

PAPILLEDEMA: AN UNUSUAL FINDING IN A PATIENT WITH HERPES ENCEPHALITIS

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Abstract- Herpes simplex virus accounts for 10 to 25% of sporadic viral encephalitis throughout the world among people of different age with two peaks, one at 5 to 30 and the other at > 50 years of age. Pathologic process includes focal brain tissue inflammation and necrosis (predominantly temporal lobe). Therefore local neurological signs and symptoms will ensue. Although CSF pressure rising due to inflammation is expected, papilledema which is defined as a noninflammatory congestion of optic disk due to raised intracranial pressure has not yet been mentioned as a sign of focal encephalitis. In this article we report a 24 year-old patient with headache, fever and some degree of cognitive disorder who was definitely diagnosed (with MRI and PCR technique) and treated for herpes encephalitis. Unexpectedly he had papilledema which led to more investigation. Most signs and symptoms disappeared during two weeks of intravenous acyclovir therapy as did papilledema to some extent. In this case, positive CSF PCR test for HSV confirmed the diagnosis. However it seems that along with starting acyclovir therapy, performing other supplementary studies (e.g. CT scan, MRI with and without I.V. contrast, CSF cytology and serologic tests for HIV) to rule out other conditions that may be associated with papilledema and focal neurological signs (like malignancies), is mandatory.

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INTRODUCTION

Herpes simplex virus involves different organs including mucocutaneous surfaces, the central nervous system and occasionally visceral organs. Herpes encephalitis, being one of the features of central nervous system involvement, produces some constitutional symptoms and focal neurological signs.

Papilledema is not considered as a sign of herpes encephalitis. Unusual clinicopathological findings, which may suggest other causes, challenge the diagnosis and necessitate other investigations. The advent of chemotherapy for HSV infections has made prompt recognition of these syndromes even more clinically important than in the past.

CASE REPORT

A 24-year-old man presented to the emergency department because of headache. He began to feel pain in periorbital area about 7 days ago. Over the succeeding days, first nausea and vomiting then fever and chills appeared. Sometimes he got

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disoriented, confused or had some degree of memory deficit. His past medical history and family history was not remarkable.

Having been diagnosed migraine or sinusitis, he had been prescribed some medications before admission to the hospital.

Physical examination revealed fever (40°C) and bilateral papilledema grade II→III (according to neurology and ophthalmology consultation). Brain CT scan revealed localized hypo dense and heterogeneous areas with perilesional edema in temporal and opercular regions (right more than left). MRI study showed abnormal signal changes in right temporal lobe and inferior aspect of right frontal lobe accompanied by post contrast (Gd-DTPA) abnormal signal enhancement (Fig. 1), which could be due to encephalitis or neoplastic lesions like lymphoma.

Considering all precautions to avoid tonsillar hernia (mannitol and dexamethasone infusion, use of fine narrow needle and post-LP 24 hours monitoring) and assuming provisional diagnosis of encephalitis or brain abscess, lumbar puncture was done and patient was administered IV vancomycin, ceftriaxone and acyclovir empirically for 48 hours.

CSF profile was compatible with aseptic meningitis (Table 1). Other CSF parameters were as follow: negative bacterial culture, negative Gram stain, no bacteria was seen, negative Indian ink, Ziehl Neelsen staining: no AFB, and negative VDRL. PCR for HCV and MTB-complex DNA was negative but positive for Herpes. CSF cytology was negative for malignancy.

Table 1. CSF profile of the patient

| Characteristic | Result |
|----------------|-----------|
| Color | colorless |
| Appearance | clear |
| WBC | 110/micL |
| RBC | 60/micL |
| Lymphocyte | 90% |
| Neutrophil | 10% |
| Sugar | 62 mg/dl |
| Protein | 42 mg/dl |

Abbreviation: CSF, cerebrospinal fluid.

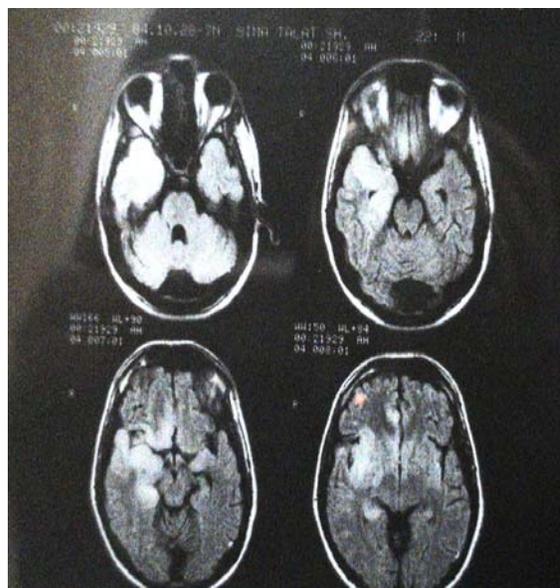


Fig. 1. MRI on admission

Serum ADA: normal, Anti Brucella-IgG: negative, HBS Ag, HIV Ab and HCV Ab were negative. Other chemical and serological laboratory tests were normal.

