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Hemiconvulsion-hemiplegia-epilepsy syndrome. Follow up of a case to adulthood

Síndrome de hemiconvulsión-hemiplejía-epilepsia. Seguimiento de un caso hasta la edad adulta

Dear Editor,

Hemiconvulsion-hemiplegia-epilepsy (HHE) syndrome is a sequel to prolonged status epilepticus, which was first recognized by Gastaut, in 1960.[1] It is characterised by the appearance of clonic epileptic seizures of long duration affecting one side of the body in the course of a febrile illness in children under 4 years. Subsequently, a hemiplegia of varying intensity is developed, which can be permanent. The crises usually originate in the hemisphere contralateral to the hemiplegia. The incidence of this syndrome has declined significantly in recent years in industrialised countries, probably due to more effective management of status epilepticus.[2]

Magnetic resonance imaging (MRI) scans show, in the early stages, hyperintensities located throughout the cerebral hemisphere on T2 sequences and diffusion with a decreased apparent diffusion coefficient, which would indicate that the underlying lesion is a cytotoxic oedema.[3] After a period of several days, these changes disappear[4] and brain atrophy becomes evident, uniformly affecting an entire hemisphere, both cortical and subcortical, with dilatation of the ventricular system. This pattern makes it possible to differentiate HHE syndrome from focal atrophies that appear in perinatal lesions with a vascular origin.[5]

This syndrome has been divided into two categories: Type I, called symptomatic, characterised by symptomatic febrile seizures occurring after acute brain processes such as meningitis, encephalitis, subdural haematomas and vascular lesions.[6] Type II, known as idiopathic, is characterised by a myoclonic status epilepticus precipitated by simple hyperthermia due to a non-specific infection, which may be followed by temporal lobe epilepsy as a sequel. This type of epilepsy usually develops after an interval varying from 1 to 3 years.[7]

Patients described usually have a good evolution, with disappearance of seizures in a few years; nevertheless, there are no conclusive results because follow up has always been short-term.[8] We describe the evolution of hemiplegia and epilepsy in a patient with HHE syndrome, monitored for over 20 years, and a review of this syndrome.

The patient was an 11-month-old girl born after normal pregnancy and delivery. Gestation was controlled, with foetal movements in the fifth month. Her weight at birth was 3,600g. She did not require resuscitation. Her psychomotor development was normal. She received vaccinations according to the immunization schedule. She presented a case of pharyngoamygdalitis with 48 hours of evolution, which was treated with amoxicillin. She was admitted to the emergency service due to hemifacial and left-limb clonic movements lasting at least 30min as well as high fever (39.2°C). Clonic focal seizures in the left limbs persisted for 48h; she presented more than 10 episodes with durations of seconds or several minutes, which required clonazepam perfusion treatment, along with intravenous phenobarbital and phenytoin.

Computed tomography scan (on admission) was normal. Electroencephalogram (EEG) (on admission) revealed: interhemispheric asymmetry with signs of brain affectation in the right hemisphere. Lumbar puncture results were: CSF glucose, 80mg/dl (blood glucose, 122mg/dl); proteins, 20mg/dl; 2 leukocytes/μl. Gram, Ziehl and cultures were negative. Blood analysis with kidney, liver and thyroid function, blood count, antinuclear antibodies, rheumatic tests, lactic acid and ammonium tests were normal. Organic acids in urine and amino acids in blood were normal. Neurotropic virus, syphilis, and *Brucella* serologies were negative. A hypercoagulability study offered results within the normal range.

At 6h after admission, she presented hypotonia and hyporeflexia in the left limbs.

The subsequent evolution of the patient brought the appearance of focal motor seizures in the left hemisphere at 2 years of age; the EEG revealed focal right temporal-rolandic paroxysmal activity (high voltage spikes followed or not by waves) on an asymmetric background path. Hypotonia resulted in spastic hemiparesis of the left hemisphere with involvement of the flexor muscles of the arm, forearm and hand as well as left equinovarus; she consequently received rehabilitation treatment and botulinum toxin, which improved spasticity and gait. An MRI showed general cortico-subcortical atrophy affecting the entire right hemisphere (fig. 1). The left focal seizures persisted for more than 12 years despite the use of various therapeutic combinations. At age 14, while in treatment with valproic acid at 1,000mg/day and lamotrigine at 100mg/day, the crises disappeared and she was consequently left in treatment with lamotrigine. The EEG confirmed the good evolution: asymmetric background with lower frequency and amplitude in the right hemisphere. There were sharp waves in the left frontal area and slow waves in right temporal-rolandic regions, with disappearance of irritative discharges. She is currently 24 years old and, despite having been without seizures for 8 years, does not want to completely stop the anti-epileptic therapy.

