Encephalitis refers to an acute, usually diffuse, inflammatory process affecting the brain. An infection by a virus is the most common and important cause of encephalitis, although other organisms may sometimes cause an encephalitis.1 Herpes simplex encephalitis (HSE) is a potentially lethal central nervous system infection that should be recognized as soon as possible. The combination of clinical history with physical examination, brain imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) and lumbar puncture should be used to establish a confirmative diagnosis. Untreated HSE is progressive and fatal within 7 – 14 days, with a mortality rate of 70% if not treated, it leaves residual neurological deficits in most survivors.2 We present a case of HSE with normal CSF analysis but typical MRI findings consistent with HSE and DNA PCR positive for Herpes simplex 1 who responded to acyclovir with complete recovery.

CASE REPORT

A 28 years old female presented with headache, fever, altered sensorium and right side weakness for one week. She was febrile and drowsy with right sided hemiplegia and papilledema. Tuberculous or bacterial meningitis, tuberculoma and abscess were at the top of the diagnosis list followed by Herpes simplex meningo-encephalitis (HSE). MRI showed abnormal signal intensity of left temporal lobe without significant post-contrast enhancement and midline shift. CSF examination was normal, gram stain and Ziehl-Neelsen stain showed no micro-organism, or acid fast bacilli. CSF for MTB PCR was negative. PCR DNA for Herpes simplex 1 on CSF was detected. Acyclovir was started and the patient was discharged after full recovery. A high index of suspicion is required for HSE diagnosis in Pakistan where other infections predominantly affect the brain and HSE may be overlooked as a potential diagnosis.

being lymphocytes, glucose level 4.3 mmol/L (normal range 2.5 – 4.5 mmol/L), Gram stain and Zeihl-Neelsen stain showed no micro-organism and acid fast bacilli respectively. CSF for MTB PCR DNA was also negative. The patient was started on intravenous ceftriaxone (2 gm 12 hourly), intravenous acyclovir (10 mg/kg/8 hourly), intravenous valproic acid, dexamethasone and prophylactic subcutaneous low molecular weight heparin. On the third day of admission, the PCR DNA for Herpes simplex 1 on CSF was detected and injectable ceftriaxone was discontinued. The patient responded to intravenous acyclovir with settling temperature and improving consciousness level and neurological deficit. Her MRI scan was repeated on the 9th day of admission which showed a remarkable improvement in mass effect and reversion of midline brain shift. The patient was discharged on the 14th day of admission having returned to her premorbid mental and physical condition.

**DISCUSSION**

Herpes simplex encephalitis (HSE) is recognized worldwide as the most frequent infectious encephalitis, and the only one with a validated specific treatment. The incidence is about one case per million per year and about 2000 cases occur annually in the USA.

However, the occurrence of Herpes simplex encephalitis with a normal CSF examination is a rarity with only a few cases being reported worldwide. In Germany, Herpes encephalitis with a normal CSF was documented to occur in five immunosuppressed patients with malignoma after whole brain irradiation. It was also documented from Turkey in two immunocompetent patients, one of whom died due to nosocomial pneumonia and the other had mild neurological deficit upon recovery from HSE. In 2009, the incidence was reported to be 5 – 10% initially in patients who represented with encephalitis.

A typical "viral profile" of CSF is the presence of red blood cells (RBCs)/µL (average = 100 WBCs/µL). As a result of the hemorrhagic nature of the underlying pathologic process, the RBC count may be elevated (10-500/µL), protein levels are elevated to the range of 60 – 700 mg/dL (average 100 mg/dL) and glucose values may be normal or mildly decreased (30 – 40 mg/dL). The gold standard for the diagnosis of HSE is DNA polymerase chain reaction (PCR) of the CSF having a sensitivity of 94 – 98% and a specificity of 98-100%.

The pathogenesis of HSE in humans is still poorly understood. Neurons are quickly overwhelmed by a lytic and hemorrhagic process distributed in an asymmetric fashion throughout the medial temporal and inferior frontal lobes. Temporal lobe involvement is documented in 60% of patients. The ability of HSV-1 to induce apoptosis in neurons, might explain the pathogenesis of encephalitis in immunocompetent adults. An atypical anergic course of Herpes simplex virus encephalitis is the proposed cause of HSE with a normal CSF examination.

Clinical presentation may vary, with focal neurological deficit occurring in only 33% as in this patient whose initial presentation was right sided hemiplegia. The typical presentation is a prodrome of malaise, fever (90%), headache (81%), and nausea, followed by acute or subacute onset of an encephalopathy manifested as lethargy, confusion, and delirium. Other manifestations include psychiatric symptoms (71%), seizures (67%), vomiting (46%) and memory loss (24%).

This patient was started on acyclovir along with steroids due to the surrounding oedema and mass effect causing midline shift. The role of steroids is still controversial and remains uncertain when used to reduce cerebral oedema. As the cellular damage in HSE is due to immune mediated inflammatory processes, steroids may be beneficial due to its anti-inflammatory effects. One non-randomized, retrospective study on human subjects compared the outcomes of patients with HSE who received steroids plus acyclovir with the outcomes of those who received acyclovir alone and the steroid group had improved outcomes at 3 months after recovery from HSE.

In conclusion, this case of HSE with normal CSF findings but typical MRI findings consistent with HSE was confirmed with PCR who responded to acyclovir and steroid therapy. A high index of suspicion is required in a country like Pakistan where other infections predominantly affect the brain and HSE may be overlooked as a potential diagnosis.

**REFERENCES**


