Case Report

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A Case of New-Onset Refractory Status Epilepticus (Norse) Due to Herpes Simplex Virus-1 Encephalitis

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Abstract

In the medical literature, the term of "New-Onset Refractory Status Epilepticus" (NORSE) is a novel term. Herpes Simplex Virus (HSV)-1 and other viral infections can be cause to NORSE. Seizures are a rare sign of HSV encephalitis, but they can occur as the first symptom. Herein, we present a case of NORSE triggered by HSV-1 encephalitis, which had been diagnosed via cerebrospinal fluid polymerase chain reaction (PCR) method and magnetic resonance imaging findings.

Keywords: Herpes Simplex Virus, encephalitis, new-onset refractory status epilepticus, seizures

Introduction

New-Onset Refractory Status Epilepticus (NORSE) is defined as the onset of refractory status epilepticus (RSE) abroad a clearly identifiable acute or active toxic, structural, or metabolic causes. NORSE should be considered a rather than a specific diagnosis, the clinical manifestation, according to a recent consensus definition document, and can be applied to a patient with new-onset status epilepticus who has no pre-existing ailment[1]. The patients with new-onset viral pathogenes (e.g., Herpes Simplex Virus-1[HSV-1]) and autoimmune disorders are included in NORSE, even if they are detected within the first 72 hours. In about half of all patients, the probable cause of NORSE can be identified[2]. Confusion, fatigue, headache, recent moderate febrile illness, behavioural changes, and memory problems are all prodromal symptoms that occur in 60 % of individuals prior to the beginning of NORSE[2,3].

Variety of infectious / non-infectious causes may lead inflammation of the brain parenchyma (encephalitis) and this can cause neurological dysfunction. Although viruses constitute most of the infectious causes, the HSV virus is the leading reason of acute encephalitis[4,5].

Herein, we present a case of NORSE triggered by HSV-1 encephalitis, which had been diagnosed via cerebrospinal fluid polymerase chain reaction (PCR) method and magnetic resonance imaging findings.

Case Report

A 46-year-old woman who had hitherto been healthy, was transferred from public hospital neurology clinic to our emergency department (ED). She had complaints of sudden onset of headache, speech difficulty and new-onset refractory seizures in last two days and she had developed epilepsy. Despite one day of antiepileptic treatment, her seizures could not be controlled. She had no notable medical history of seizures such as drug use, toxin exposure, trauma, immunosuppression, chronic illness, and fever. She had no animal contact and no history for zoonoses.

In ED, her vital signs on admission were normal. She was not oriented to time, place, and person. She was lethargic and a mild stiffness in the neck was discovered during a neurological test. Babinski sign was positive. No other suspicious abnormalities were found. There was no sign of an injury anywhere on the body. The rest of her physical examination was showed no abnormality.

Hemogram parameters, routine inflammatory markers (e.g., erythrocyte sedimentation rate and C-reactive protein), blood sugar, renal and hepatic functions, electrolytes were all within normal limits in the admission day. The hepatitis serology and human immunodeficiency virus (HIV) test were negative. The computed tomography (CT) brain scan without contrast revealed no hemorrhage or evidence of an acute ischemia. The magnetic resonance imaging (MRI)

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Table 1: Cerebrospinal fluid findings of the patient.

Variable of CSF	
Color	clear
Intracranial pressure (mmH_2O)	300
WBC ($\times 10^6$/L)	550
LY (%)	70
Protein (g/L)	697
Glucose (mg/dl)	62
Synchronous blood glucose (mg/dl)	115
Brucella Wright test	negative
EZN strain	negative
HSV-1 PCR	Positive (93.000.000 copies/ml)

brain scan was performed for further investigation. There were bilaterally inflammatory T2 signals in the hippocampus, temporal lobe, and insula, as shown on an MRI brain scan (Fig. 1). She was consulted a neurologist in the ED and was diagnosed clinically as NORSE and antiepileptic therapy was recommended.

Further, cerebrospinal fluid (CSF) examination revealed 550 leukocytes/mm^3 and elevated protein levels that indicating a serious risk of encephalitis caused by viruses. No microorganisms were seen in Gram and Ziehl Neelsen stainings from CSF (Table 1).

Abbrevations: WBC: White Blood Cell, EZN: Erlich Ziehl Neelsen EZN, HSV-1 PCR: Herpes Simplex Virus -1 Polymerase chain reaction.

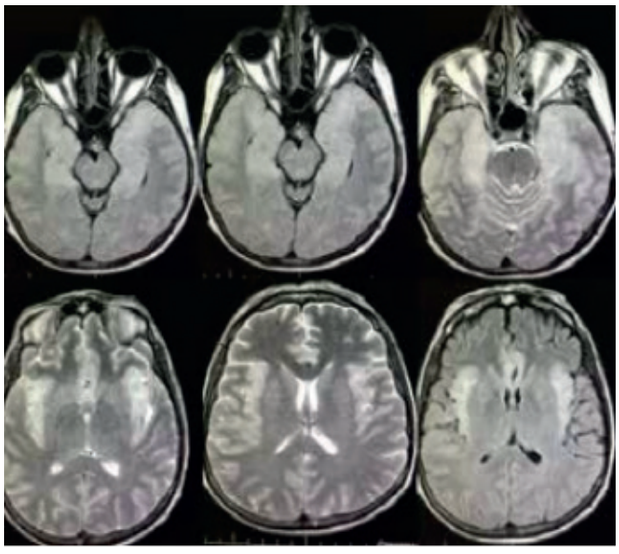

Figure 1. MRI scan of the patient shows bilaterally inflammatory T2 signals in the hippocampus, temporal lobe, and insula.

