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Case Report

Navigating diagnostic challenges: imaging strategies for herpes simplex encephalitis in resource limited settings: A case report ^{☆,☆☆}

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ABSTRACT

Encephalitis refers to the inflammatory condition affecting the brain parenchyma, leading to various neurological impairments. It can have various causes: infectious, postinfectious, and noninfectious origins. In this case, we present a 76-year-old man who presented to the emergency room with complaints of headache and behavioral changes. Initially, a Computed Tomography (CT) scan raised suspicion of herpes simplex encephalitis and prompted the initiation of treatment. Subsequently, Magnetic Resonance Imaging (MRI) and Cerebrospinal fluid (CSF) culture confirmed the diagnosis. However, despite medical intervention, the patient's condition unexpectedly deteriorated, and he unfortunately passed away after spending 2 weeks in the Intensive Care Unit (ICU). Possible factors contributing to this outcome include delayed presentation to medical care, viral resistance, or the inherent nature of the infection itself, particularly in elderly patients.

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Abbreviations: CT, Computed tomography; MRI, Magnetic resonance Imaging; HSV, Herpes simplex Virus; HSVE, Herpes Simplex Virus encephalitis; PCR, polymerase chain reaction; CSF, Cerebrospinal fluid; DWI, Diffusion weighted imaging; ADC, Apparent diffusion coefficient.

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Introduction

Encephalitis, characterized by inflammation of the brain parenchyma and associated neurological dysfunction, can stem from infectious, postinfectious, and noninfectious causes. Infectious agents account for approximately 50% of identifiable cases, with Herpes simplex virus-1 (HSV-1) being the most prevalent infectious cause of sporadic encephalitis [1,2].

Herpetic infections have been recognized since ancient Greece, and in 1944, the first adult case was reported, involving a 25-year-old man who exhibited symptoms such

as headache, fever, aphasia, and left pupillary dilatation [3].

HSV encephalitis (HSVE) exhibits a bimodal age distribution, with peak incidences observed in children under 3 years old and individuals aged 50 years or older. Diagnosis of HSVE can be challenging, and the prognosis after diagnosis is generally unfavorable. Delays or inadequacies in treatment, as well as extremes of age, are associated with higher morbidity and mortality rates [4].

Encephalitis often manifests as altered mental status, signs of brain parenchymal inflammation (e.g., fever, new seizures, focal neurologic signs), cerebrospinal fluid (CSF) pleocytosis (≥ 5 nucleated cells/mL), and characteristic abnor-

