CASE REPORT

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Human Herpes Virus-6 Meningoencephalitis in an Immunocompetent Peripartum Lady

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Abstract

We describe a case of Human herpesvirus-6 (HHV-6) meningoencephalitis in an immunocompetent peripartum lady who presented to the emergency department with febrile illness, disorientation, myalgia and altered levels of consciousness. Encephalitis occurs in immunocompromised people and is the most feared complication of HHV-6 disease. Two strains of this virus are A and B. HHV-6B is the predominant strain. This virus is characterised by lifelong latency in peripheral blood mononuclear cells and brain tissues. Hence, latent infection/reactivation occurs in immunocompromised patients. The literature is scanty about CNS involvement in immunocompetent adult patients. Meningoencephalitis developing in an immunocompetent peripartum case is unreported in Asian literature. HHV-6 infection should be kept in mind in any immunocompetent patient with meningoencephalitis of uncertain aetiology.

Key words: HHV-6, meningoencephalitis, immunocompetent, peripartum, acyclovir.

Introduction

HHV-6 is the sixth herpes virus discovered infection in humans and is nearly ubiquitous in the first two years of life with sero-prevalence rate of 95% in most studies[1]. The virus was isolated in 1986 among patients of lymphoproliferative diseases. Encephalitis occurs in immunocompromised patients and is the most feared complication of HHV-6 disease. Infection by this Beta – Herpes virus is characterised by two strains A and B. HHV-6B is the predominant strain of the virus. HHV-6A disease has been documented to cause illness in only immunosuppressed host[2]. The clinical difference is not well documented, so for the purposes of management, they are treated the same. HHV-6 is also characterised by lifelong latency in peripheral blood mononuclear cells and brain tissues following primary infection[3]. The latent infection or reactivation often occurs in immunocompromised patients and may cause fever, pneumonia, rashes, hepatitis and meningoencephalitis. Literature is scanty for central nervous system involvement in adult immunocompetent patients suffering from meningoencephalitis, especially in the peripartum period.

Case report

We describe a case of HHV-6 meningoencephalitis in an immunocompetent 25-year-old lady, who had recently delivered a baby. She had a history of pregnancy induced hypertension and was on oral Nifedipine 10 mg every 12 hourly. The records indicated her pregnancy was otherwise uneventful. She had a normal delivery of a female baby weighing 2,900 g. She was discharged the next day, in an apparently healthy condition with normal vitals.

Two days post-delivery she developed febrile illness and altered levels of consciousness. She also offered history of headache and myalgia. Physical examination revealed healthy episiotomy wound with normal gynaecological examination. Her Pulse was 120 beats per minute, regular with good volume, blood pressure 140/100 mmHg (on Nifedipine 10 mg BD). Her respiratory rate was 20 breaths per minute with a temperature of 101° F. Cyanosis was absent. She had neck stiffness, right lateral rectus palsy and normal pupils. Owing to thick throat secretions and respiratory discomfort she was intubated for 4 days. Deep tendon reflexes were brisk with bilateral extensor plantar response. Muscle strength and tone were however normal. Other systemic examination was unrevealing. As she was febrile and showed signs of meningism, a diagnosis of meningoencephalitis was clinically entertained. The details of investigations on haemogram, renal function tests, liver function tests, thyroid function tests, urine and cerebrospinal fluid (CSF) examination done are shown in Table I. The neurotropic virus panel in CSF done by real time PCR (RTPCR) is shown in Table II.

She was started on empirical parenteral Ceftriaxone, Acyclovir and Dexamethasone. Cranial magnetic resonance imaging (MRI) with contrast was performed on the second day of present hospitalisation. Neurophysician opined

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hyperintensity in left temporal lobe, rest features were normal. Antibiotics were discontinued on 4th day of hospitalisation and treatment with acyclovir and dexamethasone continued for next 7 days. Her lateral rectus palsy, fever and plantar response receded after 7 days of acyclovir and dexamethasone therapy. Patient's general condition improved with normal mental status. She recovered from the disease without any morbidity and was discharged in healthy condition on 10th day of hospitalisation.

Table I: Showing investigations done on the patient on admission and discharge.