The patient was hospitalized with a preliminary diagnosis of HSV encephalitis and NORSE. The presence of the HSV-1 pathogen in the CSF with was tested with PCR method, based on the MRI findings and her clinical presentation. HSV-DNA was found to be positive (Table 1). HSV encephalitis (HSE) was confirmed as a result. The patient was subsequently diagnosed with NORSE due to HSV infection based on these findings. The patient received antiviral treatment with 300 mg acyclovir every 8 hours through intravenous (I.V) route, antiepileptic treatment with 300 mg oxcarbazepine, and 500 mg sodium valproate twice a day orally, during his three weeks in the hospital. In addition, the patient was given 10 mg dexamethasone for three days to treat inflammation.

After three weeks of treatment, the patient was in total remission. The patient was placed on continuing orally sodium valproate antiepileptic medication 500 mg twice was given after discharge, and she returned for a follow-up visit four weeks later. No recurrent seizures were occur and she had no neurological sequels.

Discussion

The HSV is a DNA virus, that almost everybody is infected with by the time they reach adulthood. When the virus replicates in the brain, it can induce encephalitis; it's unclear whether this is due to more retrograde axonal transport after reactivation in the trigeminal ganglion, or whether it's due to reactivation of virus that's been latent in the brain. HSE is a disorder that causes both general and localized symptoms of brain dysfunction. It can also be acute or subacute. Brain infection is hypothesized to be caused through direct neuronal transmission of the virus from a peripheral site to the brain via the trigeminal or olfactory nerve, as well as indirect immune-mediated pathways causing neuroinflammation. The true mechanism of HSE is yet unknown. HSE has a bimodal age distribution, with maxima in teenagers and the elderly[4-6]. The presented case was previously healthy 46-year-old woman and with no immunosuppression.

Fever, headache, decreased mental condition, focal neurological abnormalities, and epilepsy are common acute symptoms of HSE6. The patients with new-onset viral infections (including HSV-1) were defined as NORSE, even if they are detected within the first 72 hours[2]. A case of HSE with NORSE is presented in this paper, who was diagnosed within 48 hours. The first signs were a headache, followed by convulsions, but there were no obvious signs of HSV infection, such as a skin lesion. The diagnosis of HSE was confirmed by a HSV PCR test positivity in the CSF examination and typical MRI findings.

In the available literature, the HSE cases with seizures are rarely exist[7,8]. Within 7 days of an acute central nervous system (CNS) infection, 2–67 % of individuals with encephalitis experienced acute symptomatic seizures, according to the International League Against Epilepsy (ILAE). There is a scarcity of trustworthy data from epidemiology studies on the occurrence of seizures in viral encephalitis, the likely underlying processes, and prognosis: this is especially true in resource-constrained settings, where data is restricted to passive monitoring at best[9]. Although there are above 50,000 incidences of CSF infection, encephalitis cases as causes of epilepsy per year in the United States10. Epileptic seizures in approximately 40% of patients with HSV-1 encephalitis, and they may be the first symptom and fever may be mild, and around 11% of HSE patients are afebrile at the time of admission[9]. Associated clinical manifestations include a severe headache, nausea, and vomiting, as well as signs of meningitis (neck stiffness) papilledema[4,6,9]. The presented case had generally seizures for one day as first symptom, that not respond to antiepileptic treatment. Also the case had no fever. She had mild headache and neck stiffness.

HSE is not associated with any pathognomonic clinical symptoms. Initially, focal neurologic abnormalities, CSF pleocytosis, and diagnostic imaging abnormalities may be absent. The preferred imaging study is a brain MRI as diagnostic method and PCR assay of CSF for HSV has largely superseded brain biopsy as the gold standard for diagnosis[10]. The presented case had CSF abnormalities, PCR test positivity and had pathological MRI findings.

Antiviral medication in the IV form of acyclovir is the most common treatment for HSE. Because acyclovir is largely non-toxic and the prognosis of untreated HSE is dire, patients with suspected HSE should be initiated on empirical IV acyclovir therapy as soon as possible until the diagnosis is confirmed[4,10]. Seizures in the HSE cases are treated similarly to patients with other focal epilepsies and frequently necessitating combination treatments[9,11]. The patient was treated with antiviral treatment (acyclovir/IV), antiepileptic treatment (oxcarbazepine and sodium valproate) and anti-inflammatory (dexamethasone) drugs.

All HSE cases should be treated for 14 days of IV acyclovir, followed by a repeat lumbar puncture, according to the United Kingdom guidelines, for immunocompetent individuals. If the CSF PCR tests are still positive despite the treatment, acyclovir should be completed to 21 days, with the LP performed at the conclusion of each cycle to demonstrate viral clearance before ending the medication12. As the presented case did not accept control LP, the antiviral treatment was completed to 21 days.

Conclusion

Finally, in the differential diagnosis of sudden-onset epilepsies, HSE should be examined, and cranial imaging and herpes PCR in CSF should be tested for differential diagnosis.

Informed consent: *Written informed consent was obtained from the patient for publication of this case report and any accompanying images.*

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