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Case Report

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Early diagnosis of herpes encephalitis saves lives: A case report

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ABSTRACT

Herpes simplex virus (HSV) is the most important pathogen causing endemic encephalitis. HSV-1 is responsible for 90% of the cases which is the only treatable viral encephalitis. Clinically it is characterized by decreased level of consciousness, changes in personality, convulsions, and focal neurological deficits. Diagnosis of HSV encephalitis is made by detection of HSV DNA in the cerebrospinal fluid via polymerase chain reaction (PCR) method. The mortality rate in untreated HSV encephalitis is 50-70%. In this paper a patient diagnosed as Herpes simplex encephalitis according to positive PCR, clinic findings, radiological imaging and electroencephalogram (EEG). The patient was successfully treated for 21 days with acyclovir without any complication. This case report emphasizes the value of early diagnosis and treatment.

1. Introduction

Herpes simplex encephalitis (HSE) should be considered in case of headache, high fever, and fluctuations in consciousness and personality changes. This disease has high morbidity and mortality rate so early diagnosis and treatment are very important (Cleator and Klapper, 2004; Corey, 2005; Riancho et al., 2013). Herpes encephalitis was diagnosed based on cerebrospinal fluid (CSF) examination (Tischendorf et al., 2003; Corey, 2005). CSF is abnormal in more than 95% of HSE cases. Moderate pleocytosis is found, consisting of both-mononuclear white blood cells and red blood cells (Ferrari et al., 2009). The current golden standard in the diagnosis of Herpes simplex virus (HSV) encephalitis is the detection of HSV DNA in the CSF via polymerase chain reaction (PCR) method. False negative results are most likely in the first 48 hours (Cleator and Klapper, 2004; Corey, 2005; Riancho et al., 2013). The most sensitive imaging technique in early stages is magnetic resonance imaging (MRI) (Corey, 2005). Acyclovir is the most effective agent in the treatment (Cleator and Klapper, 2004; Riancho et al., 2013). Medical history, clinical findings, radiological imaging, electroencephalogram (EEG) pattern, and PCR positivity are important cornerstones of the diagnosis. Early recognition is important because the efficacy of the antiviral treatment decreases by time in reducing morbidity and mortality. In this case report, we present a patient with HSE.

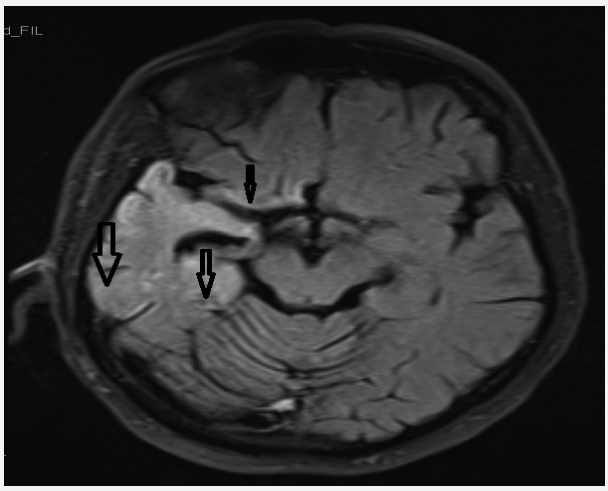

Fig. 1. FLAIR image shows high-signal changes mainly in the right temporal lobe

2. Case presentation

A 40-year-old male patient without prior disase history admitted to Departments of Clinical Microbiology and Infectious Diseases, Ataturk University Hospital, with a week-long complaints of chills, trembling, high fever, and nausea. His highest body temperature was measured as 40ºC. The patient had used antibiotics for three days prior to admission. Inappropriate behavior and personality changes were observed in addition to the patient's existing complaints. Following meaningless conversations, short lasting convulsions in his left hand and left leg, chin lock, and impairment of consciousness were observed twice. Physical examination showed the presence of somnolence and lack of cooperation and orientation. His body temperature, pulse, and arterial blood pressure were 37ºC, 96/min, and 130/70 mmHg, respectively. The meningeal irritation symptoms were negative in the neurological examination except for neck stiffness; cranial system examination was normal; and there was no motor or sensory loss. Other system examinations were normal.

The laboratory results were 13500/mm^3 for white blood cell count, 161000/mm^3 for platelet count, 14 g/dL for hemoglobin 59 mg/L C-reactive protein levels, 10/h for erythrocyte sedimentation rate, 3264 U/L for creatine kinase, 59 U/L for aspartate transaminase, 398 U/L for lactate dehydrogenase, 987 U/L for myoglobin, and 97 mg/dL for glucose levels. Lumbar puncture was performed; lymphocytes of 30/mm^3 were observed in microscopic examination; protein, glucose, and chlorine values were 96 mg/dL, 53 mg/dL, and 115 mmol/L, respectively; and HSV-DNA was detected via real time PCR (tagman, Iontek) in the CSF. CSF culture remained negative for other microorganisms that can grow in culture.

