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UNUSUAL PRESENTATION OF HERPES SIMPLEX VIRUS 2 ENCEPHALITIS: A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT The author presents a case report of an 67 years old immunocompetent male patient diagnosed with herpes simplex 2 encephalitis presenting with acute onset of fever, seizure, and right sided hemiparesis which is indeed a rare presentation. The combination of clinical history and examination, cerebrospinal fluid polymerase chain reaction (PCR) for herpes simplex virus, brain computed tomography, magnetic resonance imaging and lumbar puncture has been used to establish a diagnosis. The patient recovered well with antiviral and antiepileptic medications. Herpes simplex encephalitis (HSE) is an acute or sub acute illness that causes both general and focal signs of cerebral dysfunction. Diagnosing this disease early & providing appropriate treatment with antiviral therapy is important to achieve an optimal clinical outcome. Early administration of antiviral therapy is the only parameter that can be modified to improve the prognosis of patients with HSE.

KEYWORDS : Herpes simplex 2 encephalitis , seizure, right sided hemiparesis

Introduction:

Herpes Simplex Virus Encephalitis (HSE) is a life-threatening consequence of herpes simplex virus (HSV) infection of the central nervous system (CNS). HSE is caused mainly by HSV type 1 (HSV-1), while HSV type 2 (HSV-2) accounts for 1.6–6.5% of all HSE in adults [1]. In contrast to HSV-1 acute encephalitis, a chronic or fluctuating course may be observed in HSV-2 encephalitis [2]. Left untreated, more than 70% of cases of HSV encephalitis (HSE) are fatal and only approximately 11% of patients recover normal premorbid function [3]. The HSV encephalitis (HSE) predominantly affects the limbic system and the adjacent areas of the frontotemporal lobe. So far, the diagnosis of HSE has relied on the combination of a compatible clinical scenario, a suggestive brain computed tomography (CT) scan or brain magnetic resonance imaging (MRI) and the examination of the cerebrospinal fluid (CSF) by microscopy, biochemical analysis and polymerase chain reaction (PCR) for the presence of HSV DNA. Treatment with acyclovir has been proven to reduce mortality to approximately 20% [4]. We present a case that illustrates the importance of the clinical scenario in a patient with unusual presentation of Herpes Simplex Virus 2 Encephalitis.

Case Report:

A 67 years old immunocompetent male patient presented to casualty with complaints of high grade fever with chills since 3 days and irrelevant talk & visual and auditory hallucinations since 2 days before admission and no history of neck stiffness and vomiting. Cardiovascular system, Respiratory system & per abdomen examination was within normal limits. CNS examination revealed Glassgow Coma Scale (GCS) 15/15, no neck rigidity, all reflexes intact, normal tone and power, left plantar extensor and right flexor, pupils normal sized & bilaterally reacting to light. However, on the day of admission, he had an episode of generalized tonic convulsions with rolling of eyes, dribbling of saliva, deviation of face towards right side and right side focal facial seizures. PCR for HSV-2 DNA was positive in CSF. Bacterial as well as fungal cultures of the CSF were negative. CT Scan of brain revealed mild diffuse effacement of cerebral sulci & differentiation seen in left inferomedial temporal region. MRI Brain study revealed possibility of Viral encephalitis and acute non haemorrhagic infract in left cerebellar region. EEG study revealed epileptiform activities. Patient was diagnosed as a case of Viral Encephalitis with left cerebellar infarct and treated with acyclovir and phenytoin. On Day 2 after admission, GCS deteriorated to 7/15 and patient was put on ventilator. On day 10, GCS was 11/15 and patient was extubated. Patient made a good recovery to premorbid condition after antiviral therapy and was subsequently discharged home after 10 days post admission.

Discussion:

Patients with HSE may have prodrome of malaise, fever, headache, and nausea, followed by acute/subacute onset of an encephalopathy whose symptoms include lethargy, confusion, and delirium. However, no pathognomonic clinical findings reliably distinguish HSE from other neurologic disorders with similar presentations [5].

The following are typically the most common symptoms of HSE [6]:

- Fever (90%)
- Headache (81%)
- Psychiatric symptoms (71%)
- Seizures (67%)
- Vomiting (46%)
- Focal weakness (33%)
- Memory loss (24%)

The most frequent findings on physical examination are fever and mental status abnormalities. Meningeal signs may be present, but meningismus is uncommon.

