

Atypical Herpes Simplex Encephalitis With Extratemporal Involvement

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Abstract: Herpes simplex virus (HSV) is recognized as the most common cause of sporadic encephalitis among adults. The combination of magnetic resonance imaging, electroencephalography, and cerebrospinal fluid tests is usually diagnostic. In this article, we describe a case of atypical HSV encephalitis presenting a syndrome of febrile encephalopathy in the absence of focal neurological features, including mental and sensory disturbance, pyramidal signs, ataxia, and cranial nerve deficits, and in which magnetic resonance imaging demonstrated lesions restricted to the parietal and occipital lobes without typical localization of HSV encephalitis in the insula and inferior frontal lobe.

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Herpes simplex encephalitis (HSE) is the most common fatal nonendemic and sporadic viral encephalitis. It still has an unacceptably high mortality rate despite antiviral treatment. Although the exact incidence of HSE is not known, it has been estimated at approximately 1 case per million per year.¹ It is approximately 10% to 20% of all encephalitides.^{2,3} Magnetic resonance imaging (MRI) of the brain is the investigation of choice in HSE, and the diagnosis may be confirmed by electroencephalography (EEG) and polymerase chain reaction (PCR) test for the virus in the cerebrospinal fluid (CSF). We report a case of atypical herpes simplex virus (HSV) encephalitis presenting a syndrome of febrile encephalopathy in the absence of focal neurological features, including mental and sensory disturbance, pyramidal signs, ataxia, and cranial nerve deficits, and in which MRI demonstrated lesions restricted to the parietal and occipital lobes without typical localization of HSV encephalitis in the insula and inferior frontal lobe.

CASE REPORT

A 36-year-old man presented with a slightly elevated body temperature (up to 38.9°C), headache, and generalized seizure. He had prodromal influenza-like illness and history of mental status changes for approximately 1 week. He had trouble finding the right

words and started to use incorrect words in sentences. His headache worsened day by day. A day before admission, he noticed involuntary jerks of his left arm with rapid progression to generalized tonic-clonic seizure for approximately 2 minutes. Upon admission, he was febrile, with mild bifrontal headache. His neurological examination was normal except for the mild dysnomia. Glasgow Coma Scale score was 14. He did not have meningeal signs. He had neither significant medical history nor recent illnesses.

The brain computed tomography showed no abnormalities. Examination of CSF showed raised pressure, lymphocytic pleocytosis (140 cells/ μ L), normal glucose level, and increased protein (2 g/L). There were no red blood cells and xanthochromia. The PCR analyses of the CSF revealed DNA of HSV type 1. The T2-weighted MRI of the brain revealed bilaterally multifocal hyperintense lesions in the parietal and occipital lobes without temporal involvement. The occipital lesions demonstrated a gyral involvement pattern, whereas parietal lesions appeared in both white and gray matter (Figs. 1, 2). The EEG showed biparietooccipital delta waves without periodic complexes.

His leukocyte count was 16,200/ μ L; electrolytes, liver transaminases, folate, vitamin B₁₂, and thyroid-stimulating hormone



FIGURE 1. T2-weighted axial magnetic resonance (MR) image showing bilateral areas of hyperintensity (edema) in white and gray matter of the parietal lobes.

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FIGURE 2. T2-weighted axial MR image showing bilateral areas of hyperintensity (gyral edema) in occipital lobes.

were within normal limits. The result of the human immunodeficiency virus (HIV) antibody test was negative.

He was treated with intravenous acyclovir 10 mg/kg 3 times daily for 14 days. Upon completion of therapy, the patient made a complete recovery, and all of the cerebral lesions disappeared. T2-

weighted MR images showed complete recovery of the lesions (Figs. 3A, B).

Patients with HSE characteristically have fever, headache, confusion, clouding of consciousness, focal or generalized seizures, aphasia, personality changes, and, in some cases, coma.⁴ The presence of this clinical picture combined with abnormal findings on CSF analysis, specific cortical MRI lesions, and focal abnormalities on EEG confirms the diagnosis of HSE. The MRI findings typically include focal edema in the medial cortical region of the temporal and orbital frontal lobes, insular cortex, and angular gyrus. It may also extend to the cingulate gyrus and posterior occipital cortex.^{5,6}

Recently, cases of atypical HSE have been described.⁷ Some of these cases are often mild, presenting a syndrome of febrile encephalopathy in the absence of focal neurological features, initial CSF pleocytosis, or abnormal findings on MRI. There are, however, reports that suggest that extratemporal involvement can have focal features especially when it develops in the brain stem. In these patients, the outcomes can be poor.^{8–10}

In our patient's case, he was suspected of having seizures, headache, and dysnomia secondary to viral meningitis because of the absence of focal neurological features, including mental and sensory disturbance, pyramidal signs, ataxia, and cranial nerve deficits. The HSE was first raised by CSF findings strongly indicated by MRI and confirmed by PCR testing. The diagnosis of HSE was considered unlikely because of the mild and nonprogressive nature of his symptoms and extratemporal involvement on MRI.

