

Herpes Simplex Virus Encephalitis Complicated by Acute Ischemic Stroke

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Abstract

Introduction: Herpes simplex virus is the most common etiology for life-threatening sporadic encephalitis worldwide. Antiviral therapy with acyclovir has been shown to reduce mortality and should be started promptly in patients with clinically suspected viral encephalitis before serological confirmation of the diagnosis. Despite antiviral treatment, it is associated with significant mortality and a wide range of neurologic sequelae or neuropsychiatric disorders. Clinical presentation includes fever, headache, altered mental status, and focal or generalized seizures. In some cases, it can present with focal neurological deficits, such as an acute stroke. The aim of this study is to identify rare complications of HSVE. **Presentation:** We present a case of a 71-year-old female patient with herpes virus encephalitis and an ischemic cerebral accident. The findings of CT scan of the brain revealed an extensive right temporal hypodensity. CSF findings include an elevated protein level, normal glucose level and pleocytosis with lymphocyte predominance. The lumbar tap confirmed the presence of herpes simplex virus type 1 with polymerase chain reaction (PCR) in the CSF. Neurological manifestations include focal neurological deficit with left-sided hemiparesis and coma. After 40 days of complex therapy, an improvement in the mental state was observed. **Conclusion:** There are varying degrees of neurologic sequelae among survivors in children and adults despite the antiviral treatment. Herpes simplex encephalitis has significant morbidity and high mortality due to the lack of prophylactic treatment and preventable strategies.

Keywords

Herpes Virus Encephalitis, Focal Neurological Deficit, Altered Mental Status, Stroke Chameleon, Persistently Positive CSF

1. Introduction

Herpes simplex viral infection is among the most severe of all viral infections of the human brain. Herpes simplex virus (HSV) encephalitis is the most commonly diagnosed viral encephalitis in industrialized nations, with an annual incidence of 1 in 250,000 to 500,000. [1] Herpes simplex virus-1 is the predominant cause of encephalitis in adults, while HSVE in most neonates and early infancy is caused by herpes simplex virus (HSV)-2. [2] The clinical manifestations of HSVE include fever, mental status changes, seizures and focal neurological deficits. However, these clinical features are not pathognomonic because numerous other diseases in the CNS can mimic HSVE. The diagnostic gold standard is cerebrospinal fluid (CSF) analysis and detection of herpes simplex virus by polymerase chain reaction (PCR). However, false-negative PCR results of cerebrospinal fluid can complicate clinical decision-making. [3] [4] In contrast, a computerized tomography (CT) scan and MRI have a critical role in the evaluation of such patients. [5]

2. Case Study

This is a clinical case of a 71-year-old female patient, with a past medical history of hypertension, first presented with a fever, vomiting and altered mental status, hospitalized in the Clinic of Infectious Diseases at UMBAL “St. George”, Plovdiv. The disease started three days before hospitalization with dyspeptic syndrome, severe headache and fever over 39°C. On the day of admission, the patient was in severe condition, somnolent, with Glasgow coma scale of 11 p., with signs of intoxication and dehydration. Skin and visible mucous membranes were dry with no rash. In the neurological examination upon her admission, no alteration of the cranial nerves was identified, muscle stretch reflexes were present and normoreflexic, Babinski signs and nuchal rigidity were positive, with mild photophobia.

In the next few hours, the patient’s symptoms worsened, with left-sided hemiparesis and flexion response of the right superior arm only after repeated painful stimuli; also expressive aphasia and focal myoclonic seizure was observed;

Regarding the fact that aging and hypertension are the strongest non-modifiable risk factors for incident stroke, a head computed tomography (CT) scan was performed. (Figure 1) CT of the head revealed an extensive hypodense area in the right temporal lobe. She had no history of central nervous system disease and did not take any immunosuppressive medication. Despite evidence of ischemic stroke, given the typical location for HSVE, intravenous acyclovir therapy was initiated before the serological confirmation.

Initial laboratory findings showed the following pathological values; neutrophilic leukocytosis (WBC of 10.14; neutrophil of 78.6%), and mild hyponatremia of 130 mmol/L. (Table 1)

