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Case Report

Herpes simplex virus encephalitis mimicking acute ischemic stroke

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ABSTRACT

Background: Infections of the central nervous system might present in an acute form such as to be similar with the clinical characteristics of a stroke. This situation will hamper a correct diagnosis and a prompt treatment that can otherwise be successful.

Case Description: We present the case of a herpes virus encephalitis that came up in the emergency department with an admission diagnosis of ischemic cerebral accident. Being the symptomatology unclear, the findings of magnetic resonance of the brain oriented versus an infectious disorder. The lumbar tap confirmed the presence of herpes simplex virus (HSV) 1 virus and an antiviral therapy was administered, leading to resolution of the condition within the 3 weeks of hospitalization.

Conclusion: HSV infections may mimic stroke and therefore should be included in the differential diagnosis of atypical acute nervous conditions. In neurological events of acute nature, especially in febrile patients whose brain imaging is suspicious or inconclusive, the eventuality of a herpetic encephalitis should be kept in mind. This will lead to a prompt antiviral therapy and to a favorable outcome.

Keywords: Brain imaging, Central nervous system infections, Encephalitis, Herpes virus, Stroke, Brain MRI

INTRODUCTION

Herpes simplex virus encephalitis (HSVE) is an infectious disease of the brain tissue which in most cases is caused by herpes simplex virus (HSV)-1, with an annual incidence ranging from 0.2 to 0.4/100,000 patients.[11,13] It results from a primary infection or a reactivation of the latent virus and is clinically characterized by mental status alteration, fever, focal or generalized seizures, and headache that develop acutely.[2,16] However, in some cases, it may present with focal neurological deficits, such as mimicking acute stroke, which leads to misdiagnose and incorrect treatment.

CASE PRESENTATION

A 49-year-old male was presented to our emergency department as a stroke alert from another hospital of our country, with 2 h history of acute onset of aphasia and right hemiplegia. On neurological examination, the patient was alert, obeys commands, pupils had a diameter bilaterally of 4 mm and were both reactive to light, with right hemiplegia, motor aphasia, left

head and eyes deviation, and right indifferent plantar reflex. There was no past history of fever nor seizures.

His wife referred that 3 months ago he experienced a transient ischemic attack with dysarthria, right hemiparesis and right hemihypesthesia which lasted 15 min, but he did not see any doctor and was left untreated. She also referred that 3 years ago, he was hospitalized and treated for meningitis but with no evidence or medical files at hand.

Regarding the fact that it had an acute onset, the clinical presentation was stroke-like, a head computed tomography (CT) scan was performed and after hemorrhage was excluded from the study, intravenous thrombolysis (IVT) with Alteplase was started. At 15 min of the procedure, we noticed mild gingival bleeding and infusion of Alteplase was interrupted. After the bleeding was stopped, the patient was stable hemodynamically and started perseverating only a few words. One hour later, he had an episode of explosive vomiting and shivering, and his body temperature started to increase to 37.5°C. Two hours later, a focal myoclonic seizure of right arm was observed; therefore, the patient was set under treatment with midazolam i/v.

Later on that day, fluctuations of clinical symptoms were observed, the patient became somnolent, opened eyes only after repetitive verbal stimulus, did not obey any command, and motor aphasia was present again. Even though he was treated with antipyretics, shivering did not stop, and he became febrile to 39.5°C, and irresponsive to treatment. Hemodynamically, he showed a hypotension (90/60 mmHg) and tachycardia 130 beats/min. Over the next 12 h, the myoclonic seizures became more frequent and they were generalized twice. He became more somnolent and opened eyes only to painful stimuli, and the only motor response seen was a flexion response of the right superior limb to pain. Viral encephalitis was suspected and empiric treatment with intravenous acyclovir was started for HSVE.

Brain magnetic resonance imaging (MRI) revealed a cortical enhancement in the left frontal lobe in the diffusion-weighted images (DWIs) [Figures 1a and b]. On day 3 of admission, the patient became alert, agitated, confused, started having visual and auditory hallucinations, while no motor deficits were seen. A lumbar tap was performed to collect cerebrospinal fluid (CSF) for testing. CSF was clear; the pressure was 210 mm H_2O (range 70–180); pleocytosis 45 cells/mm^3 (range <5); proteinorrhachia 65 mg/dL (range >40) and normal range glycorrhachia compared with blood glycemia. The serological diagnosis of HSV infection was based on identification of viral DNA with polymerase chain reaction (PCR) in the CSF.

The patient was treated with intravenous acyclovir for 21 days with a dose of 10 mg/kg 3 times daily, accordingly with suggested guidelines.[17] In the meantime, he became afebrile at the end of the 1st week of treatment, and never had a seizure or seizure-like episode. At the beginning of the 2nd week, an electroencephalography was registered, suggesting complex discharges and slow waves bilaterally in the frontal areas [Figure 2].A control brain CT was performed 2 days before the end of the antiviral therapy and his discharge, with findings considered as radiologically normal [Figure 3]. The patient was discharged in a stable condition 2 days after the ending of the antiviral therapy, he showed a mild cognitive impairment on 3-month follow-up.

