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HERPES SIMPLEX ENCEPHALITIS: A DIAGNOSTIC CHALLENGE IN IMMUNOCOMPETENT YOUNG PATIENT.

Internal Medicine

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KEYWORDS

INTRODUCTION

Herpes simplex encephalitis is one of the most common and serious encephalitides of immunocompetent adults. If left untreated, this infection is associated with high morbidity and mortality (70% in untreated patients and 19% in those treated with acyclovir). Current diagnosis relies on cerebrospinal fluid examination (CSF) revealing positive results for polymerase chain reaction (PCR), a test with 98% sensitivity and 94% specificity.(1)

We presented a case of HSV encephalitis with an aggressive and fatal outcome, despite appropriate treatment. Through the presentation of this case, we review the importance of a prompt diagnosis and treatment institution to avoid unfavorable outcomes.

Case Presentation

A 22-year-old female presented to the Emergency Department after a first tonic-clonic seizure episode. Her family members reported a three-day history of fever (up to 39° C), diffuse headache and intermittent nausea and vomiting. Her medical history was unremarkable, with no comorbidities. She denied consuming alcohol, smoking or any illicit drugs. At admission she presented with fever (38,1°C), while the other vital signs where withing the normal range. Cardiac and respiratory examination were normal.

Neurologic evaluation revealed somnolence and disorientation in time and space. There were no motor focal signs, neck stiffness or other meningeal signs (Kerning and Brudzinski signs were negative). Laboratory examination revealed no signs of anemia (hemoglobin of 13.2 mg/dL).

The leukocyte count was 13,280 m/l with no immature forms. The renal and hepatic function were within the normal range. Serology tests for HIV, hepatitis B and C, syphilis and cytomegalovirus were negative.

Blood cultures were also negative. An urgent non-contrast brain CT revealed discrete diffuse effacement of the cortical sulci, and subtle loss of white-gray matter differentiation, particularly in the bilateral cortices, indicative of diffuse cerebral edema (Figure 1).

A presumptive diagnosis of meningitis was performed. The patient was started on intravenous ceftriaxone and dexamethasone. In the following twelve hours, the patient evaluated to decreased level of consciousness, and became comatose. Cerebrospinal fluid (CSF) examination revealed an elevated opening pressure (51 cm H_2O), 514 white blood cells/mm^3 (95% lymphocytes), and elevated protein level (64.2 mg/dL).

Acid-fast stain and direct mycological examination were both negative. The polymerase chain reaction (PCR) for Herpes Simplex Virus (HSV) type 1 was positive, while PCR for HSV-2, Epstein Barr, Varicella Zoster, Cytomegalovirus and Enteroviruses were negative.

A brain magnetic resonance imaging (MRI) revealed enhancement of the left temporal lobe and parahippocampal gyrus on T1-weighted image. The T2-weighted MRI also revealed hyperintensity corresponding to edematous changes in the temporal lobes (Figure 2).

The diagnosis of herpes simplex encephalitis (HSE) was performed. The patient was started on intravenous Acyclovir (10 mg/Kg every 8 hours) in 36 hours upon arrival. Despite treatment, the patient progressed to recurrent seizures and orotracheal intubation with propofol-induced coma. The patient continues to deteriorate and developed signs of brain death after seven days. No autopsy was performed since it was not available at our institution.

DISCUSSION

We presented a fatal case of HSV encephalitis in an immunocompetent patient. Herpes simplex encephalitis is a severe condition and constitutes one of the most common causes of sporadic fatal viral encephalitis in immunocompetent adults. It can present at any age and has an historical estimated incidence of between 1 in 250,000 and 1 in 1 million persons a year.(2) However, contemporary statistics performed since the introduction of routine PCR testing reveals an incidence ten times higher than reported in the end of the 20th century (1.2 cases per 100,000 inhabitants per year).(3)

For proper diagnosis, CSF analysis using molecular biology tests such as PCR to detect viral particles is considered a cornerstone. However, a negative result does not rule out the infection, specially if the CSF sample was obtained after the initiation of antiviral therapy, hence the importance of CSF analysis prior to treatment.(4) Brain image is also important to guide the correct diagnosis. The pathologic lesions of classic HSV-1 encephalitis are characteristically located in the temporal lobes.(5)

Despite the historical role of brain CT in guide diagnosis, current guidelines outline the usefulness of brain MRI in the management of patients with suspected HSE.(6)Typical radiological MRI findings in HSE are the presence of asymmetrical changes in signal intensities in the mesial temporal lobes, inferior frontal lobes and insula.(7) Guideline therapy for HSV meningitis is intravenous acyclovir (10 to 15 mg/Kg every 8 hours) for 10-14 days.

Empiric treatment with acyclovir is recommended in all patients with suspected encephalitis. Starting this antiviral treatment as early as possible is the most significant factor affecting the outcome of a patient with HSE.(8) Other factors negatively affecting the outcome 6 to 12 months after hospital discharge are coma, restricted diffusion on MRI, and older age.(9)

In the present case, some factors may had contributed to the fatal outcome. First, the lack of therapeutic response to acyclovir may be attributable to a delay in antiviral treatment. Second, despite no medical history and normal exams, an immunosuppressive state could not be completely ruled out.

CONCLUSION

We presented a fatal case of HSV encephalitis in an immunocompetent patient. Despite a well-known and high-quality evidence treatment with acyclovir, some atypical cases need a high index of clinical suspicion. This case also highlights the importance of a prompt diagnosis, and early therapeutic intervention for improving prognosis.

Conflict of Interest

The authors have no conflict of interest.

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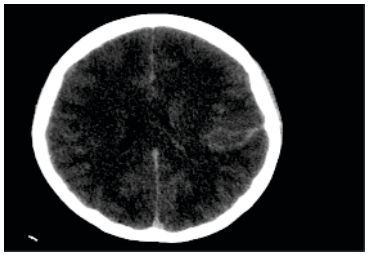

Figure 1 – Contrast enhanced brain computed tomography (CT) revealing subtle loss of white-gray matter differentiation, indicative of diffuse cerebral edema.

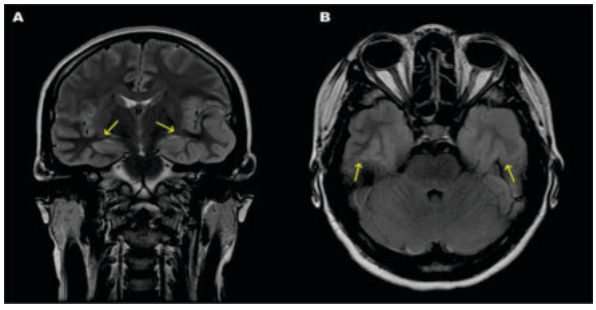

Figure 2 – The T2-weighted magnetic resonance imaging (MRI) in coronal (A) and axial (B) planes, revealing hyperintensity (corresponding to edematous changes) in the bilateral temporal lobes.

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