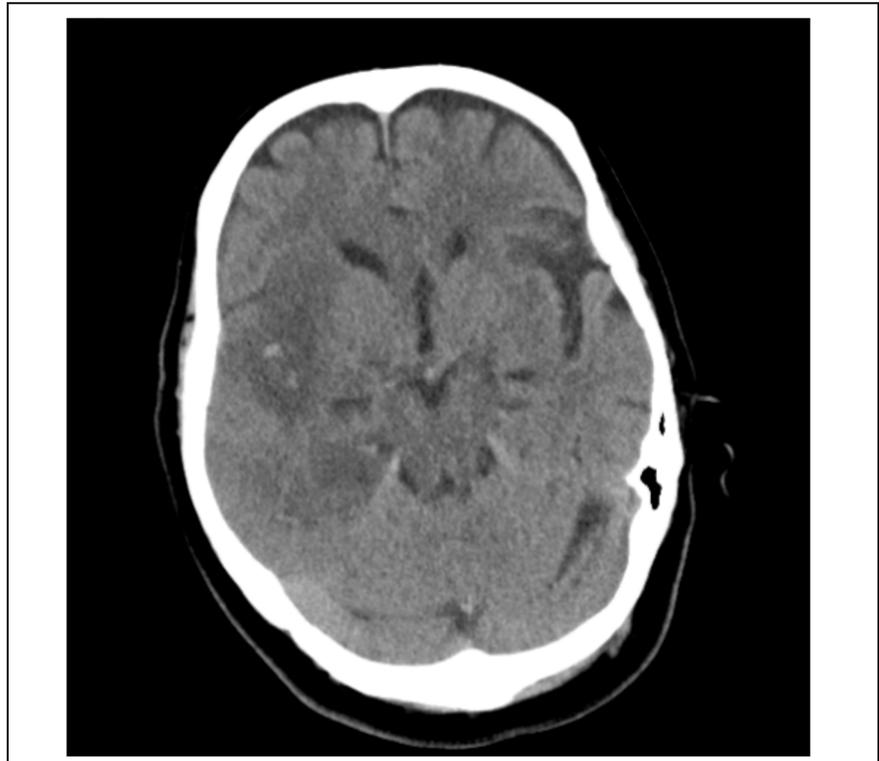


Figure 1. Simple axial computed tomography of the skull; with extensive hypodense area in the right temporal lobe with impaired differentiation, the rest of the brain structures have a normal densitometry characteristic. Asymmetric ventricular system with preserved capacity located in the middle. Free subarachnoid spaces. Bones-intact.

Table 1. Laboratory investigations.

Date	11.01.24
HGB g/l	147
RBC $10^{12}/l$	5.34
WBC $10^9/l$	10.14
PLT $10^9/l$	281
Gluc mmol/l	6
CRP mg/l	9
AST U/l	51
ALT U/l	29
Na mmol/l	130
Cl mmol/l	90
Creatinine $\mu\text{mol}/L$	69
Urea mmol/l	3.9

The Fundoscopic exam revealed no papilledema. The patient underwent a lumbar puncture and cerebrospinal fluid (CSF) analysis showed a WBC count of 64 (90% lymphocytes) and protein of 1.75 g/L. (**Table 2**)

Table 2. Cerebrospinal fluid analysis.

Date	08.09.22
Lks 10 ⁶ /l	64
U-CSF Prot g/l	1.75
Gluc-CSF mmol/l	2.3
Na mmol/l	140
K mmol/l	3.6
Cl mmol/l	108
IgG mg/l	212.77

The patient was set under i.v. treatment with Citicoline, Ceftriaxone, antiepileptic drugs, vitamins and PPI, plus reduction of intracranial pressure with Mannitol, Dexamethasone. After 5 days of complex therapy, an improvement in the mental state was observed. The patient was conscious with GCS 12 p. PCR for herpes simplex virus was positive for 40 days. Therefore, the administration of IV acyclovir continued until a negative result.

The diagnosis of HSVE was confirmed by real-time RT-PCR in CSF at the National Centre of Infectious and Parasitic Diseases.

Regarding the differential diagnosis, we discussed: meningitis caused by bacteria or encephalopathy in the course of another infectious disease. All microbiological tests from the throat swab, blood culture and gram stain of CSF were negative.

The patient was discharged from the hospital on the 42nd day with an improvement in the general condition. However, left-sided residual hemiparesis and memory loss persisted.

Three weeks later, the patient complained of diarrheal syndrome and fever. The examination revealed dehydration and the need for intravenous rehydration. The patient still had left-sided residual hemiparesis, delayed response and memory problems. The tests of a stool sample for *Clostridium difficile* toxin were positive and Vancomycin therapy was instituted.

3. Discussion

HSVE can occur in all age groups and all seasons. Although there are no diagnostic features. The most common clinical manifestations include vomiting (46%), fever (90%), headache (81%), psychiatric symptoms (71%), convulsions (67%), and memory loss (24%). [6] The radiological features are hypodensity in the temporal lobes either unilaterally or bilaterally, with or without frontal lobe involvement. However, in many cases normal CT scan cannot rule out the diagnosis, but they aid diagnosis of encephalitis etiology as well as mimicker conditions. [7] Ischemic stroke, although infrequent, can mimics herpes simplex meningitis or encephalitis. [8] [9] Also hemorrhagic stroke in adults has been reported in a few cases of HSV encephalitis. [10] In patients with clinically suspected viral encephalitis, antiviral therapy should be initiated as early as possible,

even if there is no serological confirmation.

We describe a patient who developed atypical and life-threatening complications due to HSV-1 encephalitis. This case suggests that HSV-1 should be considered among the possible causes of acute ischemic stroke and the importance of PCR amplification method of the CSF. HSV-1 encephalitis has high morbidity and mortality of up to 70% without treatment. [4] [10] [11] Normal neurological function is not restored to 97% of the surviving patients, who experience sequelae. [12] A persistently positive PCR HSV in CSF may be a risk factor for worse clinical outcomes. Herpes simplex virus encephalitis is a rare cause of ischemic stroke and must be considered in the differential diagnosis of acute ischemic stroke with atypical presentation. [13] [14] [15]

4. Conclusions

The current case presents that HSV-1 could be a possible cause for a rare combination of acute encephalitis and ischemic stroke with atypical clinical course.

Despite the observation that early MRI is more sensitive for HSV encephalitis, the typical location should guide clinicians even with a definite diagnosis of stroke.

Written Consent

Written consent was obtained from the patient for this publication.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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