Herpes simplex encephalitis in adults: A case highlighting the diagnostic superiority of MRI

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ABSTRACT

Herpes simplex encephalitis (HSE) is a rare but severe neurological condition caused by the herpes simplex virus, primarily affecting the temporal lobes and limbic system. This case report presents a 78-year-old Asian man who was admitted to the emergency department with a two-day history of fever and one day of altered consciousness. His past medical history was significant for aortic valve replacement surgery, with no other notable comorbidities. Initial clinical examination and laboratory investigations, including CT and cerebrospinal fluid analysis, were unremarkable. However, MRI of the brain revealed characteristic findings consistent with HSE, including areas of altered signal intensity in the left temporal lobe, hippocampus, insular cortex, and right thalamus. The patient was diagnosed with herpes simplex encephalitis, confirmed by MRI findings. This case underscores the importance of early neuroimaging, particularly MRI, in diagnosing HSE, which remains a clinical challenge due to its non-specific initial presentation. Prompt initiation of antiviral therapy, such as intravenous acyclovir, is critical in reducing morbidity and mortality associated with this condition.

Keywords: Cerebral ischemia, herpes simplex encephalitis, status epilepticus.

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Submitted: August 31, 2024

Accepted: May 22, 2025

To cite: Gurung K, Shrestha R. Herpes simplex encephalitis in adults: A case highlighting the diagnostic superiority of MRI. JGMC-Nepal. 2025;18(1):109-12.

DOI: 10.3126/jgmc-n.v18i1.69318

INTRODUCTION

Encephalitis is a diffuse inflammation of the brain parenchyma, leading to various neurological deficits. It may arise from infectious, post-infectious, or non-infectious causes.[1] The etiologies are broadly classified into infectious and non-infectious types. Infectious causes include viruses such as Herpes simplex virus (HSV) types 1 and 2, Varicella-zoster virus (VZV), and enteroviruses,[2] as well as bacteria like Streptococcus pneumoniae and Neisseria meningitidis.[3] Post-infectious causes include acute disseminated encephalomyelitis (ADEM), acute hemorrhagic leukoencephalitis, and Bickerstaff's brainstem encephalitis.[4] Non-infectious causes involve autoimmune conditions such as N-methyl-D-aspartate (NMDA) receptor antibody encephalitis, Voltage-Gated Potassium Channel (VGKC) antibody encephalitis, and demyelinating diseases like multiple sclerosis (MS).[3] Viruses can enter the central nervous system (CNS) via the bloodstream (hematogenous spread, e.g., arboviruses) or along peripheral nerves (neuronal spread, e.g., HSV).[2] The blood-brain barrier (BBB), which serves as a protective interface between the CNS and systemic circulation, may be disrupted in both viral and non-viral CNS diseases.[5] Herpes simplex encephalitis (HSE) is caused by HSV type 1 (HSV-1), more common in adults and children, and HSV type 2 (HSV-2), typically affecting neonates and immunocompromised individuals. HSV-1 can reach the brain via three main routes: primary oropharyngeal infection spreading through the olfactory or trigeminal nerves, reactivation of a peripheral infection, or reactivation of latent virus within the brain.

Common clinical features include fever, confusion, abnormal behavior, headache, decreased mental status, seizures, focal neurological deficits, aphasia, vomiting, coma, and signs of meningeal irritation (meningismus).[6] Cerebrospinal fluid (CSF) analysis is the gold standard for diagnosis, typically showing elevated opening pressure, increased protein, normal glucose, and lymphocytic pleocytosis. A complete blood count (CBC) may show lymphocytosis or be normal. Computed tomography (CT) is usually the initial imaging, though it may be normal early on; later findings can include hypodensities, hemorrhage, or midline shift—mainly in the temporal or frontal lobes. Contrast enhancement may take up to a week to appear. Magnetic resonance imaging (MRI) is more sensitive, typically showing T1 hypointensities and T2-weighted or Fluid-Attenuated Inversion Recovery (FLAIR) hyperintensities in the temporal lobes, often extending to the limbic system, insular cortex, and inferior frontal lobes, with sparing of the basal ganglia. Children may show atypical patterns, and immunocompromised individuals may exhibit more extensive involvement, including the brainstem and cerebellum. Electroencephalography (EEG) is usually abnormal in HSE, with the medial temporal and hippocampal regions showing high epileptogenic activity. A typical pattern includes recurrent, uniform, sharp-and-slow wave complexes in one or both temporal lobes at 2–3 second intervals. Intravenous acyclovir is the treatment of choice and significantly reduces mortality. Potential complications include cerebral edema, increased intracranial pressure, status epilepticus, aspiration pneumonitis, cerebral infarction, and lasting neurological deficits.[7]