The MRI observations included lesion areas consistent with herpes encephalitis: Fluid attenuated inversion recovery (FLAIR) in right temporal lobe, insular cortex, inferior to the frontal lobe, and posterior to the hippocampus; hyperintensity in T2s (Fig. 1, 3), especially showing involvement in the cortical-subcortical white matter; and asymmetric hyperintensity at contrast enhanced T1 (Fig. 2). Slow waves in theta frequency were captured in EEG of both hemispheres. Herpes encephalitis diagnosis established and acyclovir therapy was given at a dose of 3x10 mg/kg for 21 days. No motor or mental sequellae remained. The patient was discharged in full recovery.

3. Discussion

We report the case of 40-year-old male presenting fever, personality changes, confusion, disorientation and headache. HSV type 1 and HSV type 2 are members of the family herpes viridae. During primary and initial infection herpes virus set up a latent infection of sensory nerves at dorsal root ganglion (Cleator and Klapper, 2004). Agent may come to central nervous system via bloodstream or neural axons. Encephalitis is usually depends on reactivation of latent virus (Corey, 2005). HSV is the most important cause of endemic encephalitis (Corey, 2005; Riancho et al., 2013). The annual incidence is a million to one (Tischendorf et al., 2003). Most cases are caused by HSV 1. Herpes encephalitis occurs in all age groups and the same frequency in both men and women (Cleator and Klapper, 2004; Corey, 2005). The age distribution appears to be biphasic with peaks at 5-30 and more than 50 years of age (Corey, 2005). The patient in this case was 40 years of age. HSE is a serious disease, with high levels of morbidity and mortality (Soares-Ishigaki et al., 2012). Brain edema is believed to represent the major cause of mortality in HSE (Cleator and Klapper, 2004).

Fever, headache, focal neurological findings together with various levels of unconsciousness or seizure disorders are the characteristic findings of herpes encephalitis. Fever is present in about 90% and headache in about 80% of HSE patients (Corey, 2005; Beckham et al., 2012; Riancho et al., 2013). Other common features include disorientation (70%), personality change (70%-85%), focal or generalized seizures (40%-67%), memory disturbance (25%-45%), motor deficit (30%-40%) and aphasia (33%) (Beckham et al., 2012). Sudden onset of language abnormalities and changes in personality are important signs which are characteristic for HSE (Soto-Hernandez, 2000; Corey, 2005; Beckham et al., 2012; Riancho et al., 2013). In some patients there may be residual neurological deficit. Impairment or complete loss of short-term memory was most commonly observed sequel (Cleator and Klapper, 2004). No motor or mental sequellae remained. The patient was discharged in full recovery.

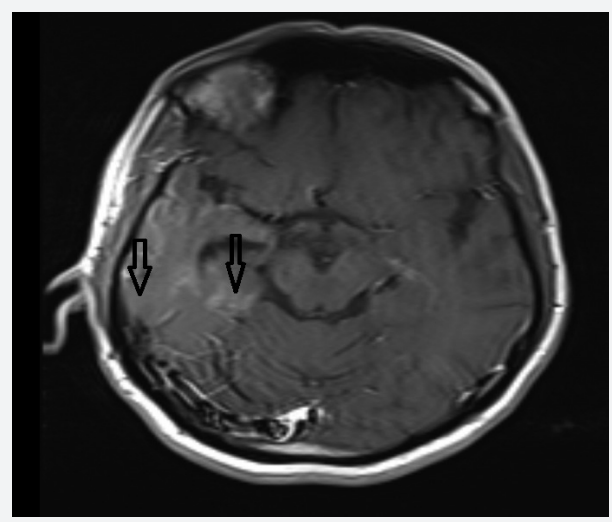

Fig. 2. Contrast enhanced T1 MRI is seen hyperintensity frontotemporal region and posterior hippocampus

