Case Report

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Herpes simplex (HSV-1) encephalitis in an infant: a case report study

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Introduction and importance: The herpes simplex virus (HSV) is the most common cause of acute sporadic encephalitis, a severe and often fatal disease in humans. It is associated with high mortality and morbidity rates in untreated patients.

Case presentation: An 11-month-old child was admitted to the hospital presenting with acute fever and seizures characterized by staring episodes and spastic movements affecting the left side of the body. Diagnostic workup revealed abnormal T2 flair hyperintense foci in bi-temporoparietal lobes and right thalamus, and bilateral otomastoiditis were detected. A positive result for HSV-1 was obtained through HSV type 1/2 polymerase chain reaction (PCR) testing, leading to a diagnosis of herpes encephalitis.

Clinical discussion: While acyclovir has proven to be an effective therapeutic option, mortality and neurological sequelae continue to be reported in a notable fraction of patients. HSV encephalitis is mainly caused by two strains of the herpes simplex virus: HSV-1, more frequently observed in children and adults, and HSV-2, commonly seen in neonates and those with compromised immune systems. MRI scans often reveal that the brain lesions are localized to certain areas, although temporal involvement may not always be evident. The symptoms of herpetic encephalitis can greatly vary, making early diagnosis and treatment vital for improving patient outcomes.

Conclusion: This case report highlights the clinical presentation, diagnostic challenges, and treatment strategies for HSV-1 encephalitis and underscores the importance of early recognition and prompt initiation of antiviral therapy in suspected cases of HSV-1 encephalitis.

Keywords: acyclovir treatment, case report, early diagnosis and treatment, herpes simplex virus (HSV)

Introduction

Encephalitis is defined as the inflammation of the brain parenchyma, leading to various neurological manifestations. This condition can arise from both infectious and non-infectious causes[1]. Among the infectious agents, herpes simplex virus type 1 (HSV-1) is recognized as a leading cause of acute sporadic viral encephalitis, which is notably the most common fatal form of the disease[2]. Annually frequency of herpes simplex encephalitis (HSE) is roughly 1 per 250 000-500 000 and had expanded significantly amid the past 20 a long time. The morbidity and mortality rates associated with untreated HSV encephalitis are alarmingly high, reaching up to 70%[2–4]. The incidence of HSV encephalitis varies worldwide, with reported rates ranging from 0.7 to 13.8 cases per 100 000 individuals across all age groups. Specifically, the incidence is 0.7–12.6 per 100 000 among adults and significantly higher in children, at 10.5–13.8 per 100 000[3].

The suspicion of encephalitis should be raised when a patient exhibits acute neurological symptoms, typically developing within 24–72 h. These symptoms include seizures, decreased consciousness, focal deficits, papilledema, and behavioral changes, often accompanied by systemic signs such as fever, rash,

HIGHLIGHTS

According to the results of the study:

- The patient presented with abrupt onset of seizures in the form of staring and spastic movements of the left half of the body and fever.
- Diagnostic workup revealed abnormal T2 flair hyperintense foci in bi-temporoparietal lobes and right thalamus, and bilateral atomastoiditis were detected. Herpes simplex virus (HSV) type 1/2 polymerase chain reaction (PCR) resulted positive for HSV-1 so the patient was diagnosed with herpes encephalitis.
- Further research and reporting of similar cases are warranted to enhance our understanding of this rare but serious neurological condition.

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lymphadenopathy, and sometimes a recent history of exposure to potential risk factors like travel or insect bites[5–7].

The gold standard for diagnosing HSV encephalitis is the cerebrospinal fluid (CSF) HSV polymerase chain reaction (PCR) test, which boasts a sensitivity of 98% and a specificity of 94%[8,9]. However, it is important to note that the PCR test may yield false-negative results during the first 4 days of illness. Therefore, it is recommended to repeat the test after the fourth day or later if the initial test comes back negative, to ensure accurate diagnosis[8,10]. The aimed this study is report of Herpes simplex (HSV-1) encephalitis in an infant.