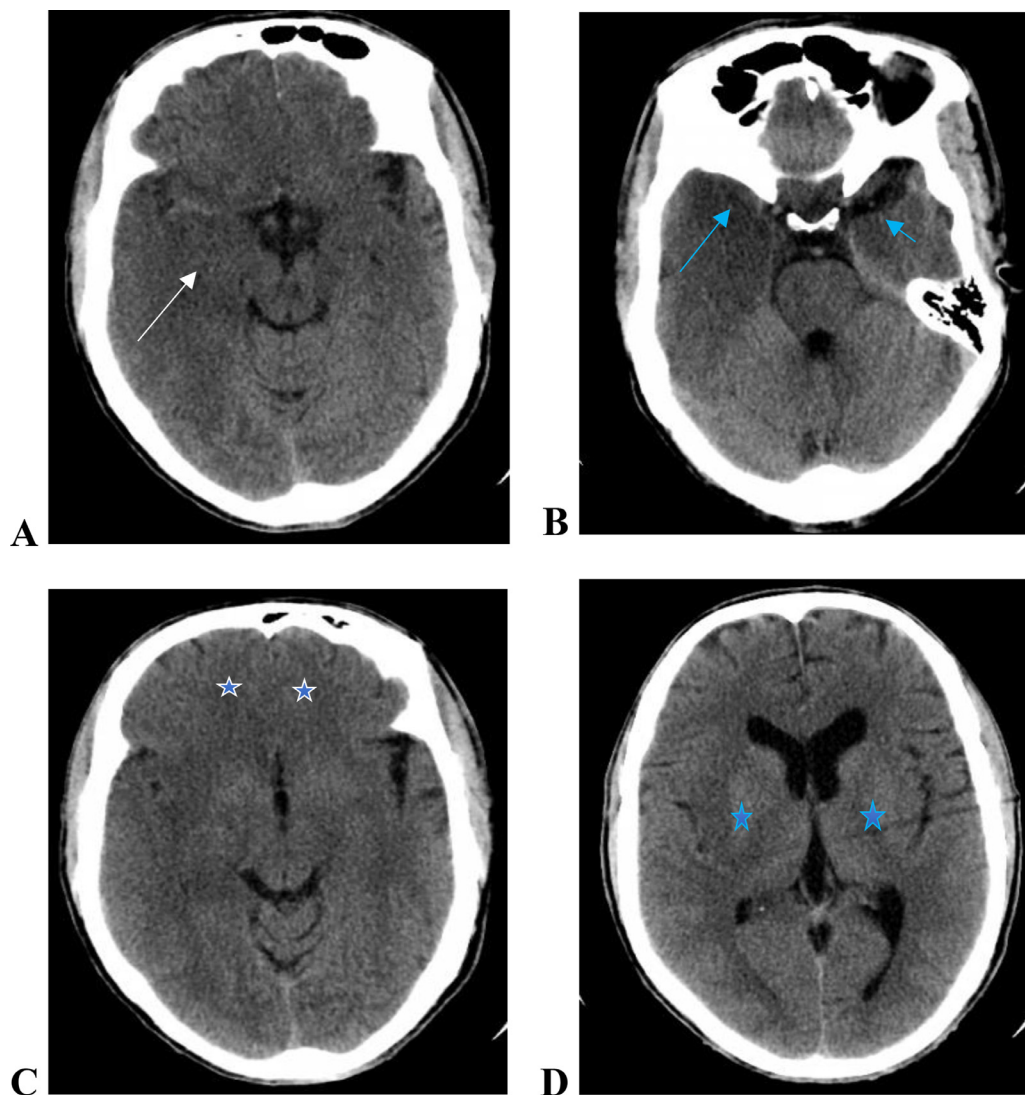


Fig. 1 – Non-contrast axial CT scan of the brain shows the following findings: medial and anterior portions of the right temporal lobe (indicated by the white arrow) exhibit low density and a loss of gray-white matter distinction(A). right insular cortex (indicated by the long blue arrow) and left mesial temporal lobe is (indicated by the short blue arrow). Both regions showed low density(B). both par-median lower frontal lobes are subtly characterized by a low density (indicated by the white stars) (C). bilateral basal ganglia, unaffected (indicated by the blue stars) (D).

