Viral Encephalitis Mimicking Acute Psychosis

Anand Jat, Saumya Shrivastava, Rahul Jain, Krishna Jain
Department of General Medicine, People’s College of Medical Sciences & Research Centre, Bhopal

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Herpes simplex virus type 1 (HSV) is known to cause encephalitis in humans which can be fatal in case of delay in diagnosis or initiation of treatment. It usually presents with fever, headache, seizures and alterations in mental status. It may also mimic behavioural or psychiatric disorders which seriously affect the early diagnosis of the disease. The mortality is almost 70% in the absence of treatment. A middle aged female presented with an acute history of fever, headache and vomiting followed by behavioural abnormalities, memory gaps and seizures. Antiviral therapy was started on suspicion of HSV encephalitis. Characteristic findings on MRI brain and positive CSF PCR for HSV DNA confirmed the diagnosis. The patient received three weeks of antiviral therapy following which she was discharged in an improved condition. This implies the advantages of early diagnosis and rapid initiation of therapy in survival of patients with this potentially fatal illness.

ABSTRACT

Herpes simplex virus type 1 (HSV) is known to cause encephalitis in humans which can be fatal in case of delay in diagnosis or initiation of treatment. It usually presents with fever, headache, seizures and alterations in mental status. It may also mimic behavioural or psychiatric disorders which seriously affect the early diagnosis of the disease. The mortality is almost 70% in the absence of treatment. A middle aged female presented with an acute history of fever, headache and vomiting followed by behavioural abnormalities, memory gaps and seizures. Antiviral therapy was started on suspicion of HSV encephalitis. Characteristic findings on MRI brain and positive CSF PCR for HSV DNA confirmed the diagnosis. The patient received three weeks of antiviral therapy following which she was discharged in an improved condition. This implies the advantages of early diagnosis and rapid initiation of therapy in survival of patients with this potentially fatal illness.

KEY WORDS: acyclovir, central nervous system, encephalitis, herpes simplex virus, infections

INTRODUCTION:

Herpes simplex virus type 1 (HSV) can cause fatal sporadic encephalitis in humans. The rapid diagnosis of central nervous system (CNS) infection with HSV is important because of the potential morbidity and mortality associated with the disease as well as the wide availability of acyclovir which has proven to ameliorate the symptoms and reduce mortality to 20%. When left untreated, more than 70% of cases of HSV encephalitis (HSVE) are fatal while only around 11% recover normal premorbid function. Diagnosis of HSVE relies upon the combination of the clinical scenario, a suggestive brain computed tomography (CT) scan or brain magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) examination by microscopy, biochemical analysis and polymerase chain reaction (PCR) for the presence of HSV DNA.

We describe one such case of a middle aged female who presented with an acute history of fever, headache, seizures and cognitive impairment and had improved with antiviral therapy.

CASE REPORT:

A 42 years old female had presented to the emergency department with complaints of fever, headache and vomiting since 3 days followed by episodes of generalized tonic clonic seizures. On clinical examination, she was found to be conscious and oriented to time, place and person with no neurological deficit. All routine investigations along with CT head and EEG were advised and treatment started with broad spectrum antibiotics and other symptomatic measures. The investigations revealed polymorphonuclear leucocytosis (total leucocyte count of 12000/mm³ with 86% neutrophils) with normal CT scan of head. EEG was suggestive of generalized seizure disorder for which anti-epileptics were added to her treatment regime. Her serum sodium was low (124meq/l) for which hypertonic saline was started.

On day 2, patient developed cognitive impairment with memory gaps. No neurological deficits were present. CSF studies were conducted which showed 155 cells/mm³ (60% polymorphs, 40% lymphocytes), protein concentration of 31.5mg/dl, glucose concentration of 92mg/dl and adenosine deaminase level of 30.26U/L. Injection dexamethasone was added to the regime.
On day 3, patient developed marked meningeal signs with high grade fever, tachycardia, memory gaps and disturbed consciousness. In view of the present status and lack of improvement with broad spectrum antibiotics, a diagnosis of viral meningo-encephalitis was suggested and injection acyclovir was started in divided doses. IgM / IgG for HSV 1 and 2, CSF PCR for HSV DNA and MRI brain were advised. MRI brain revealed white matter hyperintensity in right temporal lobe, para-hippocampal and perisylvian regions on T2 weighted images and flair sequence (Figure 1) which was suggestive of viral encephalitis with probable herpetic cause.

**DISCUSSION:**

HSVE can occur at any time during the year and affects both sexes, children and adults. Pathologically, it is an acute necrotizing encephalitis with preferential involvement of fronto-temporal, cingulate and insular cortex. The onset is usually abrupt, with the clinical course rapidly progressing over several days.

The common manifestations include a fairly rapid development of fever, focal signs, seizures and alteration in mental status. Some patients have a slowly progressing prodromal phase at the beginning, followed by a rapid decline while others show behavioral or psychiatric disorders with amnesia or language disturbances. These may seriously affect the early diagnosis of herpetic infection, since other psychiatric and/or neurological conditions are usually considered initially to be the cause. Acute anemia and recent memory loss may occur in 20% of cases. Personality changes may be subtle and easily missed. On suspicion of HSVE, antiviral treatment should be started before a definitive diagnosis is made.

It is the combination of clinical features and laboratory findings that establishes the diagnosis of HSVE. CT head may be normal in the first 4–5 days of symptom onset. MRI brain remains the most sensitive neuroimaging for early diagnosis and for defining the distribution of cerebral injury. It typically shows changes of focal oedema in the temporal lobes, frontal lobes, insular cortex and cingulate gyrus. EEG is abnormal in practically all cases. CSF may show a normal or raised pressure, lymphocytic pleocytosis (10–200 cells/mm3), normal glucose and raised protein (0.6 to 6 g/l). CSF PCR for HSV DNA is 100% specific and the sensitivity of this test exceeds 90%. False negative results may occur when CSF samples are obtained too early in the course of encephalitis. Real-time PCR is a recent modification of conventional PCR for HSV.

Treatment for HSVE should be initiated on suspicion of the disease itself. The primary areas of concern relate to the appropriate dosing and adequate duration of therapy. Intravenous acyclovir at a dose of 10mg/kg every 8 hours is the standard treatment. It is a guanosine analogue that first becomes phosphorylated by viral thymidine kinase and then by cellular enzymes. The triphosphorylated product is a competitive substrate for viral DNA polymerase and following incorporation results in termination of viral replication. An alternative oral drug which can be used.
is valacyclovir.\(^{[7,8]}\)

Corticosteroid administration in the acute stage of HSVE represented one of the significant independent predictors of outcome in HSVE. The exact effectiveness of such combination therapy in HSVE has not yet been established. However, corticosteroids have been administered empirically with aciclovir treatment in some patients to improve brain oedema. There have been recent reports about the effects of corticosteroid administration with aciclovir treatment in an animal model of HSVE.\(^{[9,10]}\) The mechanisms that underlie these clinical benefits of steroids differ from that in other diseases and further studies will be required to validate these results.

In the present case, real time PCR for HSV DNA came out to be positive three days after the onset of CNS symptoms. Ayclovir was continued upto 3 weeks and patient was rehabilitated with family support to gain her near to normal life.

CONCLUSION:

The present study supports that a strong clinical suspicion is the most important criterion for initiation of antiviral treatment. Since the widespread availability of HSV DNA PCR, most atypical or milder cases are now being identified. It is also concluded that presence of behavioural or psychiatric disorder with amnesic or language disturbances may lead to a delay in the diagnosis of HSVE.

REFERENCES: