

CASE REPORTS

ACUTE ENCEPHALITIC SYNDROME DUE TO COINFECTION WITH HERPES SIMPLEX VIRUS AND SCRUB TYPHUS

Parminder Kaur, Roosy Aulakh

Department of Pediatrics, Government Medical College and Hospital (GMCH) 32, Chandigarh, India

ABSTRACT

Acute encephalitis is the clinical diagnosis in children with acute onset of fever, headache, vomiting, change in sensorium and seizures as a result inflammation of the brain parenchyma and cerebral dysfunction. The cause may be any infection - viral, protozoal, bacterial. We hereby report a case of encephalitis with dual etiology being herpes simplex virus and scrub typhus.

ARTICLE HISTORY

Received 20 December 2019
Accepted 24 March 2020

KEYWORDS

scrub typhus, Herpes simplex virus, encephalitis

Introduction

Various causative agents have been implicated in the etiology of encephalitis. Some systemic infectious diseases such as dengue fever¹, chikungunya², scrub typhus² and leptospirosis⁴ may present with brain function derangement. Acute encephalitis is mostly caused by 'neurotrophic' viruses, many of which are vector-transmitted (arthropod-borne) arboviruses. In India, Japanese encephalitis (JE) virus is the predominant etiology.⁵ Other viruses implicated are herpes simplex virus (HSV)⁶ and mumps virus⁷, a few enteroviruses⁸ and Epstein-Barr virus.⁹ Diagnosis of encephalitis is made by a combination of clinical, laboratory, neuroimaging, and electrophysiologic findings. There have been case reports in literature regarding co-infection with dengue, scrub typhus and leptospirosis as the etiology of undifferentiated febrile illness¹⁰ but no such data has been found on coinfection between herpes virus and scrub typhus encephalitis.

Case Report

An 11 years old male child presented to our emergency with fever for 15 days, generalized tonic clonic seizure lasting for about 30 minutes four days prior to admission and altered sensorium with irrelevant talk post convulsion. On hospitalization, child was in altered sensorium with Glasgow Coma Scale (GCS) of E2M4V2. Other vital parameters were within normal limit. There was neck rigidity with hepatomegaly. Other systemic examination was normal. A provisional diagnosis of acute febrile encephalopathy was made and child was started on intravenous (IV) ceftriaxone (100 mg/kg/day in two divided doses), IV acyclovir (30 mg/kg/day in three divided doses), IV artesunate (2.4 mg/kg/dose at 0, 12 hours, 24 hours and then once daily dose) and an IV phenytoin (20 mg/kg loading followed by 5 mg/kg/day in two divided doses maintenance

dose). On investigations, complete blood count showed hemoglobin 9.2 gm/dl, total leucocyte count (TLC) of 26,000 cells/mm cube (neutrophil 80%, lymphocytes 16%) and platelets 1,20,000/cumm. Renal and liver function tests, serumelectrolytes, venous blood gas and blood sugar were normal. Malarial antigen test, Widal test and dengue IgM antibodies by ELISA were negative. Blood culture was sterile. Scrub typhus IgM was positive with OD ratio being 1.58 (<1.0 negative and >1.0 positive). Cerebrospinal fluid (CSF) examination revealed a cellular fluid with proteins 74 mg/dl and sugar 56 mg/dl. CT brain was normal. EEG was not done during hospital stay. A diagnosis of scrub encephalopathy was made, and child was started on doxycycline (5 mg/kg/day in two divided doses). Acyclovir and artesunate were stopped after 48 hours. On day 5th of admission, there was worsening of GCS (E2M4V1) for which the child was intubated and put on T piece ventilation. In view of raised intracranial pressure (ICP) hypertonic saline was given. On day 8 of hospitalization, in view of non-response, the stored CSF sample was sent for herpes simplex virus (HSV) PCR. CSFHSVPCR was positive. IV acyclovir was restarted and within 48 hours GCS improved to E4M5V4 and child became a febrile. Child was extubated. IV acyclovir was continued for total of 14 days.

Discussion

HSV encephalitis (HSE) is a life-threatening infection of the central nervous system (CNS) with mortality rates of upto 70% in the absence of therapy. Antiviral therapy is most effective when commenced early, hence highlighting the importance of prompt diagnosis.^{11,12} Patients typically have malaise, irritability, and nonspecific symptoms lasting 1-7 days followed by acute onset of fever and focal neurologic signs.^{13,14} In our patient, there was fever for 15 days and one episode of seizure. There was no focal neurological deficit, though there was marked irritability. Untreated HSE is progressive and often fatal in 7-14 days. Polymerase chain reaction (PCR) of the cerebrospinal fluid (CSF) is the diagnostic method of choice for HSE. In our case also the CSF HSV PCR was positive. Elbers et al in their study¹⁴ reported CSF pleocytosis in 94%, elevated CSF protein in 50%, EEG changes in 94%

CONTACT Dr Parminder Kaur

Email: kaurparminder1991@yahoo.in

Address for Correspondence: Dr Parminder Kaur, House no 3079, Rajpura town, District Patiala, Punjab 140401.

