

A CASE OF HERPES ENCEPHALITIS MISDIAGNOSED AS ISCHEMIC INFARCT

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[Un caso di encefalite erpetica erroneamente diagnosticata come ictus]

ABSTRACT

Herpes simplex encephalitis is a medical emergency and a potentially lethal infection that should be recognized as soon as possible, because specific therapy has a dramatic influence upon survival and reduces the extent of permanent brain injury. In this case report we discuss about a patient who had a clinical presentation and an history not suggestive, initially confused with a more common acute illness due to an ischemic stroke. Due to this misdiagnosis lumbar puncture was not performed, and diagnosis was made by neuro-imaging findings.

Key words: Encephalitis, Herpes Virus Simplex, Ischemic Stroke.

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Introduction

Human herpes viruses (HSV) consist in a family of several enveloped DNA-containing viruses. Each displays neuro-invasiveness in immunological competent or immunological compromised hosts, or possesses the ability to induce latent or persistent infections of humans.

HSV-1 encephalitis is the most common non epidemic encephalitis in the western countries: exhibits no seasonal, gender, or racial predilections and has an incidence of approximately 1 in 250,000 to 500,000 persons per year⁽¹⁾. HSV-1 enters in the central nervous system (CNS) via sensory neural pathways and latently infects trigeminal ganglia. Reactivation of HSV-1 and retrograde transmission of the virus to the CNS are assumed to cause most cases of human encephalitis⁽²⁾.

Clinical picture is considered typical with headache, fever, and confusion developing over hours to days; hemi-paresis, and focal or generalized seizures may also be included⁽³⁾.

This clinical features of “encephalopathy” are not ever suggestive for an univocal diagnosis, and other few conditions may mimic the same clinical picture, as cerebral ischemic lesions and brain gliomas. In some cases also neuro-imaging may be ambiguous, leading to diagnostic difficulties if cerebrospinal fluid examination is not available.

We report a case of herpes virus encephalitis (HVE) presenting clinical finding initially suggestive for a cardio-embolic stroke. This review further confirms that diagnosis of encephalitis is based on laboratory studies and a combination of clinical, radiological, and possibly pathological data, because no pathognomonic clinical findings reliably distinguish HVE from other neurological disorders with similar presentation.

Case report

A 66-years-old man was evaluated in a consultant setting for altered mental status. Five days prior the patient complained for headache and fever (39.5°

C), which responded rapidly to antibiotic therapy. Admission in emergency ward of our hospital followed when he suddenly developed depersonalization state, with memory loss and decreased psychomotor activity.

On neurological examination the patient appeared mild disoriented to person and place, but well communicating without aphasic speech. Deep tendon reflexes were brisk and symmetric, without Babinski or meningeal signs. Muscle strength in superior and lower limbs was normal; nystagmus or other signs of cranial nerves involvement absents.

In the clinical history patient reported Crohn's disease treated with immunosuppressive drugs and corticosteroids; ischemic heart disease submitted to coronary artery bypass surgery; diabetes mellitus treated with insulin and hypertension.

Chest X-ray was unremarkable; EKG with normal heart rhythm and complete right bundle branch block. Laboratory tests did not reveal leukocytosis (white cells count was 5.3 thousand/ μ ml) or electrolyte imbalance; CRP was 2,0 mg/dl.

Trans-thoracic echocardiography revealed an atrial septal aneurysm without mitral valve prolapse or right-left shunt. An urgent CT scan of the head showed a soft area of hypo-density in the right temporal lobe, assessed as ischemic.

Based on the patient's atrial aneurysm, the cerebral lesion was effectively hypothesized as ischemic in nature and due to cardiac systemic embolism. Lumbar puncture was not performed, but patient was placed on antibiotics and acyclovir because it was not clear whether fever was responsible for his acute presentation.

Follow-up CT scan after two days revealed a complete area of hypo-density (5.3 centimetres in the greatest diameter) involving anterior and medial region of temporal lobe, extended to orbital surface of frontal lobe in the same side with slight swelling effect (fig. 1).

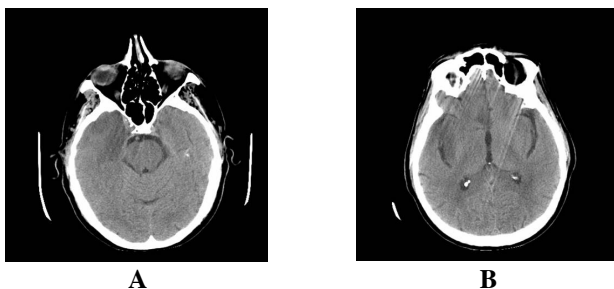


Fig 1: CT scan of the head showing hypo-density in the right temporal lobe (A) involving Hippocampus and medial aspect of the lobe. B. hypo-density in medial region of the right frontal lobe, with consensual involving of the insular lobe.

Acyclovir administration was not discontinued, and general clinical conditions began to improve slowly but progressively. Patient remained afebrile for the rest of his stay in hospital, and psychic alterations subside with residual amnesia for recent facts.

EEG recorded in this sub-acute phase did not shows lateralized epileptiform discharges, or the typical temporal focal slowing. We noted only subtle abnormalities lateralized to right hemisphere correlate with radiological extent of lesions.