CASE PRESENTATION

A 78-year-old Asian man presented to the emergency department with a two-day history of fever and one-day history of altered consciousness. According to his attendant, he had been well until the onset of continuous fever with chills and rigors. His temperature had not been recorded at home. One day later, he became confused. There was no history of loss of consciousness, seizures, vomiting, chest pain, dyspnea, abdominal pain, or limb weakness. Bowel and bladder habits were normal. He had undergone aortic valve replacement surgery two years prior but had no other significant medical history. He did not smoke or drink. On examination, he was febrile (102°F), with a pulse of 92 bpm and blood pressure of 150/90 mmHg. Physical examination was unremarkable, and his Glasgow Coma Scale (GCS) score was 15/15. Laboratory tests revealed a white blood cell count of 10,540/µL (83.7% neutrophils, 13.3% lymphocytes). Urinalysis, renal function tests (RFT), and liver function tests (LFT) were normal. Serological tests for Scrub Typhus, HIV, HBsAg, HCV, Leptospira, and Brucella were negative. Non-contrast CT (NECT) of the brain was normal (Figure 1). Cerebrospinal fluid (CSF) analysis showed 3 lymphocytes/µL. Hemoglobin A1c (HbA1c) was 7.42%. Brain MRI revealed altered signal intensity in the left temporal lobe, hippocampus, and insular cortex, appearing hyperintense on T2-weighted (Figure 2) and FLAIR (Figure 3) images. Diffusion-weighted imaging (DWI) showed hyperintensity with corresponding signal loss on the apparent diffusion coefficient (ADC) map (Figure 4, Figure 5), indicating true diffusion restriction. Effacement of ipsilateral sulci was present, with no susceptibility on SWI, ruling out hemorrhage. The right thalamus also showed T2/FLAIR hyperintensity without DWI restriction. These findings were consistent with herpes simplex encephalitis.

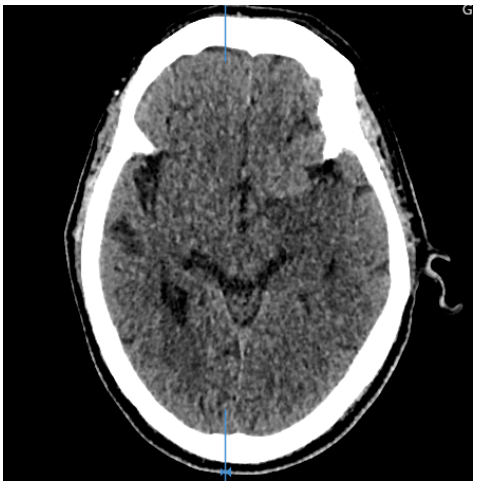

Figure 1: Non-contrast computed tomography (NECT) head axial view showing no altered densities in brain parenchyma

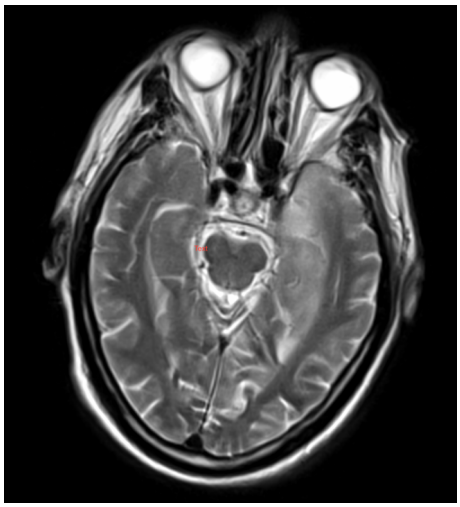

Figure 2: T2 weighted axial view image of brain showing high signal intensity in left temporal lobe

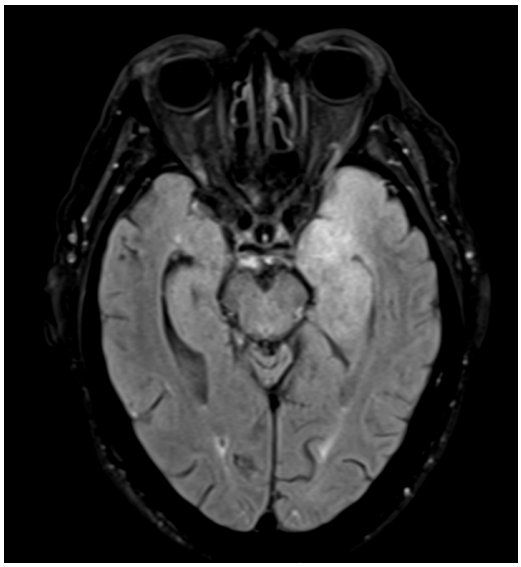

Figure 3: FLAIR axial view image of brain showing high signal intensity in left temporal lobe and left hippocampus