Cerebrospinal fluid (CSF) examination : CSF analysis displays elevated levels of mononuclear cells and proteins. As the disease progresses, both protein and WBC count raise. The protein level averages approximately to 100mg/dl. Elevated protein is reported in 80% of patients which rises to the striking levels as the disease progresses [7]. Early in infection, the neutrophils might be dominant, a lymphocytic pleocytosis of about 10-500 cells/mm^3 occurs in 85% of HSE patients, while less than 8% of patients with biopsy or PCR-proven disease are reported to have a normal CSF cell count. RBCs are frequently detected in the CSF [8]. The presence of red blood cells is not diagnostic for HSE. Also there might be a mild hypoglycorrhachia [9]. Nearly 5-10% of patients have a normal CSF results on the first admission. The later observations should be carry out especially in children in whom the presentations include fever, encephalopathy, altered mental state, and initially normal CSF examinations. However, repeating the CSF analysis even within 24 hours will usually reveal abnormalities.

Electroencephalogram (EEG) : In 80% of the patients there is typical findings in EEG .There is a temporal focus showing periodic lateralized epileptiform discharge as well as the background slowing [10]. These findings are suggestive but not pathogonomic. In the early stages of disease, the abnormal electrical activities usually involve one temporal lobe and then spread to the contralateral temporal lobe as the disease evolves [11]. These changes in EEG are observed within the first 5-7 days of illness [12].

Computed tomography (CT) :

CT findings may be characteristic late in illness and consist of low-density, contrast-enhanced lesions in the temporal lobe, mass effect, edema, and hemorrhage; early in the illness, when diagnosis is critical , CT findings are more often unremarkable. 30-40% of patients might have normal CT scan. Follow up imagings 1-2 weeks after the disease onset demonstrate more widespread abnormalities with involving contralateral lobe, insula and cingulate gyrus.

Magnetic Resonance imaging (MRI) :

MRI is more sensitive and specific than CT for evaluating viral encephalitis. Findings include hyperintensity of the temporal lobe on T2-weighted images with gadolinium enhancement. MRI findings may be abnormal at the initial evaluation of HSVE because of its high sensitivity to the changes in brain water content[13].

Polymerase chain reaction (PCR) :

PCR analysis can confirm the positive results one day after the onset of symptoms. However, the negative result does not essentially exclude the diagnosis . In the patients with a high likelihood of HSE (e.g. typical EEG, MRI or CSF pleocytosis) a negative test only reduces the disease likelihood to about 5%. In patients with the low likelihood of HSE, a negative CSF HSV PCR result reduces disease likelihood to less than 1 % [14]. In another study, it has been shown there wasn't any obvious correlation among HSV-1 load in the CSF and the severity of clinical signs or the findings in cranial imaging and the overall outcome [15]. PCR analysis allows the antiviral therapy to be performed efficiently and helps to detect the existence of a resistant strain of the virus [16] . Quantitative HSV PCR is known to be valuable in determining the prognosis of HSV encephalitis. In one study, the morbidity and mortality rates were higher in patients with a high copy number than in those with lower copy numbers. However, the amount of HSV-1 DNA in the CSF decreases following the Acyclovir therapy.

Treatment:

Acyclovir decreases the mortality rate to 19%, six months after the beginning of therapy. Importantly, 38% of patients, irrespective of age, recover and return to the normal function. However, conversely, most patients are left with significant neurologic impairment[16]. Returning to the normal activity is more likely in young patients with the better consciousness state than older patients who are semicomatose or comatose. New therapeutic protocols, such as anti-inflammatory agents and antiapoptotic agents should be explored.

In the present case, The combination of clinical history and examination, cerebrospinal fluid polymerase chain reaction (PCR) for herpes simplex virus, brain computed tomography, magnetic resonance imaging and lumbar puncture has been used to establish a diagnosis. The patient recovered well with antiviral therapy of acyclovir and antiepileptic medication in the form of intravenous phenytoin.

Conclusion:

Herpes simplex virus (HSV)-2 should be considered in the aetiological investigation of chronic encephalitis in an immunocompetent patient. Our findings indicated that utilising HSV-2 PCR in the cerebrospinal fluid should be an important diagnostic consideration.

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