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Aphasia in a patient with acute hepatic encephalopathy associated with multifocal cortical brain lesions☆

Afasia en paciente con encefalopatía hepática aguda asociada a lesiones corticales cerebrales multifocales

Dear Editor,

Acute hepatic encephalopathy (AHE) is typically characterised by a wide range of neuropsychiatric manifestations including behavioural, cognitive, or mood changes associated with asterixis and different degrees of alteration to the level of consciousness, which may progress to stupor or coma in some cases.[1] This situation may be due to acute liver failure, cirrhosis, portal hypertension, or a transjugular intrahepatic portosystemic shunt.[2,3] Brain magnetic resonance imaging (MRI) of patients with AHE may reveal signal alterations in different brain areas, caused by vasogenic and cytotoxic oedema related to the toxic effect of ammonia in the brain.[4,5] These alterations may disappear after resolution of the encephalopathy,[5] or may progress to cortical laminar necrosis in cases with poor outcomes.[6] Presentations with focal manifestations are very infrequent in AHE, and may lead to diagnostic errors.

Clinical case. The patient was a 50-year-old man who was diagnosed in 2002 with portal vein thrombosis secondary to protein S deficiency, which was treated with a transjugular intrahepatic portosystemic shunt (TIPS) and oral anticoagulation. He was admitted to another hospital in May 2015 due to a sudden loss of consciousness which progressively and spontaneously improved over the following hours. The patient was transferred to our hospital to rule out the possibility of cerebrovascular accident, since he presented difficulties speaking after recovering a normal level of consciousness. During the neurological examination at admission, the patient was awake and presented mild asterixis in both hands; the most striking finding, however, was the presence of mixed aphasia characterised by hypofluent speech with presence of frequent phonological paraphasias in spontaneous language and difficulty understanding complex commands. Word repetition was preserved, although he showed difficulties repeating simple sentences. The neurological examination yielded otherwise normal results. The blood test revealed chronic anaemia, altered liver profile (ASAT 58 IU/L, total bilirubin 3.3 mg/dL) and moderately elevated levels of ammonia (91 μmol/L). The peritoneal fluid analysis and a brain computed tomography showed no abnormalities. However, the brain MRI showed altered high intensity signal on the fast fluid-attenuated inversion recovery (FLAIR), T2-weighted, and diffusion-weighted imaging (DWI) sequences in the left frontal parasagittal, insular, temporal, and cingulate cortices, as well as the right insular cortex, with no abnormal diffusion restriction in the apparent diffusion coefficient (ADC) map (Fig. 1A). The MR-angiography showed permeability of the intra- and extracranial vessels. An EEG study revealed presence of a delta rhythm with bi- and triphasic waves suggestive of toxic-metabolic dysfunction, with no associated epileptiform activity. We finally diagnosed the patient with acute aphasia as a manifestation of AHE associated with multifocal cortical brain lesions, predominantly involving the left insular and temporal cortices, and in the context of a TIPS. The patient received cathartic therapy, with aphasia progressively improving and resolving several weeks later. An additional MRI scan performed 2 months later showed that the cortical lesions had completely disappeared (Fig. 1B).

Discussion. Few cases have been described of patients with TIPS who, in the context of AHE, developed focal neurological signs associated with presence of cortical lesions in neuroimaging.[7–9] Two of the patients described in the literature presented sudden loss of consciousness with posterior aphasia, with brain MRI scans showing cortical lesions with a similar location to that described in our patient.

Correlation of the level of ammonia with the type of manifestation and the clinical severity of encephalopathy is a controversial issue.[10] In our case, as in that reported by Babington et al.[7], blood ammonia levels increased only moderately. This suggests that the pathophysiology of these pseudo-ictal discharges may involve factors other than ammonia, such as inflammatory mechanisms or other potential toxins,[1,11] the individual susceptibility of the brain to the toxic effect of ammonia, or the rate of increase of ammonia levels in the brain, favoured by TIPS.

Diagnosis of AHE in case of acute focal symptoms in patients with liver disease or TIPS is important since it may have prognostic consequences. It is well known that

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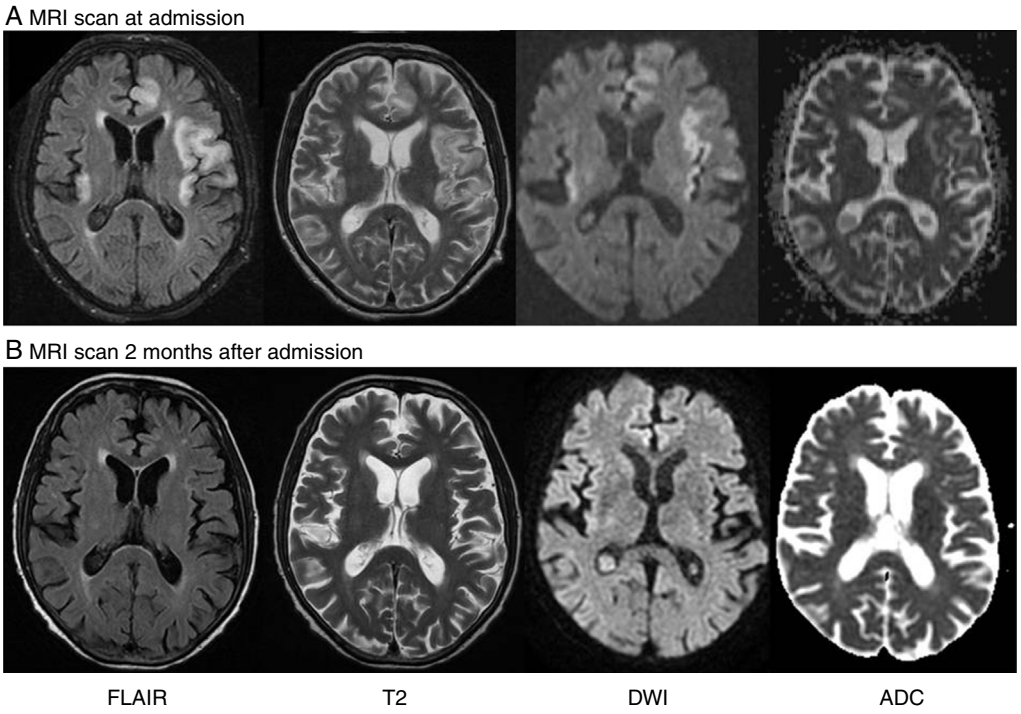

