HSV encephalitis with normal initial CT scan - a case report with a review of the literature

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ABSTRACT

Introduction. HSV-1 is the most common cause of viral encephalitis with a high mortality rate if left untreated and causes frequent diagnostic difficulties. It commonly involves the
temporal, inferior frontal lobes and the limbic system. HSV can be differentiated by a combination of symptoms, laboratory tests and neuroimaging findings.

**Case report.** A 29-year old female with HSV encephalitis, who, despite prevailing symptoms of altered mental status, had no abnormalities on initial CT head scan. Three MRI follow-up examinations revealed imaging findings with characteristic evolution. Despite CSF results being negative for HSV antibodies, the combination of symptoms, CSF analysis, and characteristic MRI findings were highly suggestive to diagnosing HSV encephalitis and to implement proper treatment.

**Discussion.** In case of radiological changes in temporal lobe, the involvement of the Herpes simplex encephalitis (HSE) should always be considered. Although the laboratory tests happen to be inconclusive or even falsely negative, neuroimaging often helps to determine the diagnosis. Despite HSE being a severe neurological disorder, initial CT scans can be normal. MRI has become superior, especially at the early phase of the disease and is capable of determining the extensiveness of lesions.

**Key words:** herpes simplex virus; magnetic resonance imaging; encephalitis; cerebrospinal fluid

**Introduction**

HSV-1 remains the most common cause of sporadic encephalitis in adults and older children. The estimated morbidity is about 70%. The onset is nonspecific, usually flu-like and delays antiviral treatment. Clinical manifestations include seizures, vomiting, focal neurological deficit and memory loss. There is a 70% mortality rate in untreated patients and more than half of the untreated survivors have severe neurological deficits. The diagnosis is based on clinical manifestation, neuroimaging, and the presence of anti-HSV antibodies and/or HSV-DNA in the CSF. Due to misleading initial symptoms and late appearance of anti-HSV antibodies in CSF the MRI became critically important in early diagnosis. [1-3]

Lesions typically occur as bilateral, but asymmetrical T2WI and FLAIR hyperintensities, commonly showing restricted diffusion on DWI. Additional MRI findings e.g. gyral enhancement and hemorrhage often appear in later stages of the disease [4-5].

**Case Report**

A 29-year old female was admitted to the Neurology Department with history of impaired consciousness, dysfasia, severe headache, malaise, vomiting, loss of appetite and fever. Due to neurological manifestations, the medical history was taken from the family and co-workers, who reported sudden onset of symptoms, a few days before admission to the hospital.

On admission, the patient’s general condition was determined as severe, she remained conscious but with disturbed logical communication and allocrhetic orientation. Furthermore, the physical examination revealed impaired gait, mild fever (38.6 °C), nuchal rigidity but neither evident paresis nor sensory deficits.
The additional laboratory blood tests showed normal leukocyte count (7,700 cells/mm3), elevated D-dimer level - 4019,66 ng/ml FEU [<550] and low TSH level - 0,260 ulU/mL [0,4-4,0].

Lumbar puncture was performed, obtaining light watery cerebrospinal fluid with elevated levels of protein (93,5 mg/dl), pleocytosis 12 cells/µL, Nonne-Apelt test slightly positive.

In the cerebrospinal fluid, antibodies for Herpes simplex virus were not found neither in IgG nor in IgM class, while in blood serum, antibodies for HSV were detected both in IgM and IgG class.

Furthermore the determination of antibodies against Borrelia burgdorferi in CSF and serum were performed with negative results. Also HIV screening test proved to be non-reactive.

CT head scan without contrast administration showed no abnormalities.

MR imaging was performed on a GE 1.5 T Signa scanner. T2WI and FLAIR images revealed poorly demarcated, mainly cortical, right hemisphere hyperintensities, non-enhancing after contrast administration in T1WI and showing only slight oedema. The affected areas involved the whole temporal lobe, including the hippocampus and showed high signal in DWI sequence. The restricted diffusion was also noticeable in left hippocampus, without any hyperintensity on T2WI and FLAIR in this localization. The ventricular system was not expanded.

