Eight Year-Old Girl With Herpes Simplex Encephalitis, Dysentery and Auditory Agnosia: A Case Report

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Despite advances in antiviral therapy over the past 2 decades, herpes simplex encephalitis (HSE) remains a serious illness with significant risk of morbidity and mortality. HSE includes a range of clinical presentations, from aseptic meningitis and fever to a severe rapidly progressive form with mental status changes (clouding of consciousness, confusion, disorientation, personality changes) and sometimes seizures (focal or generalized), dysphagia, or other focal neurological signs. Symptoms vary in intensity early in the disease, but tend to progress rapidly. Brain CT Scan and MRI can play an important role in determining the diagnosis and extent of the disease. This case report refers to an 8-year-old girl, diagnosed with herpes encephalitis that presented with seizure, bloody diarrhea and decreased level of consciousness and restlessness who recovered clinically after acyclovir treatment.

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Introduction

Despite advances in antiviral therapy over the past 2 decades, herpes simplex encephalitis (HSE) remains a serious illness with significant risk of morbidity and death. HSE is the most common cause of sporadic viral encephalitis, in countries with global vaccination against mumps with a predilection for the temporal lobes and a range of clinical presentations, from aseptic meningitis and fever to a severe rapidly progressive form involving altered consciousness(1). Clinical features of HSE include fever with mental status changes (clouding of consciousness, confusion, disorientation, personality changes) sometimes with seizures (focal or generalized), dysphagia, or other focal neurological signs. Symptoms vary in intensity early in the disease, but tend to progress rapidly. Brain CT Scan and MRI can play an important role in determining the diagnosis and extent of the disease (2,3).

The patient was an 8-year-old girl referred to our hospital with fever and seizure. Fever has been initiated 3 days before admission, accompanied with frontal headache. In 3 days she was treated with co-amoxiclav and penicillin at outpatient setting. On the third day, she developed tonic seizure with upward gaze lasting 5 minutes and then was hospitalized and treated with ceftriaxone and phenytoin. After seizure she had problem in recognizing her parents. After second seizure she was referred to our hospital.

On admission she was febrile and disoriented. Neurological examination revealed no sign of meningeal irritation or neurological focal sign and deep tendon reflexes were normal. Complete blood count (CBC) with differential included: (WBC: 3200, polymorphonuclears: 62%, lymphocytes: 35%, band: 3%, hemoglobin: 9.4 mg/dl, platelet: 188000). Erythrocyte sedimentation rate (ESR) was 27 and C - reactive protein (CRP) was 3+. During evaluation first episode of low volume bloody diarrhea initiated, after 15 hours she had 3 other episodes of bloody diarrhea. Stool smear included: (WBC: 2-3 per HPF

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and RBC: 10-15 per HPF). Stool culture was sterile. Then amikacin added to treatment plan. On second day of admission she developed focal seizure, restlessness, decreased level of consciousness and signs of meningeal irritation. She was admitted at pediatric intensive care unit (PICU) and lumbar puncture was performed. Cerebrospinal fluid (CSF) index included: (Appearance: clear, WBC: 185 per HPF, RBC: 1 per HPF, PMN: 5%, Lymphocytes; 95% Glucose: 45mg/dl, protein: 42 mg/dl). CSF culture was sterile. With respect to cellular pattern of CSF and suspicion to HSE, intravenous acyclovir was initiated.

CSF examination for viral nucleotide sequences by polymerase chain reaction (PCR), Brain MRI and electroencephalogram (EEG) were performed. PCR was positive; EEG showed slow waves and Brain MRI showed edema and hyperintensity in temporal area T2 W (Figure 1) and hypointensity in T1 W (Figure 2).

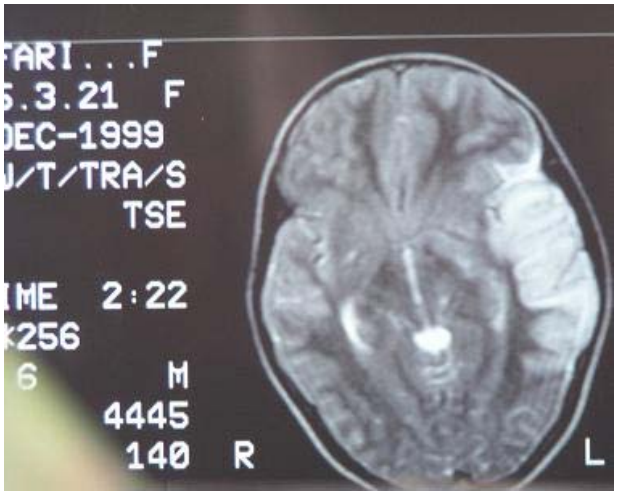

Figure 1. Brain MRI (edema and hyperintensity in temporal area T2W)

