Three consecutive cases of Herpes simplex virus encephalitis despite normal cell count in the cerebrospinal fluid

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Introduction

Herpes simplex encephalitis (HSE) is a neurological emergency. Diagnosis is based on medical history and neurological examination, cerebral spinal fluid (CSF) analysis, CSF polymerase chain reaction amplification (PCR), and neuroimaging, preferably MRI.

In HSE patients, CSF pleocytosis (increase of cells number 5-500, manly lymphocytes) is the typical CSF finding. Fewer than 5 leukocytes have been reported only in 3- 8 % of HSE cases.

Method

The aim of this paper is to report three consecutive patients with a definite diagnosis of HSE (by CSF PCR positive for HSV1 DNA) but with normocellular CSF.

All the three patients were admitted through the emergency department, within few days each other. Starting symptoms were confusion and fever, two developed speech disturbances in the following days. Two of them had focal epileptic seizures during hospitalization. Median duration from the onset of first symptom to hospital admission was 3 days.

Results

Serum analysis showed no leucocytosis, but hyponatremia in two cases (121 and 130 mmol/l).

CSF cell count was normal in 100% of patients (lymphocytes count:1-3), one patient had elevated protein levels (81 mg/dl). In the suspect of viral encephalitis, a CSF PCR for herpes simplex virus were ordered, the results of which were received 24-48 hours later and were positive for HSV-1 DNA. Therapy with acyclovir was started immediately after lumbar puncture.

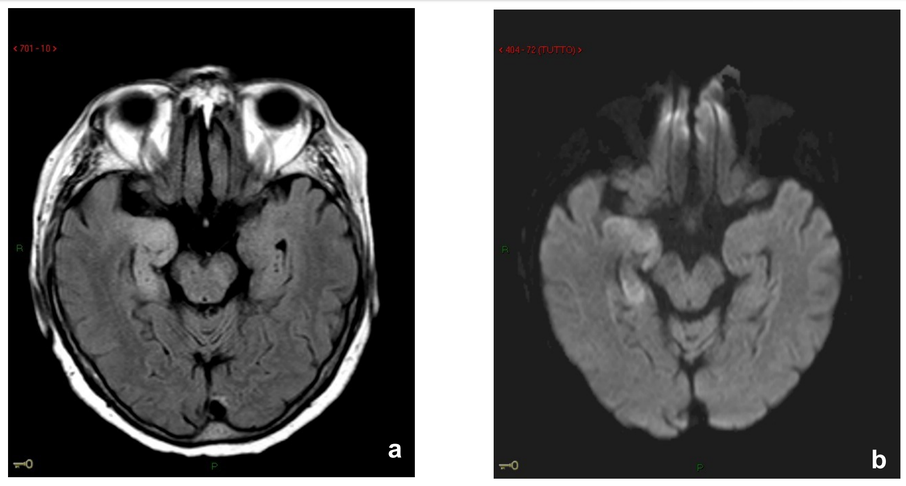
EEG performed during hospitalization showed slow waves in the temporal lobe in one case and periodic lateralized epileptiform discharges (PLEDs) originating from the temporal lobes in two cases.

MRI showed in all the patients attenuation and mild mass effect in temporal lobes and insula. One patient (in ASA theraphy because of previous ischemic heart disease) worsened at day 9 and CT scan showed haemorrhage in the encephalitic area that required urgent surgical intervention.

Conclusion

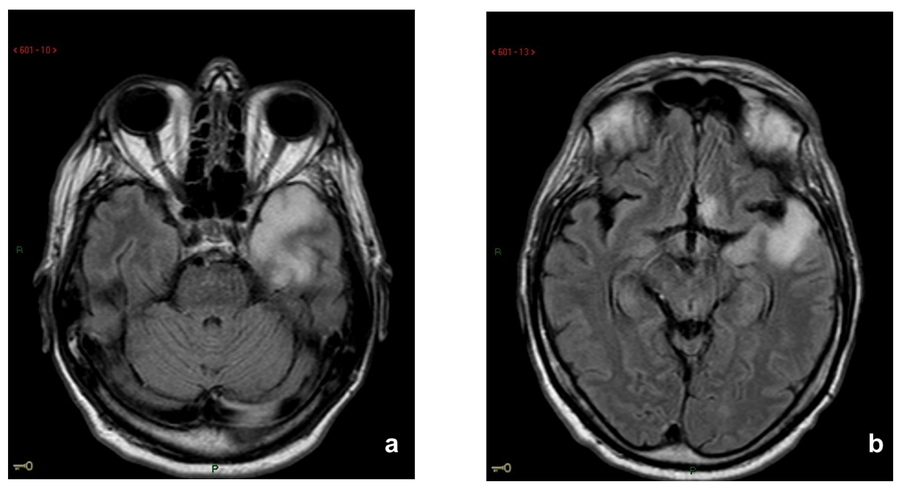
Correct immediate diagnosis and introduction of antiviral therapy is paramount in HSE as it changes the prognosis of the patients. The decision to start therapy is mostly based on clinical presentation and the detection of CSF pleocytosis. Here we describe three HSE cases of immunocompetent patients with typical presentation, but with atypical cellular response in the CSF. Albeit absence of CSF pleocytosis in HSE has been described as a rare finding in the past, our cases showed that it is more common than what was generally known. Conclusion: Clinicians should not exclude central nervous viral infection merely on the base of the absence of CSF pleocytosis. Examination of HSV DNA by PCR in the CSF is mandatory in the suspect of encephalitis, even without CSF pleocytosis. Moreover, in presence of high clinical suspect of HSE, empiric acyclovir treatment is recommended.

Case 1



Patient 1 (a) Axial Fluid-attenuation inversion recovery sequence showing mild hyperintensity in right temporal lobe. (b).axial diffusion-weighted image showing restriction in the same area.

Case 2



Patient 2: (a) Axial Fluid-attenuation inversion recovery sequence showing an area of high signal intensity in the left anterior medial temporal lobe and (b) left basal frontal area.

Case 3

Patient 3: (a) Axial Fluid-attenuation inversion recovery sequence showing an area of hyperintensity in the left temporal and hippocampus area and (b) in the left insular area, (c) Axial computed tomography showing acute cerebral hemorrhage in the left temporal lobe and intraventricular blood

	Patient 1	Patient 2	Patient 3	Normal values
BLOOD				
CRP	<0.1	0.3	< 0.1	< 0.4 mg/dl
Leukocyte	9.9	9.7	8.5	4-10 x 10^3 µl
Neutrophile	7.6	7.9	6.1	2-7 x 10^3 µl
Lymphocyte	1.6	1.2	1.6	1.5- 4 x 10^3 µl
Na	121	143	135	135-145 mmol/l
CSF				
Leukocyte	1	3	1	<4/ µl
Erythrocyte(/mm3)	3	1	0	0/ µl
Glucose	74	94	64	50-80 mg/dl
Protein	35	81	39	20-50 mg/dl
HSV 1 PCR	+	+	+	neg

Table 1: CRP, C-reactive protein; CSF, cerebrospinal fluid; PCR polymerase chain reaction

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