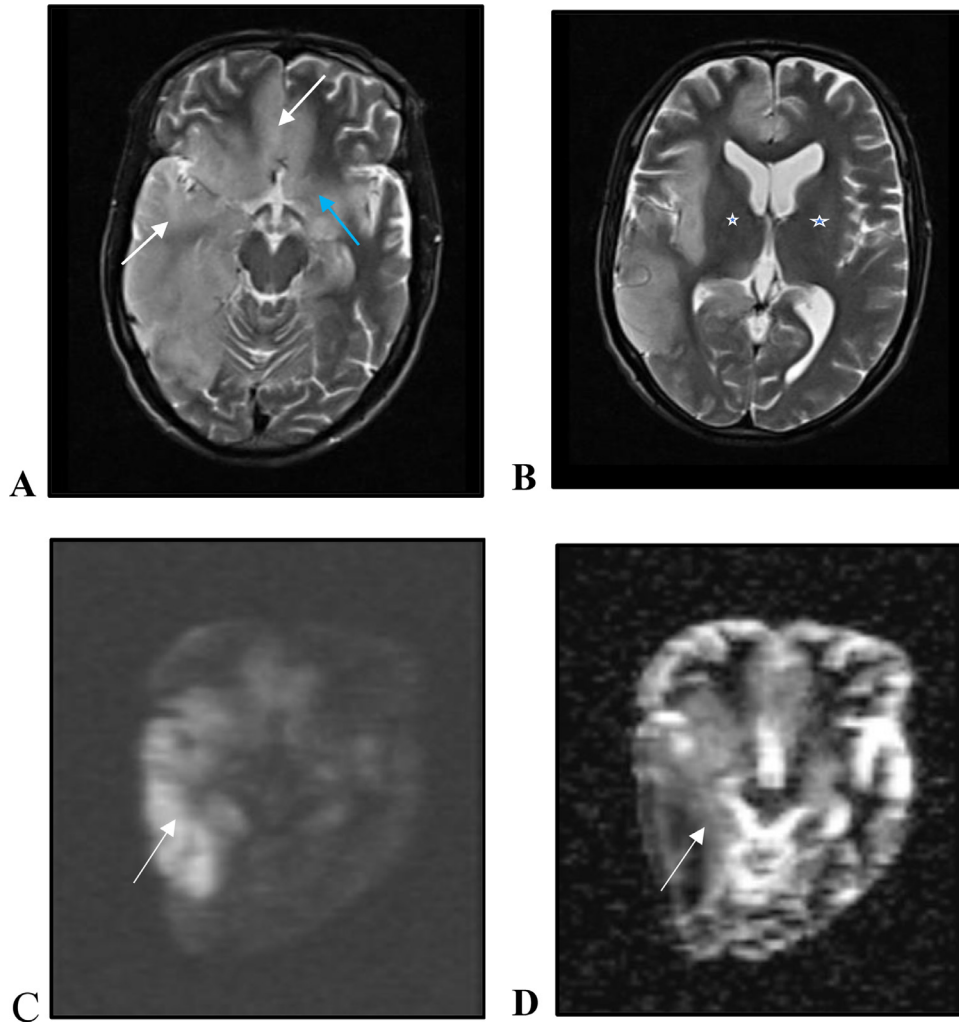


Fig. 2 – Axial non-contrast brain MRI, T2 (A&B), DWI (C) and ADC (D) shows the following findings: There is high T2 signal intensities with swollen gyrus and effacement of surrounding sulci in the right temporal lobe (indicated by short arrow), bilateral lower paramedian frontal lobes (indicated by long arrow) and left mesial temporal lobe (indicated by blue arrow) (A). bilateral basal ganglia remain unaffected (indicated by white stars) (B). (C) DWI and (D)ADC images demonstrate subtle restricted diffusion in the areas of the brain where the signal intensity changes are observed (white arrows).

malities observed in brain CT or MRI scans [5]. Therefore, familiarity with the typical presentation and radiological findings is crucial for early recognition and treatment of HSVE [1,3].

Currently, the diagnosis of herpes simplex virus (HSV) infection relies on identifying typical brain imaging findings on MRI/CT scans, CSF abnormalities, and confirmation through CSF polymerase chain reaction (PCR) testing [7].

MRI is considered superior to CT scans, and in immunocompetent adult patients, typical imaging findings involve asymmetrical bilateral involvement of the limbic system, medial temporal lobes, insular cortices, and inferolateral frontal lobes. The basal ganglia are usually unaffected. Therefore, in cases where there is clinical suspicion, early empirical treatment should be initiated. Prompt initiation of acyclovir has been shown to improve outcomes, and the addition of broad-spectrum antibiotics may be necessary until bacterial infection can be ruled out [8,9].

Case presentation

A 76-year-old male patient presented to the Emergency department with a complaint of headache lasting for 5 days and altered behavior for 2 days. Upon examination, no significant findings were noted, except for slurred speech. Due to the unavailability of an MRI machine on site, a CT scan (Fig. 1) was performed, and a lumbar puncture was conducted after the patient arrived at the emergency room. Considering a high suspicion of meningitis, empiric treatment covering both bacterial and viral causes (including acyclovir) was initiated in the emergency setting. The patient's cerebrospinal fluid (CSF) analysis and PCR results were awaited. The CSF analysis revealed leukocytosis with 100% lymphocytes, elevated protein levels, normal glucose levels, negative gram stain, and a viral PCR result that confirmed the presence of HSV-1, which became available after 2 days. Subsequently, the patient was

admitted to the hospital and continued receiving intravenous acyclovir and antibiotics. Despite a week-long hospital stay, the patient's condition did not improve, and he eventually lapsed into a coma. In order to assess for possible intracranial complications, an MRI scan was ordered at a nearby health-care facility. Following the MRI (Fig. 2), which did not reveal any additional complications, the patient was transferred to the Intensive Care Unit (ICU) while receiving the same care based on the initial working diagnosis. Unfortunately, after 14 days of hospitalization, the patient experienced a sudden deterioration and succumbed to the illness.