Case presentation

The patient, an 11-month-old girl residing in a village near Gorgan, Iran, was the fourth child born to consanguineous parents, delivered vaginally at full term (39 weeks). Her birth weight was 3150 g, placing her in the 10th–25th percentile for her age, and at the time of hospitalization, she weighed 8500 g, which is between the 5th to 10th percentiles. Her height was 77 cm, and head circumference (HC) was 47 cm, both metrics falling within the 50th–75th percentile. There was no notable history of hereditary, neurological, psychological, or congenital diseases within the family. The neurological examination findings of the patient were as follows:

Mental status: Glasgow Coma Scale: GCS score of 8 (E2V2M4), eyes: open to pain, verbal: crying inconsolably, motor: spontaneously moving extremities

Cranial nerves: pupillary reactions: unequal and sluggish, limited assessment of extraocular movements due to infant's decreased level of consciousness, facial expression: grimacing in response to stimuli, hearing: startles to loud noises

Motor function: muscle tone: increased tone in all extremities, spontaneous movements noted, but decreased overall activity, occasional tremors observed

Sensory function: limited assessment due to infant's decreased level of consciousness

Reflexes: reflexes diminished and difficult to elicit due to infant's condition, plantar responses: not assessable

Coordination and gait: unable to assess coordination or gait in an infant of this age

Meningeal signs: neck stiffness not assessable due to infant's age, Brudzinski's sign and Kernig's sign not applicable in this age group

Autonomic function: temperature regulation impaired with fever present, heart rate and respiratory rate elevated, sweating noted on forehead

Cognitive function: inability to engage in age-appropriate play activities, decreased responsiveness to familiar faces or voices

Seizure activity: three seizures during her stay, characterized by staring and spastic movements of the left half of her body.

At the age of 11 months, she was hospitalized due to fever and seizures. Upon examination, she was found to be asleep with an oxygen saturation of 99% and a heart rate of 135 beats per min. She experienced three seizures during her stay; two were spaced 6 h apart, lasting ~ 3 min each, characterized by staring and spastic movements of the left half of her body.

Prior to this admission, she had been hospitalized for 5 days at another center where she received supportive care, underwent an ultrasound, and had several tests (white blood cell count (WBC) : 11.6, hemoglobin (Hb) : 8.4, creatinine (Cr) : 0.4, blood urea nitrogen (BUN) : 4, blood sugar (BS) : 126). The brain ultrasound revealed an echogenic area measuring 24 × 23 mm in the right temporoparietal region. Abdominal and pelvic ultrasounds showed a 4 mm gallstone and multiple echogenic foci in the gallbladder, but the bladder appeared normal. The heart echocardiogram (echo, TTE) detected trivial mitral regurgitation (MR) and trivial pulmonary insufficiency (PI) with no evidence of vegetation or clot.

Due to a Glasgow Coma Scale (GCS) score of 8/15 and suspected encephalitis, she was admitted to the Pediatric Intensive Care Unit (PICU). A comprehensive set of tests including complete blood count (CBC), blood urea nitrogen (BUN), creatinine (Cr), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), blood culture (B/C), urine analysis (U/A), urine culture (U/C), electrolytes, liver enzymes, and arterial blood gas (ABG) were ordered. Routine blood examination shown the Table 1.

COVID-19 PCR test was negative. CSF RNA analysis for Influenza H1N1 was negative, but PCR testing for HSV types 1

Table 1

Routine blood examination performed.