©2020 Pediatric Oncall

and diagnostic imaging abnormalities in 88% patients with HSE. However, in our patient, though there were only raised proteins in CSF, the fluid was acellular and neuroimaging was normal. It was only on CSF PCR that HSV encephalitis was picked up. The neuroimaging of HSE consists of acute necrotizing encephalitis mostly localizing asymmetrically to the orbito-frontal and temporal lobes and involvement of the cingulate and insular cortex.¹⁵ Computed tomography (CT) scanning is usually normal within the first 4-6 days, MRI being much more sensitive. In our case CT head was done, that too early in the course which explains the normal neuroimaging in our case of herpes encephalitis.

Similarly, the important neurological manifestations of scrub typhus are meningitis, meningoencephalitis, seizures, and altered sensorium and rarely focal neurological deficits.¹⁶ There is limited literature on the neuroimaging finding of scrub encephalitis, except a single report of MRI brain showing small ring enhancing lesions in the corpus callosum and hyperintensities on FLAIR and T2-weighted sequences in periventricular and deep white matter regions of the brain.¹⁷ Scrub typhus encephalopathy should be suspected in a case with fever of more than week duration and altered sensorium and convulsions with scrub typhus immunoglobulin M enzyme linked immunosorbent assay positivity.¹⁶ In our case also, there was fever of more than one week and altered sensorium with seizures and scrub typhus IgM was positive. Dual infection with scrub typhus and HSE has not been reported earlier. This case highlights the need to rule out dual infection in patients with acute febrile encephalopathy if there is no improvement with treatment.

Compliance with Ethical Standards

Funding: None

Conflict of Interest: None

References:

1. Kumar R, Tripathi S, Tambe JJ, Arora V, Srivastava A, Nag VL. Dengue encephalopathy in children in Northern India: clinical features and comparison with non-dengue. *J Neurol Sci.* 2008;269:41-8.
2. Chandak NH, Kashyap RS, Kabra D, Karandikar P, Saha SS, Morey SH, et al. Neurological complications of Chikungunya virus infection. *Neurol India.* 2009;57:177-80.
3. Varghese GM, Trowbridge P, Janardhanan J, Thomas K, Peter JV, Mathews P, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis.* 2014;23:39-43.
4. Khan SA, Dutta P, Borah J, Chowdhury P, Topno R, Baishya M, et al. Leptospirosis presenting as acute encephalitis syndrome (AES) in Assam, India. *Asian Pac J Trop Dis.* 2012;2:151-3.
5. Joshi R, Kalantri SP, Reingold A, Colford JM., Jr Changing landscape of acute encephalitis syndrome in India: A systematic review. *Natl Med J India.* 2012;25:212-20
6. Panagariya A, Jain RS, Gupta S, Garg A, Sureka RK, Mathur V. Herpes simplex encephalitis in North West India. *Neurol India.* 2001;49:360-5.
7. John TJ, Maiya PP, Jadhav M, Christopher S, Mukundan P. Mumps virus meningitis and encephalitis without parotitis. *Indian J Med Res.* 1978;68:883-6.
8. Sapkal GN, Bondre VP, Fulmali PV, Patil P, Gopalkrishna V, Dadhania V, et al. Enteroviruses in patients with acute encephalitis, Uttar Pradesh, India. *Emerg Infect Dis.* 2009;15:295-8
9. Kalita J, Maurya PK, Kumar B, Misra UK. Epstein Barr virus encephalitis: Clinical diversity and radiological similarity. *Neurol India.* 2011;59:605-7.
10. Yong LS, Koh KC. A case of mixed infections in a patient presenting with acute febrile illness in the tropics. *Case Rep Infect Dis.* 2013;2013:562175.
11. Whitley RJ. Herpes simplex encephalitis: adolescents and adults. *Antiviral Res.* 2006; 71: 141-148.
12. Whitley RJ, Kimberlin DW. Herpes simplex encephalitis: children and adolescents. *Semin Pediatr Infect Dis.* 2005; 16: 17-23.
13. Tyler KL. Herpes simplex virus infections of the central nervous system: encephalitis and meningitis, including Mollaret's. *Herpes.* 2004 Jun;11 Suppl 2:57A-64A.
14. Elbers JM, Bitnun A, Richardson SE, Ford-Jones EL, Tellier R, et al. A 12-year prospective study of childhood herpes simplex encephalitis: is there a broader spectrum of disease? *Pediatrics.* 2007; 119: e399-407.
15. Kennedy P, Chaudhuri A. Herpes simplex encephalitis. *J Neurol Neurosurg Psychiatry.* 2002; 73: 237-238
16. Mahajan SK, Rolain JM, Kanga A, Raoult D. Scrub typhus involving central nervous system, India, 2004-2006. *Emerg Infect Dis.* 2010;16:1641-3.
17. Chua CJ, Tan KS, Ramli N, Devi S, Tan CT. Scrub typhus with central nervous system involvement: A case report with CT and MR imaging features. *Neurol J South East Asia* 1999;4:53-7.