Figure 1 (A) Brain MRI revealing cortical and subcortical hyperintensity in both insular areas, the left temporal lobe, and the parasagittal frontal lobe on T2-weighted and FLAIR sequences. DWI showed cortical signal alterations in all these areas, with no abnormal diffusion restriction in the ADC map. (B) A second MRI scan performed 2 months later revealed that lesions had disappeared.

patients undergoing early, aggressive treatment for AHE have a better prognosis for recovery of neurological deficits and resolution of brain lesions. However, results may not be favourable, with the condition even resulting in the death of the patient, if the aetiology of these lesions is uncertain and treatment is started late.[4,8]

Conflicts of interest

None.

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Psychiatric manifestations and dysautonomia at the onset of focal epilepsy in adults: Clinical signs indicating autoimmune origin[☆]

Manifestaciones psiquiátricas y fenómenos disautonómicos en el comienzo de epilepsia focal del adulto. Señales clínicas de un origen autoinmune

Immune alterations may be the cause of some of the epilepsies considered to date to be cryptogenic, and they usually respond to immunotherapy. Some of the clinical features of this type of epilepsy are a personal or family history of autoimmune or neoplastic disease, subacute onset with high seizure frequency, multiple seizure foci, early resistance to antiepileptic drugs, neuropsychiatric symptoms, and in some cases rapidly progressive cognitive impairment.[1] Presence of signs of inflammation in magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) studies and the detection of antineuronal antibodies may help establish diagnosis.[2] Diagnosis and early treatment may have a crucial impact on seizure control and cognitive comorbidity.[3,4] We describe the cases of 3 patients with adult-onset focal epilepsy. Psychiatric symptoms and dysautonomia led to the suspicion of autoimmune aetiology, which was confirmed by antibody tests.

The first patient was a 24-year-old man with no relevant personal history who experienced an epileptic seizure with head version to the left, disorientation, and generalised rigidity and postictal period. Two weeks previously, he had presented behavioural alterations, insomnia, and auto- and hetero-aggression which progressed to mutism and catatonia. He also presented self-limiting episodes of profuse sweating. No paroxysms were observed in the EEG. A brain MRI scan (Fig. 1A and B) revealed hyperintensities in the frontal lobe bilaterally and in the posterior corpus callosum, with no contrast uptake. CSF and serum analyses confirmed the presence of anti-NMDA receptor antibodies (qualitative study) and tumour screening ruled out occult neoplasm. He received antiepileptic treatment during hospitalisation, as well as treatment with corticosteroids and immunosuppressants (cyclophosphamide and rituximab). A follow-up MRI scan showed that the size of the lesions had decreased. Psychiatric symptoms improved 2 weeks later, and the patient was discharged, presenting no further epileptic seizures and without receiving treatment. A follow-up laboratory test at one year showed negative results for serum anti-NMDA receptor antibodies.

The second patient was a 35-year-old woman with type 2 diabetes mellitus, vitiligo, and anxiety disorder of one year's progression, under follow-up with the psychiatry department. The patient responded poorly to benzodiazepines. She had fallen and lost consciousness on 3 occasions, which had been interpreted as syncope. The patient subsequently experienced complex partial seizures with symptoms of temporal lobe epilepsy in the dominant hemisphere, with piloerection, brief episodes of disorientation, jaw automatisms, and motor aphasia. These symptoms manifested daily for one year. Baseline brain MRI results were normal. Neuropsychological tests revealed difficulty performing verbal and visual memory tasks. After receiving 2 drugs in monotherapy, she continued experiencing seizures 2-3 times per week. She was admitted to the long-term continuous video-EEG monitoring unit, and experienced 74 seizures with symptoms of left anteromedial temporal lobe epilepsy. Interictal findings were located in the anteromedial region of the left temporal lobe. A second MRI scan revealed enlargement and hyperintensity of the amygdala and left hippocampal head (Fig. 1C). Presence of anti-LGI1 antibodies in the plasma was confirmed (levels of 275 pM; normal range: negative). Treatment with corticosteroids was started and seizures disappeared after 3 weeks. The patient was treated with oxcarbazepine for one year. A follow-up brain MRI scan (Fig. 1D) showed decreased severity of the findings in the initial scan; a new plasma study confirmed negative results for anti-LGI1 antibodies. Results from the neuropsychological study performed at one year were normal. The patient is currently receiving no treatment and remains asymptomatic.

The third patient was a 62-year-old man with no relevant personal history, who was admitted due to a 2-month

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