Biochemistry	Case	Unit
WBC	6400	mm
RBC	3.87	mil/cumm
Hb	8.4	gr/dl
Hct	25.9	%
MCV	66.93	fl
MCH	21.71	Pg
Plt	322 000	µl
Poly	58	%
Lymph	40	%
BUN	7	mg/dl
Cr	0.5	mg/dl
Na	137	mEq/l
K	5.1	mEq/l
Calcium	8.2	mg/dl
Phosphorus	3	mg/dl
Mg	2.2	mg/dl
Blood sugar	81	mg/dl
AST	75	U/l
ALT	18	U/l
ALP	130	U/l
ESR	45	—
CRP	+3	—
Blood group , Rh	A+	
B/C	No growth after 48h	
U/C	No growth after 24h	
U/A		
Color	Yellow	
Blood. Hb	Negative	
Urine protein	Negative	
PH	5	
Specific gravity	1014	
Appearance	Clear	
Ketones	Negative	

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; fl, femtoliters; gr/dl, grams per deciliter; Hb, hemoglobin; Hct, hematocrit; K, potassium; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; Mg, magnesium; mg/dl, milligram per deciliter; mil/cumm, million per cubic millimeter; mm, millimeter; mmHg, millimeters of mercury; mmol/l, millimoles per liter; Na, sodium; pg, picograms; Plt, platelet; RBC, red blood cell count; Rh, rhesus; U/l, unit per liter; WBC, white blood cell count; µl, microliter; µmol/l, micromoles per liter.

Table 2

PCR test.

Test name	Specimen	Result
RNA analysis for Influenza H1N1 (PCR)	CSF	Negative
HSV type ½ PCR	CSF	Positive for HSV-1
COVID-19 RT-PCR		Not-detected

CSF, cerebrospinal fluid; HSV, herpes simplex virus; PCR, polymerase chain reaction; RT-PCR, real-time PCR.

and 2 was positive for HSV-1, leading to a diagnosis of herpetic encephalitis (Table 2).

CSF analysis showed white blood cells (WBC) of 23(/μl), 90% lymphocytes, and protein of 25 mg/dl. CSF pressure was 13 cmH2O and the patient didn't have papilledema (Table 3). CSF analysis showed in Table 3.

The treatment regimen included a single intravenous dose of acyclovir 130 mg, followed by 85 mg administered three times daily (TDS) for 19 days. Additional treatments included cefotaxime 430 mg IV, vancomycin 130 mg IV (as the patient was referred with a reduced level of consciousness and based on the clinical findings, we suspected meningitis, so we gave the patient meningitis treatment until the diagnosis of herpes simplex encephalitis was confirmed) , phenobarbital 20 mg IV, and calcium gluconate 8 cc IV. Daily measurement of head circumference was advised, averaging 44 cm during her stay. Nutritional support through a high-protein diet and physiotherapy for the left limb due to hemiplegia were also part of her care plan. The patient has been followed-up for 6 months, and hemiplegia on the left side is observed. Occupational therapy continues for the patient.

Brain MRI identified abnormal T2/flair hyperintense foci in the bi-temporoparietal lobes and right thalamus, along with bilateral otomastoiditis, though the brain computed tomography (CT) scan was normal. MRI findings showed in Fig. 1.

Discussion

HSV holds the distinction of being the predominant cause of acute sporadic encephalitis, an affliction striking ~2–4 individuals per million annually and noted for its catastrophic impact on human health[11,12]. This condition is associated with a daunting 70% mortality and morbidity rate in cases left untreated. Despite the high efficacy of acyclovir in managing herpetic encephalitis, mortality rates persist at 11–19%, with survivors often facing neurological sequelae[11,13].

HSV encephalitis can be attributed to two strains of the virus: HSV-1 and HSV-2. While HSV-1 is chiefly responsible for cases in children beyond the neonatal period and in adults, HSV-2 predominantly affects neonates and individuals with compromised immune systems. Thus, the majority of herpes encephalitis cases are linked to HSV-1 infections[14,15]. Brain MRI evaluations frequently reveal that lesions primarily affect the temporal lobes, the insula, and the basal regions of the frontal lobes in children and adults. Conversely, neonates more commonly exhibit involvement of the insula, parietal, and occipital lobes, as observed with lesions in bi-temporoparietal lobes in our case. It is important to note that the absence of temporal lesions does not preclude a diagnosis of herpetic encephalitis, underscoring that a satisfactory outcome hinges on prompt diagnosis and initiation of treatment[11,16,17].