Discussion

The herpes simplex virus is the leading cause of nonepidemic and sporadic viral fulminant encephalitis [10]. Clinical manifestations typically begin early during the infection, and detectable changes on brain imaging can be seen within 2-3 days of symptom onset on MRI, while CT scans may show these changes commonly after 3 days. This makes MRI the most sensitive radiological investigation. Typical MRI findings of herpes simplex encephalitis include asymmetrical involvement of the limbic system, including the medial temporal lobes, insular cortices, inferolateral frontal lobes, and cingulate gyri, while the basal ganglia are usually unaffected [11]. Gliomatosis cerebri and infarcts in the middle cerebral artery (MCA) territory can be confused as differential diagnoses; however, intact basal ganglia, non-localized pattern of damage against MCA territory infarction, and the presence of acute symptoms differentiate herpes simplex encephalitis [12].

In our case, the observed neuroimaging findings on CT scan showed loss of gray-white matter distinction and reduced density in specific brain regions, such as the right temporal lobe, right insular cortex, left mesial temporal lobe, and both paramedian lower frontal lobes, which raised clinical interest. The sparing of the bilateral basal ganglia further helped differentiate it from MCA territory infarction and contributed to the diagnostic evaluation. With the presence of fever and behavioral changes, along with these CT scan findings, the diagnosis of herpes simplex encephalitis was favored. Considering the higher mortality associated with this condition and the importance of early treatment initiation, empirical management was crucial in our patient, followed by CSF analysis and MRI imaging, if available, for confirmation.

While CT scans are less sensitive in detecting herpes encephalitis, showing late abnormalities, they can still be an appropriate diagnostic modality in resource-limited settings. In our case, due to limited resources, CT was initially performed and helped in making the diagnosis of HSV encephalitis and initiating early treatment. A recent article [15] mentioned that the sensitivity of CT for HSV encephalitis increases with time from symptom onset: 0% at Day 0-2, 80% at Day 3-10, and 89% after Day 10. On the other hand, MRI sensitivity for HSV encephalitis decreases after 10 days from symptom onset: 100% at Day 0-2, 100% at Day 3-10, and 75% after Day 10. Considering our patient presented on the fifth day of symptoms, CT had a sensitivity of 95%. Therefore, in resource-limited settings,

CT can play an important role in detecting encephalitis if performed after 2 days of symptom onset [6,14].

Herpes simplex encephalitis is typically fatal in elderly patients, highlighting the importance of early diagnosis and the use of antiviral medications for improved prognosis. In resource-limited settings, relying on clinical symptoms and utilizing supportive diagnostic modalities like CT, along with early empirical treatment, can benefit the patient. When viral PCR and MRI are not available, utilizing the resources at hand allows for early initiation of treatment, which can impact treatment efficacy. Despite the early initiation of antiviral medication in the emergency department based on high clinical suspicion and CT scan findings, the patient's outcome was not satisfactory. Possible contributing factors for this lack of improvement may include delayed presentation to the emergency department, advanced age, potential antiviral resistance, and the nature of the infection itself [13].

Conclusion

Herpes simplex is a common cause of infectious encephalitis and diagnosing it can be challenging in resource-limited settings. However, maintaining a high level of suspicion in patients with fever and behavioral changes, and utilizing available resources such as CSF analysis and CT scans, can be highly valuable. While PCR and MRI are the preferred diagnostic methods, CT scans can be suitable in settings with limited resources, showing a sensitivity of up to 95% on the fifth day of symptom onset. Despite treatments, herpes simplex encephalitis still carries a high mortality rate, especially in older patients. Prompt treatment initiation and maximizing available resources have the potential to improve the final outcome.

Patient consent

The patient confirms their understanding of the consent form and voluntarily consents to the publication of their case report, including associated images. A copy of the consent form has been provided to the patient for their records.

Data availability statement

The datasets used in this study will be made available by the corresponding author upon reasonable request.

Ethical considerations

Written informed consent was obtained from the patient representative to publish this case report and its accompanying images.

Contributions of authors

All authors made substantial contributions to the conception, design, execution, data acquisition, analysis, and interpretation of the study. They were also involved in drafting, revising, and critically reviewing the article. The final version of the article was approved by all authors for publication. They have agreed on the journal to which the article has been submitted and take responsibility for all aspects of the work.

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