MRI of the brain was obtained one week after presentation, which confirmed the diagnosis of herpes virus encephalitis (fig. 2). Imaging in RM T1-weighted, T2-weighted and FLAIR sequences revealed the typical involvement in the limbic regions after herpes virus infection: temporal lobe, uncus and adjacent para hippocampal gyrus, orbital region of the frontal lobe (gyrus rectus), insula and cingulated lobe with basal ganglia sparing. Gadolinium-enhanced T1-weighted images revealed patchy parenchymal and gyral enhancement.

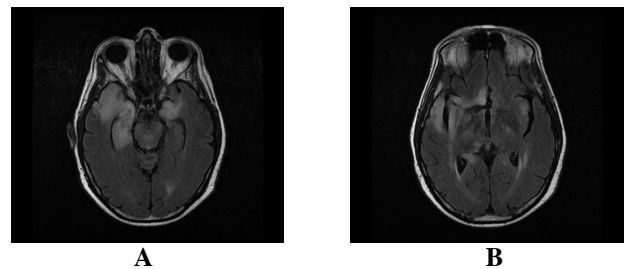


Fig 2: T2-weighted MRI reveals hyperintensity corresponding to edematous changes in the right temporal lobe (A). In the same side abnormal intensity of signal is present in the inferior frontal lobe and insular lobe (B). Partial involvement of the left temporal lobe can be observed (A).

Discussion

HSV tends to attack a part of the brain known as "limbic system", a set of interconnected brain structures responsible for the integration of emotion, memory, and complex behavior. This disease is important to recognize because there is an effective drug treatment: acyclovir⁽⁴⁾. Acyclovir is well tolerated and very effective in inhibiting viral replication, and delay even during first hours from onset of symptoms greatly increases axonal spread to newly infected regions in the brain. Prompt treatment reduces substantially both mortality and morbidity⁽⁵⁾. Today it has become an established practice that treatment for HVE is commenced on suspi-

cion, before a specific aetiological diagnosis was possible⁽⁶⁾. Therefore we have started acyclovir immediately, and treatment was constantly maintained until diagnosis has become clear.

But our case present further instructive features that it is worth to discuss. Diagnosis of HVE can be clouded by confounding factors, especially when CSF examination is not obtained. Although the patient had fever on presentation, he was afebrile throughout his hospital course, which is uncommon in a infective disease. In the same way white cells count, ESR, and CRP, although no specific, were not elevated.

Further the clinical picture was lacking of other suggestive features, as focal neurological symptoms and seizures. Likewise EEG, although generally regarded as a non-specific investigation, is a sensitive indicator of cerebral involvement in case of encephalitis⁽⁷⁾. But our EEG does not show specific features that may give clues to the diagnosis.

Crucial aspects in the history and clinical course of our case are the behavioural changes (altered level of consciousness, disorientation) and the cognitive dysfunctions (memory disturbances), started after remission of a febrile disease accompanied by headache. Diagnosis was orientated to an acute vascular cerebral event, because of predisposing conditions linked to a potential stroke: age, hypertension, diabetes mellitus, cardio-pathy.

It is noteworthy that the patient had a CT scan of the brain without contrast with hypo-density within a temporal lobe mildly swollen. Temporal lobe localization is more suggestive for an encephalitis than a vascular brain lesion. The diagnosis of acute hemorrhagic leuko-encephalitis, which is localized in the same regions involved in HVE, can be excluded for the absence of typical hemorrhagic lesions, considered rare and only "focal" in HVE⁽⁸⁾.

Although the frequency is low, primary brain tumours including glioblastoma can masquerade as an acute viral encephalitis⁽⁹⁾. Gliomas demonstrate MRI findings of hypo-intensity on T1 images and hyper-intensity on T2 images, can be focal, multifocal or diffuse, and though no usually also headache, fever, and seizures may be seen in patients with high grade gliomas. A recent report⁽¹⁰⁾ describe the case of a patient presenting sudden onset of cognitive impairment and headache for 2 days, and brain MRI showing left temporal lobe hyper-intensity, and cerebrospinal fluid cytology revealing a mild pleocytosis. Initially improved after medical treatment with a presumptive diagnosis of HVE,

after 8 months the patient complained of recurrent seizures. A follow-up brain MRI revealed marked increase in size and surrounding perilesional oedema in the left temporal lesion on T2-weighted images and a new contrast-enhancing lesion on T1-weighted images. Stereo-tactic brain biopsy revealed a glioblastoma. In the opinion of authors of this report, the atypical encephalitic presentation of glioblastoma should be considered if definitive evidence for the diagnosis of HVE cannot be obtained.

We have not prospected to familiars of our patient the possibility of a craniotomy for open-brain biopsy and definite pathological diagnosis. Lumbar puncture has been refused, but spinal fluid examination has limited relevance after acute phase: detection of specific nucleic acid provided by PCR is timing dependent because highest yield is obtained during the first week after symptom onset, much less in the second week and only occasionally after that⁽¹¹⁾. Only sierological tests are sensitive enough to detect even low amounts of antibodies from spinal fluid, compared with antibody levels in the serum⁽¹²⁾.

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