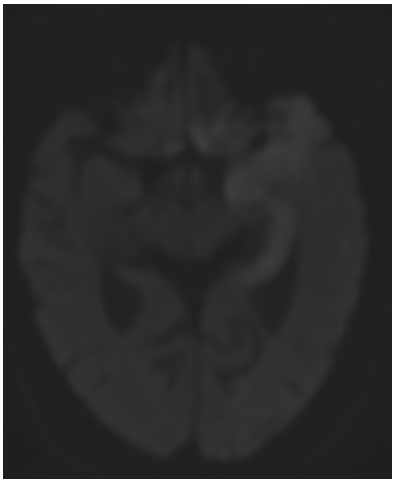

Figure 4: Diffusion weighted imaging of brain showing high signal intensity in left temporal lobe and left hippocampus

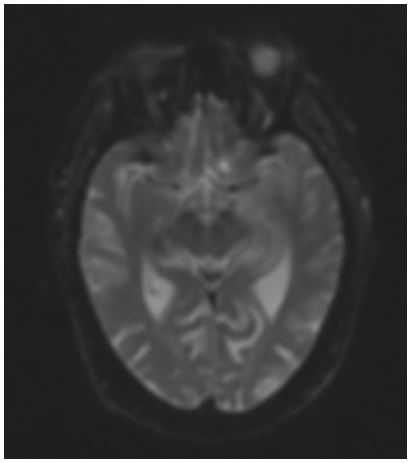

Figure 5: Apparent diffusion coefficient (ADC) image of brain showing high signal intensity in left temporal lobe and left hippocampus

DISCUSSION

Herpes simplex encephalitis (HSE) occurs in both neonatal and adult forms.[8] Its annual incidence is about 1 in 250,000 to 500,000, with a significant rise over the past 20 years.[9] The neonatal form results from vertical transmission via the birth canal, with symptoms appearing within the first month.[8] The adult form usually spreads through the nasopharynx and remains latent in the trigeminal ganglion, reactivating during immunosuppression, trauma, or stress. HSV-2 shows no age, sex, or seasonal preference. HSE primarily affects the limbic system, especially the anterior and medial temporal lobes, insular cortex, subfrontal area, and cingulate gyri, typically bilateral but asymmetrical. Children more often have extratemporal and extralimbic involvement, with the basal ganglia usually spared.

Non-contrast CT (NCCT) may be normal early on, but later shows hypodensity and mild mass effect in temporal lobes and insula. Early enhancement is rare but patchy or gyriform enhancement can appear later. MRI is preferred, showing gyral swelling and an indistinct gray-white interface on T1-weighted images. T2-weighted images reveal cortical and subcortical hyperintensity, sparing white matter. FLAIR is the most sensitive, detecting changes before T1 or T2 sequences. True diffusion restriction appears on DWI and ADC maps. Contrast-enhanced MRI may show patchy parenchymal and meningeal enhancement. SWI can detect petechial hemorrhages. MR spectroscopy often reveals reduced N-acetylaspartate (NAA) and lipid-lactate peaks.

Differential diagnoses include acute cerebral ischemia, neoplasm, status epilepticus, and other encephalitides. Ischemia follows vascular territories and often involves basal ganglia, usually without fever or flu-like illness but with neurological deficits like weakness or slurred speech. Status epilepticus mimics HSE but is usually unilateral, involving cortex with transient, widespread postictal edema. History and follow-up aid differentiation. Diffuse astrocytomas involve white matter or both white matter and cortex. HHV-6 encephalitis typically affects the medial temporal lobe; however, distinguishing it from HSE is difficult if extrahippocampal lesions occur.[10]

CONCLUSIONS

Herpes simplex encephalitis remains a diagnostic challenge due to its diverse clinical presentations and similarity to other neurological conditions. In this case, the patient's atypical symptoms and initially normal CT and cerebrospinal fluid findings highlight the critical role of MRI in detecting hallmark features like temporal lobe involvement and diffusion restriction. Prompt diagnosis

and treatment are essential to improve outcomes and prevent severe complications such as cerebral edema, raised intracranial pressure, and lasting neurological deficits. This case emphasizes the importance of maintaining high clinical suspicion and early use of advanced imaging in patients with acute encephalitis, especially when initial tests are inconclusive.

ACKNOWLEDGEMENT

We would like to thank the patient for his cooperation.

CONFLICTS OF INTEREST: None declared

SOURCE OF FUNDING: None

AUTHORS' CONTRIBUTION

KG contributed to the conceptualization of the study, data collection, manuscript preparation, and editing. RS contributed to conceptualization, data analysis, and editing. Final editing and confirmation have been given by all authors.

PATIENT CONSENT

The patient has provided informed consent for the publication of the case.

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