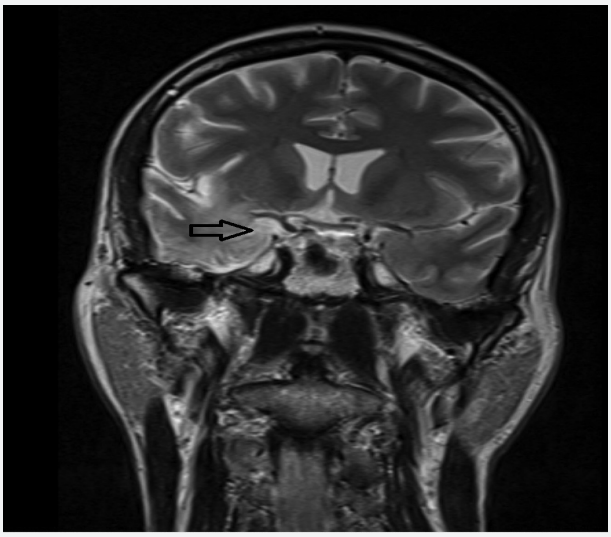

Fig. 3. T2 weighted MRI showing hyperintensity in right temporal lobe

Examination of CSF is the single most important diagnostic test in suspected cases with HSE. CSF has lymphocytic pleocytosis between 10 and 1000 white blood cells per µl. Although rare cases with an initially normocellular CSF have been reported (Beckham et al., 2012). The presence of a normal CSF analysis in HSE is unusual, especially in non-immunocompromised patients (Tischendorf et al., 2003; Beckham et al., 2012; Riancho et al., 2013). In our case, the patient was not immunocompromised and had no evidence of underlying malignancy. A history of hypertension and diabetes mellitus were not present. CSF is usually hemorrhagic. The hemorrhagic encephalitis can be seen in HSV type 1, varicella zoster, rubella, Epstein-Barr virus or amoeba infection in immunocompromised patients (Kim et al., 2001). CSF protein is often moderately elevated and glucose is normal in more than 90% of patients with HSE (Cingue et al., 1996; Beckham et al., 2012). Our patient revealed mild increased CSF protein.

Anti-HSV IgG antibody becomes detectable in CSF generally after two weeks. The detection of HSV DNA in CSF was a more sensitive indicator of encephalitis (Zeytinoğlu et al., 2000; Cleator and Klapper, 2004; Corey, 2005). Hence, in our case a lumbar puncture was made on the first day of hospitalization for HSV DNA detection in CSF. During admission to our clinic HSV-DNA in patients CSF was positive.

An EEG would have been useful in the diagnosis and management HSE in these patients. EEG is valuable but not specific. EEG will reveal nonspecific slow wave activity during the first five-seven days of illness. After, more characteristic paroxysmal sharp waves or triphasic complexes with a temporal predominance (80%) can be found (Cleator and Klapper, 2004). In our case, slow wave activity in EEG pattern was identified.

The most sensitive imaging technique in early stages is MRI. The MRI shows frontobasal and temporal lesions on T1 weighted images and hiperintense lesions on proton density and T2 weighted images at an earlier stage (Cingue et al., 1996; Soto-Hernandez, 2000; Cleator and Klapper, 2004; Corey, 2005). The lesions are characteristically located in the temporal and frontal lobes. But cingulate gyri and occipital lobes may also be involved (Cleator and Klapper, 2004; Corey, 2005). MRI angiography in our patient did not reveal any segmental narrowing or bleeding. In our case, frontal, temporal lobe lesions were present in addition to a hippocampus.

PCR is the gold standard for diagnosis (Soto-Hernandez, 2000; Zeytinoğlu et al., 2000; Corey, 2005). The amount of HSV DNA found in CSF appears to be correlated with prognosis. The higher viral load detected during the acute stages of infection, the poorer the outcome. PCR was found to have a sensitivity of 95-100% and high specificity of 98-100%. PCR is not infallible and negative results may be obtained. For example samples taken in early stages of disease or where acyclovir therapy has been instituted prior to lumbar puncture (Tischendorf et al., 2003; Beckham et al., 2012; Riancho et al., 2013).

Even if there have been a lot of improvements in antiviral theraphy HSE has still high mortality and morbidity rates (Corey, 2005; Beckham et al., 2012; Riancho et al., 2013). Acyclovir is the most effective agent in treatment. Immediate administration of acyclovir therapy can improve the survival rates. The administration of acyclovir at a dose of 10 mg/kg intravenously three time per day for 14-21days (Tischendorf et al., 2003; Ferrari et al., 2009; Beckham et al., 2012). Newer antivirals, such as penciclovir, valaciclovir and famciclovir are now in use (Cleator and Klapper, 2004). Foscarnet is alternative therapy for acyclovir resistant patients (Beckham et al., 2012). Acyclovir treatment was given to our patient. In our case patient recovered without any complication.

In our patient, clinical presentation, CSF findings, MRI and the presence of HSV DNA in the CSF established the diagnosis of HSV encephalitis. We believe that early diagnosis and treatment of cases with HSE may decrease morbidity and mortality significantly.

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