There have been several cases of HSE which have extratemporal involvement and where the patient is immunocompromised or has HIV infection.^{8,11} In our patient, we ruled out HIV infection and immunocompromised state by a negative HIV antibody test and blood count.

Wasay et al¹² found that extratemporal involvement in HSE has been variably reported in 10% to 30% of the cases. The most affected extratemporal lesions were seen in the frontal and parietal cortices and also in the occipital lobe, basal ganglia, and brain stem. In a study of 28 patients with HSE from northern India, MRI showed bilateral asymmetric frontotemporal lesions in 12 cases and isolated temporal lesions in only 4 cases.¹³ Cases of atypical HSE have been described.^{14,15} Brohi et al¹⁴ described a patient with HSE, showing involvement of the pons, midbrain, and frontal lobe on MRI. Tada

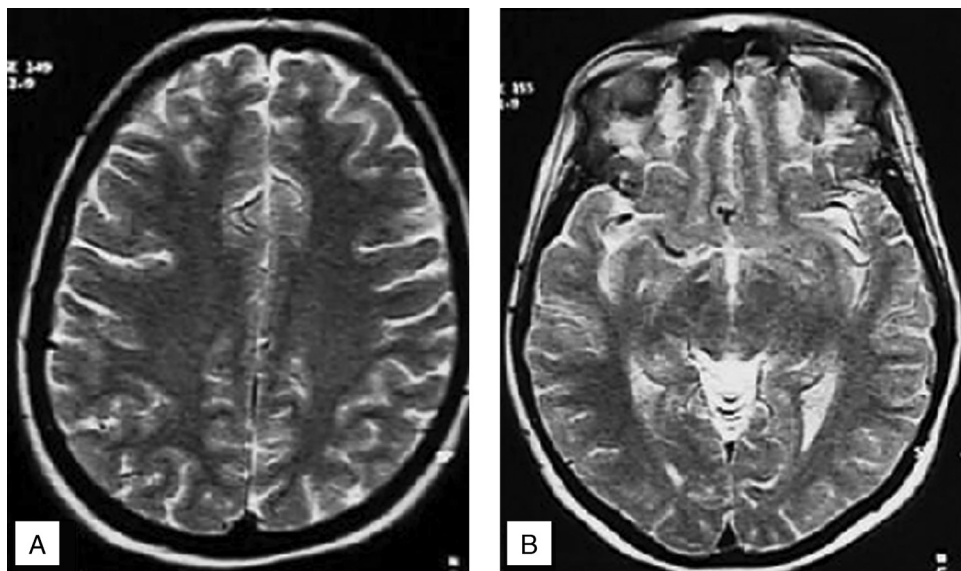


FIGURE 3. A and B, T2-weighted axial MR images showing complete recovery of the lesions after acyclovir treatment.

et al¹⁶ have reported optic nerve enlargement and lesions in the region of the left geniculate body and left occipital lobe. Atypical forms of HSE occurred in approximately 20% of the patients. These patients usually present with focal or generalized seizures, and neurological examination is normal except for mental status.⁷ The MRI abnormalities can occur even in patients with mild or atypical forms of HSE. However, cranial MRI of our patient demonstrated that his disease was atypically localized to the parietooccipital lobes bilaterally. The diagnosis was confirmed by PCR testing.

CONCLUSION

Extratemporal involvement is uncommon in patients with HSE, and the signs and symptoms of HSE may be atypical like those in our patient. These cases also emphasize the importance of performing HSV CSF PCR study on all patients presenting with febrile encephalopathy even in the absence of focal neurological findings and abnormal findings on MRI scanning. Early diagnosis and treatment of HSE are very important. If these patients are untreated, encephalitis has a high case-fatality rate of approximately 70%. Even if it is treated in a timely fashion, approximately 40% to 50% would be expected to make full neurological recovery.¹⁷ Thus, early recognition can prevent serious morbidity.

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