Table 3

Cerebrospinal fluid (CSF) analysis.

White blood cells (WBC)	23	(/μl)
Lymphocytes	90	%
Protein	25	mg/dl
Glucose	44	mg/dl
RBC	7	
Appearance	Normal	
Pressure	13	cmH2O

RBC, red blood cell.

The wide spectrum of clinical presentations of herpetic encephalitis, coupled with primary symptoms like fever, headaches, fatigue, and vomiting that are often nonspecific, complicates the diagnosis. Only 38% of non-neonatal children manifest with neurological symptoms such as seizures, which can facilitate earlier detection[11,18]. The case under discussion involves an infant presenting with acute onset seizures and fever. Our initial differential diagnosis included meningitis, encephalitis, and intracranial infection. Despite a normal EEG, the detection of temporoparietal lobe involvement on MRI and the presence of HSV-1 DNA in PCR analysis confirmed the diagnosis, aligning with the established diagnostic gold standard for herpetic encephalitis, which includes CSF analysis, MRI, and EEG[19,20].

Although HSV encephalitis is relatively rare, its primary symptoms necessitate heightened clinical awareness to ensure early treatment, which significantly influences prognosis[21,22].

Neurological outcomes in children with HSV central nervous system (CNS) infection are challenging to forecast, and the prognosis remains cautious despite timely diagnosis and treatment. Mortality from HSV CNS infection is uncommon in children but more prevalent in neonates, typically as a component of disseminated infection. Infants under 12 months, especially neonates, are at the highest risk of HSV CNS infection. CNS infection is linked to enduring neurological consequences, even in children discharged from the hospital without any identified neurological impairments. It is advised to provide meticulous neurodevelopmental monitoring for all children[23–25].

Conclusion

This case report delineates the clinical manifestations, diagnostic hurdles, and therapeutic management of HSV-1 encephalitis, marked by the sudden emergence of seizures characterized by staring and spastic movements on the left side of the body, accompanied by fever. The diagnostic process uncovered abnormal T2 flair hyperintense foci in bi-temporoparietal lobes and right thalamus, along with bilateral otomastoiditis. The positive HSV type 1/2 PCR for HSV-1 led to the diagnosis of herpes encephalitis. A 20-day acyclovir treatment regimen effectively halted the fever and seizures, highlighting the critical need for early detection and immediate antiviral intervention in suspected cases. Moreover, this case stresses the importance of vigilant monitoring for potential complications and long-term neurological outcomes in survivors. Further investigation and documentation of similar instances are imperative to deepen our comprehension of this infrequent yet grave neurological disorder.