She was in stupor 2 days after antiviral therapy and treated with manitol because of brain edema detected in MRI. After second day her consciousness was improved gradually and on fourth day improvement was continued to normal level, but she could not talk. On fifth day she could walk but her gait was ataxic and she developed auditory agnosia that continued after one month of follow up despite early rehabilitation

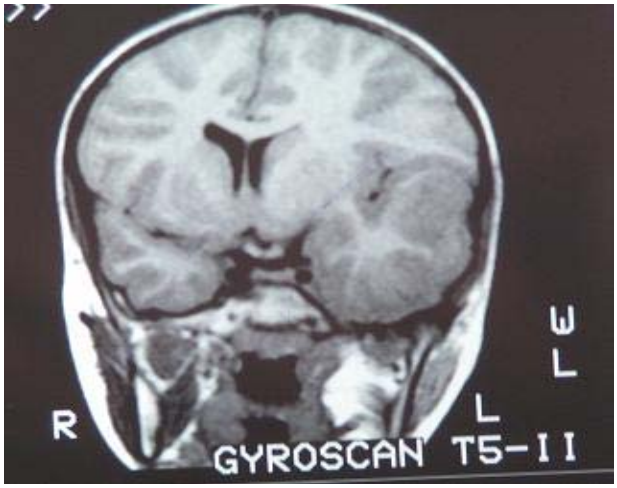

Figure 2. Brain MRI (hyperintensity in T1W)

Discussion

This case highlights the wide spectrum of symptoms in HSE. It is a serious but potentially treatable and often misdiagnosed condition. It should be strongly suspected in any patient with a clinical presentation suggesting encephalitis i.e. fever, headache, behavioral abnormality, hallucinations, seizure and memory impairment (2,3). Demonstration of anti-herpes antibody titers in the CSF is significant but more important is the polymerase chain reaction (PCR) which involves the detection of viral DNA in the CSF and has a sensitivity of 95% and a specificity of 99% (equal to or more than brain biopsy) (4,5). Brain MRI, EEG and above all, a strong clinical suspicion are sufficient to early diagnosis of HSE (5,6). This is extremely important in India for instance as Japanese encephalitis (JE), and cerebral malaria (CM) is common there and many cases of HSE may be mistaken with one of them. Even unusual presentations like mild or subacute encephalitis, neurological focal deficits, Psychiatric syndromes (Kluver-Bucy), brainstem encephalitis, benign recurrent meningitis, myelitis and raised intracranial pressure are well known (6-8). In this case dysentery and age of onset obscured the

correct diagnosis despite clinical probability of symptoms. We conclude that HSE is commonly misdiagnosed. It was not suspected in the patient referred to us because the clinical presentation is highly variable and protean (3). Early therapy of acyclovir can make a significant difference. We agree with most authors that IV acyclovir (oral has no response) should be given in all cases suspected of HSE even while confirmatory investigations are in progress (9-11). The recommended antiviral treatment for HSE is a 14-day course of acyclovir given IV, in a dose of 10 mg/kg eight-hourly (5,6). More so, one-third of the patients develop mild to severe neurological sequelae like aphasia, cognitive impairment, personality or behavioral abnormality, epilepsy, anosmia, and the Kluver-Bucy syndrome (6-8). To prevent relapse and sequelae, a higher dosage and longer duration of therapy (14-21 days) is more appropriate (6,7). No final decision has yet been made on the most appropriate strategy for HSE, but at present the recommendation is to obtain an early etiological diagnosis, with immediate initiation of acyclovir therapy (8,9). Bale (12) and Kimberlin (13) suggested that infants with herpes simplex virus infections should receive acyclovir, 20 mg/kg every 8 hours for 21 days, and older children should be treated with 20 mg/kg every 8 hours for at least 21 days. Because of the substantial morbidity associated with neonatal and childhood herpes simplex virus encephalitis, ongoing studies are evaluating the role for prolonged suppressive therapy with acyclovir in neonates with herpes simplex virus infections (14).

Conclusion

Encephalitis produced by the herpes virus is a disease that is dreaded because of the high mortality rate and the devastation it causes in living conditions of survivors. Our aim is to stimulate the clinical suspicion of HSE so that pharmacological treatment can be established even while diagnostic tests are being carried out. We suggest early evaluation and follow-up of the manifestations of focal sequelae related to the frontotemporal regions.

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