Investigations	On Admission (Day 1)	On Discharge (Day 10)	Reference Range
Haemogram			
Haemoglobin (gm%)	11.7	10.5	13 - 16.2
Total Leucocyte Count (c/cmm)	19,050	9,630	4,000 - 10,000
Platelet Count (million/cmm)	326	231	150 - 410
Packed Cell Volume (%)	36.1	32.9	40 - 50
Blood Sugar Random (BSR) (mg%)	111	83	
Renal Function Tests			
Blood Urea (mg/dL)	14	20	19 - 43
Serum Creatinine (mg/dL)	0.5	0.6	0.8 - 1.5
Serum Sodium (mEq/L)	141	137	135 - 148
Serum Potassium (mEq/L)	4.0	3.7	3.5 - 5.5
Liver Function Tests (LFT)			
Total Bilirubin (mg/dL)	0.6	Not done	0.2 - 1.3
Direct Bilirubin (mg/dL)	0.4		0 - 0.4
Indirect Bilirubin (mg/dL)	0.2		0 - 0.8
SGOT (U/L)	33		17 - 59
SGPT (U/L)	22		21 - 72
Alkaline Phosphatase (U/L)	156		38 - 125
Total Proteins	6.5	Not done	
Serum Albumin (g/dL)	3.3	Not done	
Prothrombin Time	11.8 Seconds	Not done	
C Reactive Protein (mg/dL)	0.8	Not done	0.3 - 1
Widal Test	Negative	-	
Dengue Ns1 Antigen	Non Reactive	-	
HIV 1/ HIV2	Non Reactive	-	
HBsAg	Non Reactive	-	
Hepatitis C Virus Antigen	Negative	-	
TSH/FT3/FT4	0.88/1.97/1.20	-	
Peripheral Blood Smear	Normocytic	Normocytic	
	Normochromic	Normochromic	
	Polymorphs 86%	Polymorphs 72%	
	Lymphocytes 14%	Lymphocytes 28%	
	with Adequate Platelets	with Adequate Platelets	
Urine Albumin Dipstick	Trace	Nil	Nil
Sugar	Nil	Nil	Nil
PUS Cells	1-2/HPF	Nil	Nil
Cerebrospinal Fluid			
Volume ExaminedColour	2 MLColourless and Clear		
Coagulum	Absent		
Cobweb	Absent		
Cells	20 Cells/HPF		
Polymorphs	30%		
Lymphocytes	70%		
RBCs	Nil		
Proteins	92 mg/dL		
Sugar	63 mg/dL		

Table II: Neurotropic virus panel on Cerebrospinal Fluid (CSF).

Method – Real Time Polymerase Chain Reaction (RTPCR)	
Name of the Virus	**Result**
Human Herpes Virus 6 (HHV6)	Detected
Herpes Simplex Virus (HSV1)	Not Detected
Herpes Simplex Virus (HSV2)	Not Detected
Parvovirus B19	Not Detected
Epstein Barr Virus (EBV)	Not Detected
Varicella Zoster Virus (VZV)	Not Detected
Adenovirus	Not Detected
Enterovirus	Not Detected
Parechovirus	Not Detected
Varicella Zoster Virus (VZV)	Not Detected
Cytomegalovirus (CMV)	Not Detected
Human Herpes Virus 7 (HHV7)	Not Detected

Discussion

HHV-6 infection has been associated with complications of varying severity in haematopoietic stem cell transplant (HSCT) recipients and to a lesser degree among solid organ transplant recipients. Mayo clinic data reported an incidence of HHV-6 encephalitis in 1.7% (9/571). While incidence was low the mortality rate in these patients was 50% and those who survived had high rates of persistent neurologic disease deficits[4]. Management of such patients described is controversial and ill defined, although, the treatment in immunocompromised patients with HHV-6 encephalitis, treatment is more rewarding with Acycolvir, Ganciclovir or valganciclovir[5-8]. HHV-6 viral infection is able to persist in the latent form in central nervous system or sometimes in cervical canal which may reactivate with resultant neurological diseases[9]. Yilmaz *et al* described 17 cases of HHV-6 meningoencephalitis in immunocompetent adults,

including their own case. Exact figures on mortality were not shown as database literature was inconclusive and did not describe this information completely[10].

HHV-6 infection in immunocompetent adult individuals may manifest as a mononucleosis – like illness presenting with fever, lymphandenopathy and hepatitis. HHV-6 also has the ability to be chromosomally integrated (CiHHV-6), occurring in <1% of total population who newly acquire the infection and pass on the disease via vertical transmission. Yao *et al*[9] examined for evidence of HHV-6 infection in CSF of encephalitis patients using PCR and HHV-6 antibody reactivity. HHV-6 DNA was detected in 40% encephalitis patients while the controlled group remained negative. Integrated chromosomal DNA complicated the result as among 1 - 2% of the general population CiHHV-6 is inherited from their parents, as demonstrated by some authorities[2]. In immunocompromised patients PCR of HHV-6 DNA is often used for work-up with cell free CSF sample. This is considered as PCR technique of choice for the purpose. We did not use cell free CSF for the test. However, HHV-6 DNA was strongly positive suggestive of HHV-6 related CNS disease.

HHV-6 infection of CNS is reported with variable degrees of involvement in the pons, cerebral cortex, thalamus and medullary cord. HHV-6 exculsively involves medial temporal lobes (hippocampus and amygdala). Frontal lobes and cerebral lobes can also be involved. The MRI may show high signal T2W with mild enhancement[10]. The changes resolve as the condition improves. In our case the changes were noted in temporal lobe showing hyperintensities in the left side of temporal lobe that resolved post-therapy.

Infectious Disease Society of America recommends foscarnet or ganciclovir as first-line therapy for HHV-6 encephalitis; however, acyclovir who used in other cases with good outcome[11]. The present case received acyclovir therapy with steroids for 10 days. Patient was reviewed two weeks later with normal vitals and without neurological deficits.

Conclusion

HHV-6 is a well known infection commonly seen in immunosuppressed patients. Central nervous system infection resulting from HHV-6 in an immunocompetent host in the peripartum period with meningoencephalitis is rare. Data on this immunocompetent peripartum patients is unreported in the literature though limited cases of encephalitis are described among pregnant women. HHV-6 should be kept in mind when patients present with meningoencephalitis even among apparently immunocompetent people.

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