Therefore all antibiotics except for acyclovir were discontinued. Within 14 days, most of signs and symptoms subsided and papilledema decreased. MRA and MRV study, done 3 weeks later, confirmed the recovery (Fig. 2).

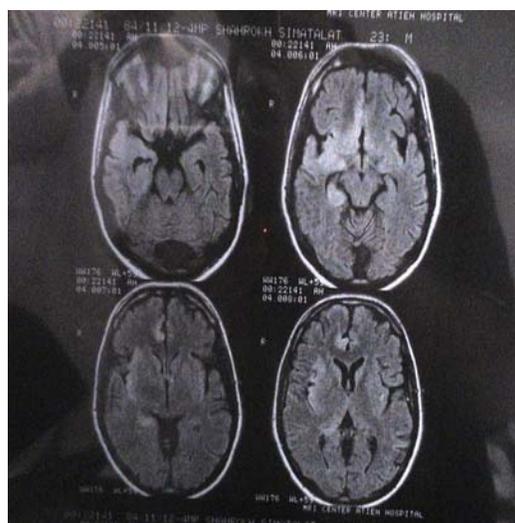


Fig. 2. MRI two weeks later

DISCUSSION

The neuropathological picture of HSE is characteristic, consisting of acute necrotizing encephalitis that almost always localizes, often asymmetrically, to the orbitofrontal and temporal lobes with involvement of the cingulate and insular cortex (3).

The clinical hallmark of HSV encephalitis has been the acute onset of fever and focal neurological (especially temporal-lobe) symptoms like prominent olfactory or gustatory hallucinations, anosmia, unusual or bizarre behavior or personality alterations, or memory disturbance (1). Clinical differentiation of HSV encephalitis from other viral encephalitides, focal infections or noninfectious processes is difficult (1). Our case typically has followed most of these symptoms.

Papilledema, which takes 24-48 hours to occur and 6-8 weeks for fully developed form to resolve during adequate treatment, has been reported in few cases of herpes encephalitis (11, 12). It may reduce visual acuity by causing hyperopia, but in most cases vision is normal apart from blind spot enlargement, so without precise physical examination it remains unclear. Sudden reduction of intracranial pressure or systolic perfusion pressure may precipitate severe visual loss in any stage of papilledema (2). Its presence in our case suggested other causes like malignant lesions (e.g. leukemia), abscesses or arteriovenous malformations which were ruled out by CSF cytological study, lumbar puncture and neuro-imaging study.

Magnetic resonance imaging (MRI) provides the most sensitive method of detecting early lesions and is the imaging of choice in HSE (4). It can noninvasively establish many of the potential alternative diagnoses of HSE.

Examination of the cerebrospinal fluid (CSF) is of considerable value and should always be done after computed tomography or MRI. The exception is where cranial imaging shows evidence of severe cerebral oedema and brain shift, in which case we prefer to delay lumbar puncture until the oedema is reduced with steroids or mannitol to avoid brain herniation (5).

The most sensitive and specific noninvasive method for early diagnosis of HSV encephalitis is the demonstration of HSV DNA in cerebrospinal fluid by PCR. In an experienced laboratory a PCR test for HSV in the CSF of a patient with HSE during the first week can detect viral DNA in about 95% of cases (4, 6). False negative results are most likely to occur very early, for example, within the first 24-48 hours, or late, for example after 10-14 days or when blood is present in the CSF (7). The specificity of the test is over 95% in experienced laboratories with the ability to avoid contamination (3, 6).

Intravenous antiviral chemotherapy reduces the mortality of HSV encephalitis from about 70% to less than 30% and also reduces morbidity (9, 10). Even with therapy, however, neurological sequelae are frequent, especially in persons over 35 years of age. A better outcome is seen in younger patients below the age of 30 years and in those in whom the duration of encephalitis was four days or less and the Glasgow coma score was above 6 when acyclovir was started (8). Most authorities recommend the administration of intravenous acyclovir to patients with presumed HSV encephalitis until the diagnosis is confirmed or an alternative diagnosis is made (1). The same rules were observed in our case and he left the hospital without any sequelae.

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