only few cases reported as secondary generalisation. Movement disorders such as chorea, ballismus, choreoathetosis and myoclonus occurs as a post infectious sequelae. Myoclonus may be cortical or subcortical. Recurrent HSV encephalitis has been reported with subcortical epileptic myoclonus. Cortical epileptic myoclonus is a rarest acute presentation of HSV encephalitis affected patients. Pharmacologic therapy involves

one or a combination of GABAergic agents such as valproic acid (800–3000 mg/d), piracetam (8–20 g/d), clonazepam (2–15 mg/d), levetiracetam (1000–3000 mg/d), or primidone (500–1000 mg/d).

Rhabdomyolysis is known to occur in infectious aetiology owing to tissue hypoxia, activation of lysosomal enzymes, low oxidative and glycotic enzyme activity and mechanisms implicating endotoxins. Various viruses have been implicated to cause rhabdomyolysis of which Influenza type A and B being most common worldwide followed by varicella zoster. Other viral aetiology being HIV, coxsackie virus, Ebstein-barr virus, echo virus, cytomegalovirus, HSV and west nile virus. Disseminated Herpes simplex virus infection being an aetiology, HSV encephalitis leading to rhabdomyolysis is rare. Serum creatinine kinase activity greater than five times the normal value accepted to the criterion for the diagnosis of rhabdomyolysis. Myoglobinuria doesn't occur without rhabdomyolysis but rhabdomyolysis doesn't necessarily lead to myoglobinuria. Urine myoglobin must exceed 100mg/dl. Although elevated serum myoglobin and myoglobinuria are reliable factors, their sensitivity and specificity are affected by many factors. Serum myoglobin rises before the rise in CK and drops rapidly than the decline in CK. Management by intravascular volume replenishment and forced alkaline diuresis.

Conclusion

HSV type 1 encephalitis being most common sporadic occurrence, has high morbidity and mortality despite the available antiviral therapy. Untreated cases has mortality as high as 70 percent. Under high clinical suspicion patient should be started on empirical antiviral therapy as early in the onset of disease to prevent neurological sequelae. Patient with HSV PCR negative obtained after 72 hours of onset of neurological signs, in the absence of other supporting evidence reduces the likelihood of disease to <1%, hence empirical antiviral therapy can be discontinued.

Course of HSV type 1 encephalitis is complicated by seizures, motor deficits, cognitive and memory deficits. Other rare complications of rhabdomyolysis and atypical presentations of seizures ought to be diagnosed for early intervention and management to prevent mortality.

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