In controlled MRI examinations, performed after 5 and 10 days, T2WI and FLAIR sequences showed an evolution of the inflammatory process at right hemisphere, which involved additional structures such as insula and mediobasal area of the right frontal lobe. Furthermore, similar new T2WI/FLAIR hyperintensities appeared symmetrically in left hemisphere additionally including uncinate gyrus. The affected areas demonstrated contrast enhancement.

The wakefulness EEG examination revealed pathological changes, spatially undifferentiated while quiescent. There was mixed polymorphic delta-theta rhythm, at a frequency of 1.2-7.1 Hz and amplitude of 140 µV. Moreover, the EEG demonstrated predominance of delta waves over the right hemisphere and few slow sharp waves over the frontal lobes. During Acyclovir treatment, control wakefulness EEG was performed and showed partial resolution of those changes.

During hospitalization, one tonic-clonic seizure secondarily generalized occurred. The patient received empirical antiviral treatment (acyclovir), antiedematous (mannitol, furosemid), chemotherapheutic (metronidazol) and anti-epileptic drugs.

The patient also underwent a psychological examination which mainly showed slowing of psychomotor functioning and neuropsychological deficits congruent with structural brain damage. Furthermore, the allopsychic disorientation, anterograde and partial retrograde amnesia were diagnosed. The emotional state included fluctuations from apathy and passivity to anger outbursts and aggressive behavior. A final psychological assessment revealed amnestic syndrome and organic personality disorder.

The patient’s condition partially improved. After being discharged she was hospitalized two more times at the Neurological Rehabilitation Ward and Neurology Ward due to memory impairment and allopsychic disorientation. The MRI T2WI and FLAIR images demonstrated post-inflammatory gliosis involving the temporal and the frontal lobe at the right hemisphere. The psychological assessment confirmed persistent short-term memory loss and allopsychic
disorientation, which significantly interfered daily functioning. In addition, the disturbance of speech fluency, lack of criticism, anosognosia also endured.

**Discussion**

Inconclusive laboratory tests’ results cause physicians to turn towards other diagnostic methods. Neuroimaging has a vital role in the investigations of such patients. CT scanning may not reveal any abnormalities. [3, 6]

MRI without contrast administration is superior to CT in detecting the early cerebral lesions in the course of viral encephalitis, and should be performed by choice in all patients with suspected encephalitis as soon as possible. Presented patient had no abnormalities in CT scan. [3]

Although Garnerod J et al. stated that MRI specificity for HSV encephalitis, between 3–10 days after symptom onset, is 100%, a negative MRI does not exclude HSV encephalitis diagnosis [5-6].

Memory loss can be associated with damage caused to hippocampus and medial temporal lobe. Indeed, the described patient demonstrated bilateral hippocampus involvement. Apart from that, there were also extratemporal lesions, however, they are less common [4, 7].

Apart from T2WI/FLAIR hyperintensities our patient also presented restricted diffusion. Although those high signal areas (T2WI and FLAIR) coincided with the hyperintensities on DWI, another restricted diffusion hyperintensity in the left hippocampus was reaveled. Literature shows several cases of patients presenting symptoms of HSV encephalitis with nonspecific laboratory findings, negative PCR, initial normal CT and MRI, where DWI abnormalities became a key to a proper diagnosis. Renard D. et al. compared lesion borders in FLAIR and DWI images with the result of DWI showing more extensive abnormalities in 14% of the areas. Furthermore, DWI appeared to be slightly more sensitive to FLAIR in acute-subacute HSE, except for the thalamus, where FLAIR seemed to be superior. DWI is propably the most sensitive sequence for detecting HSE in the acute phase for the early diagnosis of herpes encephalitis [5, 8-9].

MRI is the gold standard in all cases with suspected encephalitis, especially if the initial CT scan remains normal. It should be performed as soon as possible after hospital admission. DWI becomes superior to other MRI sequences in the early stages of the disease and in lesions extensiveness imaging.

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