Imaging findings and outcome in herpes simplex encephalitis: study of 14 cases

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Authors: M. CHAABOUNI\textsuperscript{1}, S. Haddar\textsuperscript{2}, S. Chaabouni\textsuperscript{2}, A. Arous\textsuperscript{2}, H. Abid\textsuperscript{2}, K. Ben Mahfoudh\textsuperscript{3}, J. Mnif\textsuperscript{2}; \textsuperscript{1}SFAX, SF/TN, \textsuperscript{2}Sfax/TN, \textsuperscript{3}SFAX/TN
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Purpose

To illustrate imaging findings in herpes simplex encephalitis (HSE) and to evaluate the role of diffusion-weighted imaging (DWI) in the diagnosis of this viral encephalitis, its relationship with the stage of the illness and its prognosis.

Methods and Materials

This is a retrospective study including 14 patients diagnosed with HSE from January 2004 to June 2011. The mean age was 36.7 years, ranging from 5 months to 87 years (4 children and 10 adults). The sex-ratio was 7 males/7 females.

These patients were hospitalized for fever (n = 12), seizures (n = 8) and behavioural changes (n = 9). Cerebrospinal fluid (CSF) analysis was performed in all cases, showing a normal formula (n = 3) or lymphocytic meningitis (n = 11). All patients benefited from an initial brain imaging: computed tomography (CT): n = 8; magnetic resonance imaging (MRI): n = 10. CT images were acquired before and after injection of iodinated contrast material.

A spin-echo sequence was used to obtain axial T2-weighted and axial and/or sagittal T1-weighted images before and after administration of gadolinium chelate. Six of our patients benefited from a FLAIR sequence and DWI with calculating of the apparent diffusion coefficient (ADC) value.

The diagnosis was given by a positivity of polymerase chain reaction (PCR) (n = 9) or a rise in the serum antibody titre for Herpes simplex virus (HSV) (n = 5). HSV type 1 was incriminated in all cases.

Long-term imaging was performed in 10 cases: CT (n = 5) and/or MRI (n = 10).

Aciclovir was administrated for all patients. Clinical outcome was variable: favourable or sequelae or death. Sequele was divided into moderate, severe and major.

To simplify statistical study, we defined good outcome as favourable evolution or moderate sequelae, and poor outcome as severe or major sequelae or death.

The data were expressed as means and frequencies. Statistic significance was analyzed using Chi-square test or Fisher's exact test followed by multiple logistic regression. P<0.05 was considered to be statistically significant.
Results

We noted predominance of supra-tentorial gray matter involvement: cortex (n = 13) and basal ganglia (n = 4). The temporal lobe was interest in ten cases. Frontal lobe involvement was present in nine patients. Lesions were seen in the cingulate gyrus (n = 4), the insular lobe (n = 11), and, in four patients, in the basal ganglia (Fig. 1 on page 7).

Imaging abnormalities appeared hypodense on CT (Fig. 2 on page 5) and hyperintense on T2 and FLAIR in all cases. Diffusion sequence showed hypersignal in 5 cases with low ADC (Fig. 3 on page 4) corresponding to cytotoxic oedema, and isosignal with high ADC value in only one case (Fig. 4 on page 3) corresponding to vasogenic oedema.

A mass effect was observed only once and meningeal enhancement in 3 cases.

Imaging follow-up showed lesion stability (n = 3), aggravation (n = 8) or sequelae (n = 3) (Fig. 5 on page 8). Hemorrhagic lesions were found in 4 cases (Fig. 6 on page 6). Control MRI with DWI was obtained only once, demonstrating high ADC value (Fig. 7 on page 10, Fig. 8 on page 11).

Clinical outcome after acyclovir administration: favourable (n = 2), sequelae (n = 9) and death (n = 3). Clinical follow-up of patients with initial low ADC demonstrated different clinical outcome: favourable (n = 2), sequelae (n = 3) and death (n = 1).

We studied relations between clinical outcome and imaging findings on CT, conventional MRI sequences and diffusion. We didn't obtain significant correlation except a valid relationship between the number of lesion's locations and prognosis (p = 0.049) (Table 1).

<table>
<thead>
<tr>
<th>Prognosis</th>
<th>Good</th>
<th>Poor</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions number</td>
<td>2.25</td>
<td>7.25</td>
<td>0.049</td>
</tr>
</tbody>
</table>

*Table 1: relation between lesions number and prognosis.*

A number strictly higher than 4 lesions was correlated to poor outcome (Fig. 9 on page 9).
Fig. 4: A 30-year-old man, presenting with fever, seizure and abnormal behaviour. MRI axial images T2 (A), FLAIR (B), diffusion (C) and ADC map (D) : bilateral hyperintensities T2 and FLAIR in temporal and basi-frontal lobes. Lesions were isointense on diffusion with high ADC value.
**Fig. 3:** A 63-year-old woman. Aural and visual hallucinations + behavioural changes. Proof of herpes infection on CSF analysis. MRI axial images T1 (A), FLAIR (B), diffusion (C) and ADC map (D) : cortico-sub-cortical lesion in the left fronto-insular lobes, hypointense T1, hyperintense FLAIR and diffusion with low ADC value.
Fig. 2: A 56-year-old woman. Fever, confusion. Specific antibody in CSF, negative PCR. CT at day 4: axial image (A) : left temporal hypodensity. MRI at day 5: T2 axial (B) and coronal (C) images : inflated and hyperintense aspect of the cortex in insular, cingulate and temporal lobes.
**Fig. 6:** Control MRI of the same patient in fig 2. Appearance of a left temporal hematoma without mass effect.
Fig. 1: A 55-year-old woman. Mental disorders in febrile context. Specific antibody in CSF, Negative PCR. CT at day 7 : axial image (A): hypodensity of the cingulate gyrus and right insular lobe. MRI at day 10 : T2 axial (B) and coronal (C) images : cortical oedematous lesions, hyperintense, in right temporal lobe, bilateral insular lobe and cingulate gyrus. There is also lesion of the right lentiform nucleus (B).
Fig. 5: Control MRI of the same patient in fig 1 at day 18: T2 axial (A), T1 axial (B) and T1 coronal with gadolinium (C) images: appearance of a cortical-gyriform-T1 hypersignal with enhancement after injection of gadolinium: laminar cortical necrosis. Outcome: death.
Fig. 9: ROC curve demonstrating the relationship between lesions' number and poor outcome. The under-curve area was 0.844. The level point was 4.5 lesions.
Fig. 7: A 34-year-old man. Fever + behavioural changes. PCR positive. MRI axial FLAIR (A), diffusion (B) and ADC map (C) : right insular lesion, hyperintense on FLAIR and diffusion with low ADC value.
**Fig. 8:** Control MRI of the same patient in fig 7, after three months: extension of lesions becoming bilateral, hyperintense on FLAIR (A), isointense on diffusion (B) with high ADC value (C).
Conclusion

- MRI, particularly through the new sequences, contributes to early diagnosis of HSV encephalitis by demonstrating suggestive abnormalities.

- From our study, low ADC values are usually observed in acute stage and high ADC values in chronic stage.

- We don't find a relationship between the initial ADC value and the clinical outcome.

- We had demonstrate a statistically valid relationship between the number of lesion's locations and prognosis. A number strictly higher than 4 lesions was correlated to poor outcome.

References


Personal Information

Mohamed CHAABOUNI
Radiologist
Department of Radiology
H. Bourguiba hospital - Sfax - Tunisia
E-mail: medchaabouni@yahoo.fr