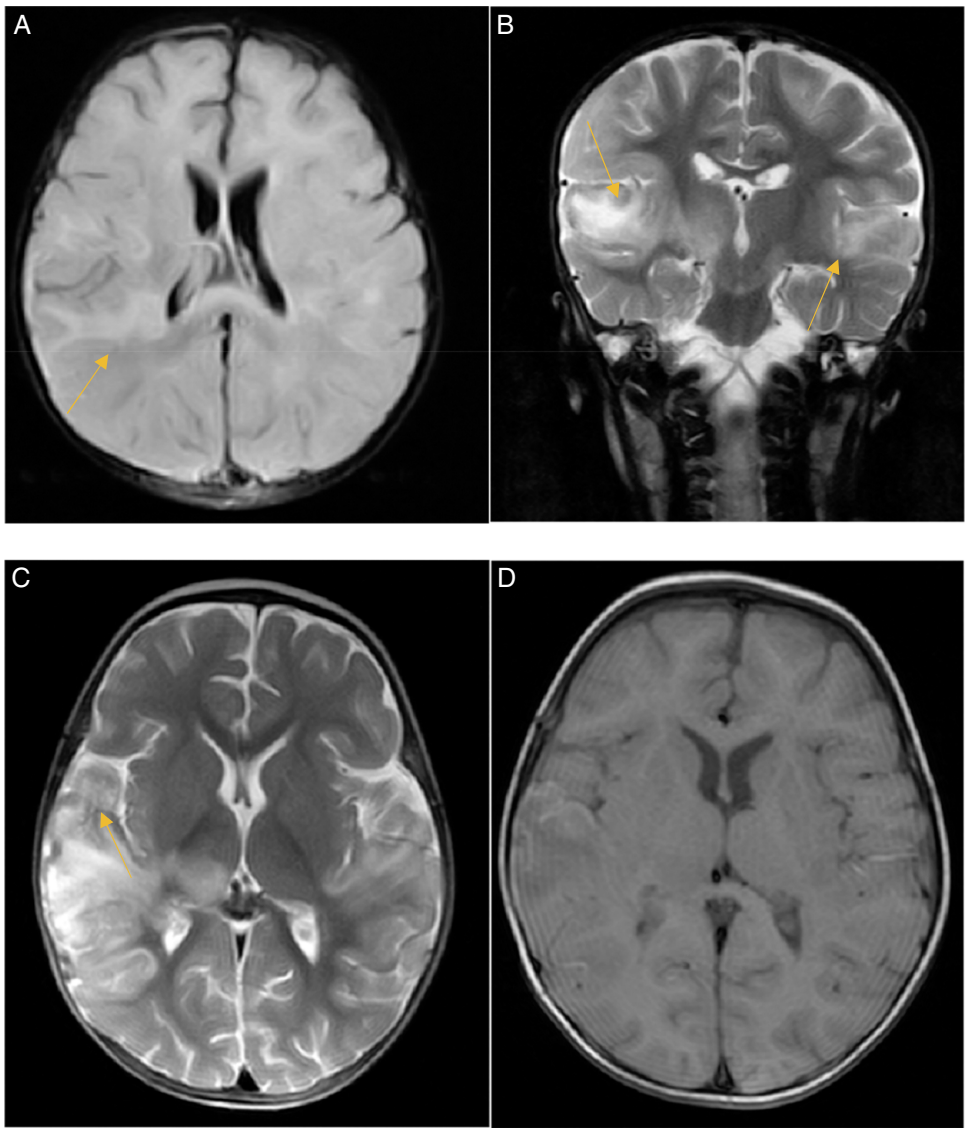

Figure 1. MRI findings. (A) Increased signal on right temporoparietal region in FLAIR sequence in axial section. (B) Increased signal on right and left temporoparietal region with right side predominance in coronal section on T2WI. A "ribbon-like sign" on a brain MRI refers to a radiological finding where there is a linear or ribbon-shaped area of abnormal signal intensity in the brain, typically seen on T2-weighted or FLAIR sequences. This finding can be associated with various conditions such as demyelinating diseases (e.g. multiple sclerosis), inflammatory disorders, infections like herpes simplex encephalitis (HSV) or certain neurodegenerative conditions. The appearance of a ribbon-like sign can provide important diagnostic information to help guide further evaluation and treatment. Based on the clinical presentation of the patient and the findings in the cerebrospinal fluid, our diagnosis was herpes encephalitis. (C) Increased signal on right temporoparietal region in axial section on T2WI. (D) Increased signal on right temporoparietal region in sagital section on T2WI.

Ethical approval

NA.

Consent to participate

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. The whole research was done under the permission of the Ethics Committee of Golestan University of Medical Sciences and also Genetic Testing for parents was done because of their.

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Author contribution

S.A.H. and S.G. diagnosed, and managed this patient and interpretation. P.S.H. and S.D. wrote the first manuscript draft, M.G.G. and P.S.H. revised the manuscript and finalized the draft

Conflicts of interest disclosure

The authors declare that they have no conflicts of interests.

Research registration unique identifying number (UIN)

For register of research needs to pay charge. we are in international sanction so unable pay or transfer register fee.

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Data availability statement

The datasets are available from the corresponding author on reasonable request.

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