DISCUSSION

HSVE can often have poor prognosis and is associated with significant morbidity and mortality (20–30%), despite prompt diagnosis and treatment.[1] HSVE-1, which might be a life-threatening condition, rarely present as a stroke mimic and it is reported that the proportion of stroke mimics varies from 1% to 16%.[18] We must say that stroke mimics are a true challenge for neurologists to distinguish from classical strokes and even though there are not seen serious complications after IVT in stroke mimic, it is crucial for the proper diagnosis to be done as soon as possible to avert unnecessary IVT and if HSVE, to initiate antiviral treatment.[7]

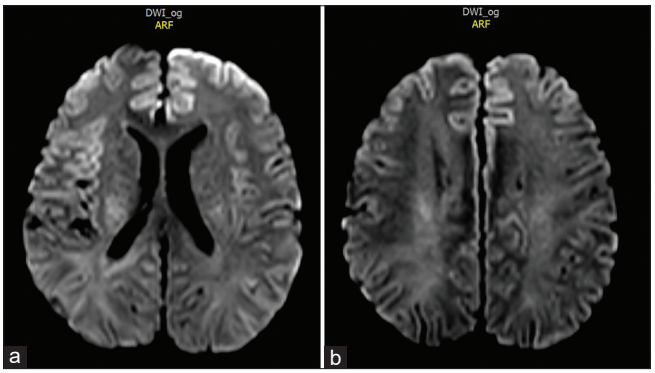

Figure 1: (a) (left inset) and (b) (right inset): cortical enhancement in the diffusion-weighted images images, showing an acute involvement of the left frontal lobe.

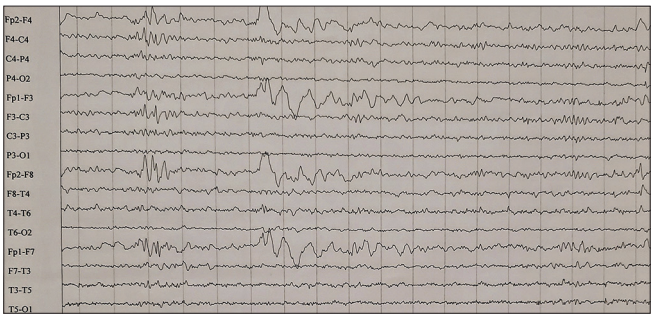

Figure 2: Electroencephalographic findings: slow waves and complex discharges were registered in bilaterally the frontal derivations.

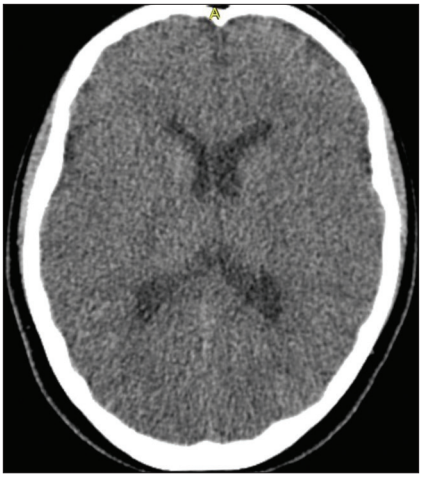

Figure 3: A control computed tomography, performed before the discharge, was interpreted as normal.

High index of clinical suspicion, prompt diagnosis, and early treatment are the mainstays of therapeutic success in herpetic encephalitis.[10] Sources suggest that acyclovir treatment should be started as early as possible on clinical suspicions, and this must be done while waiting further confirmation, such as the lumbar puncture results or serology.[10] Furthermore, the imaging studies can be inconclusive, and not all cases have a typical appearance, both clinically and radiologically.

Performing a lumbar puncture might be controversial if the patient has a thrombolysis recently; however, in our case, the CSF fluid was collected during the 3rd day of hospitalization. Instead, the thrombolysis was attempted upon admission and subsequently stopped due to gingival hemorrhage. The setting of a febrile patient, with unsatisfying response to antipyretics, while in a deeply confusing state and subsequent myoclonus, will raise the suspicion of a neuroinfection.

Since we are living in the SARS-CoV-2 era and several investigations have shown the involvement of the central nervous system along the course of the disease, with encephalitis being one of the occurrences, we must consider this virus as well. We excluded at the admission facility the possibility of a COVID-19 infection in our patient, through a Rapid test and a PCR test, which resulted both negative.[6]

Brain MRI is the imaging study of first choice, because it ensures a fast diagnosis and untangles HSVE from its mimics. Its typical findings are bilateral but asymmetrical involvement of frontotemporal lobes with cytotoxic edema, hemorrhage, or necrosis; however, in some cases, HSVE might develop unilateral lesions looking like ischemic stroke.[14,15] Cortical enhancement might be an initial suspicion sign in the DWIs of the brain magnetic resonance, with the temporal lobe showing a clear predilection for the herpetic foci.[8] Nevertheless, other localizations have been reported as well.[4]

As shown in our case and from a large database of other reports, when having a patient with unusual symptoms of stroke, HSVE must be under consideration as a differential diagnosis.

CONCLUSION

HSV is the most common cause of viral encephalitis and it might have a wide spectrum of clinical presentations. Rarely, it will mimic the clinical picture of an acute ischemic stroke.[5,9] More frequently, the clinical symptomatology will be similar to that of the occlusion of the middle cerebral artery, the same as in our patient, making it difficult for clinicians to diagnose correctly and timely, resulting in delaying of antiviral treatment.[3] Such cases must serve as "red flags" for the approach of HSVE diagnosis and differential diagnosis.

Among clinical caveats to mention and that would raise suspicion on a herpetic neuroinfection is the almost constant febrile nature of the occurrence, apart from the fluctuating neurological symptoms that sometimes characterize a transient ischemic attack. The latter is frequently missed on plain CT scan images; hence, the importance of a lumbar tap whenever there are clinical doubts. Of course, if thrombolysis is started, a delay of at least 48 h should separate this therapeutic intervention from the puncture to avoid unnecessary risks. This is valid also for patients while in treatment with oral anticoagulants, and algorithms suggesting the necessary diagnostic workup before performing the puncture are available, while evaluating carefully the risk/benefit ratio of the procedure.[12]

In all cases, an appropriate antiviral therapy could be started while waiting laboratory confirmation of the infective agent, to enhance the chances of a full recovery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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