The pathogenesis of HHE syndrome is controversial. Some authors suggest that a primary viral infection could cause, directly or through proinflammatory cytokines, a cerebrovascular disorder, which would in turn cause hemiconvulsion, hemiplegia, and cytotoxic oedema.[9-11] Other authors believe that the injury is a direct result of prolonged seizure activity. The most convincing hypothesis is that the repeated crises may cause a brain lesion by altering neuronal energy metabolism.[12-14] Several factors may contribute to the pathogenesis of the syndrome, such as the beginning of the crises in the first year of life (when

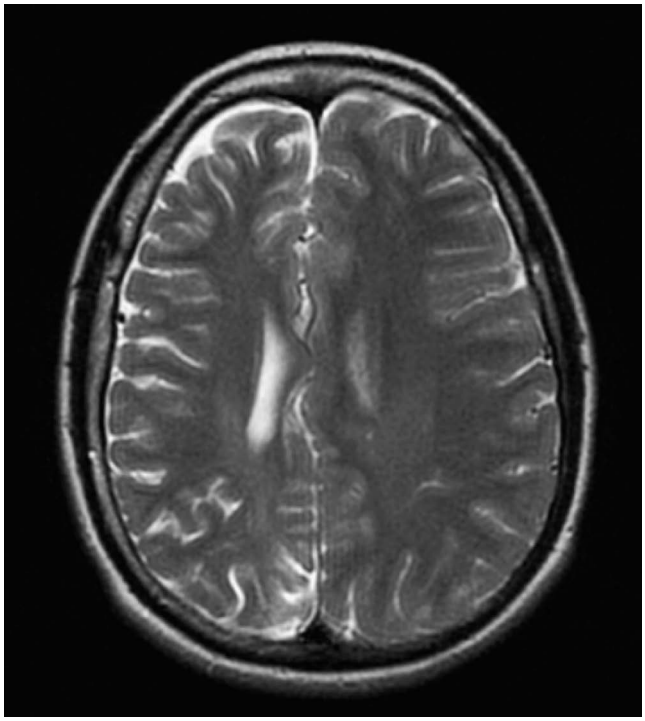

Figure 1 Brain MRI, in axial T2 sequence: a general atrophy of the entire right cerebral hemisphere with homolateral ventricular dilatation in the absence of vascular lesions can be observed.

the brain is more prone to intrahemispheric diffusion), possible unnoticed long-term seizures, alteration of neuronal energy metabolism, genetic factors that may predispose towards prolonged febrile seizures and systemic factors such as hypoxia, hypoglycaemia, low blood pressure and hyperthermia.[3]

This syndrome has been associated with hypercoagulability, such as factor V Leiden[15] or protein S deficiency.[16] However, the ischemic theory would not explain the general atrophy of the hemisphere in the absence of evident ischemic lesions or the absence of arterial obstruction in the angio-MRI.[8] Hemiplegia in HHE syndrome differs from postictal or Todd paralysis in that it lasts for longer than 7 days. The degree of hemiparesis correlates with the degree of brain atrophy seen in the MRI.[12]

We must rule out underlying metabolic disorders in these patients through the identification of organic acids in urine. This has previously been described as a presentation form of a case of L-2-hydroxyglutaric aciduria,[17] as well as subjacent cortical dysplasias.[18]

The onset of epileptic seizures is associated with fever in 75% of patients[19] (as is the case in our patient) and prior small seizures appear in 25%.[20] Initially flaccid hemiplegia becomes spastic, although the intensity may decrease in many occasions,[19] and may even disappear in 20% of cases.[1] However, even in these cases, there is some degree of spasticity with hyperreflexia and pyramidal data. Mental retardation has been described in connection with hemiplegia in 80% of cases;[20] although our patient presented a significant degree of hemiparesis, she showed no obvious cognitive problems. Hemiconvulsion-hemiplegia syndrome is followed by epilepsy, leading to the onset of HHE syndrome by the appearance of partial seizures in 56%-70% of cases.[1,6,20] Of these, 85% do so within 3 years from the beginning of the hemiconvulsion.[20]

The abnormalities seen in the EEG consist of slow waves that are either unilateral or predominantly unilateral,[20,21] consistent with clinical seizures, although they have also been described in the hemisphere contralateral to the atrophied one.[5] The HHE syndrome should not be mistaken for Rasmussen syndrome, in which continuous myoclonic jerks appear, affecting one side of the body and gradually developing into hemiplegia, with mental retardation and even death of the patient, or with significant sequelae after an active period of months or years.

Seizures in HHE syndrome can usually be well controlled. In selected cases, they may require surgery; callosotomy is preferable to hemispherectomy, since the latter can leave significant language sequelae. A 90% decrease of generalised seizures has been described with callosotomy, although partial, sensory-type seizures remained unchanged. In general, a reduction of over 50% is obtained in the number of seizures.[22] In epilepsies beginning in the first year of life, HHE syndrome should be considered. Occasionally, brain structure abnormalities are related to chromosomal deletions; however, no alterations in the genotype are known in this syndrome.

The therapeutic approach to status epilepticus, considering it a medical emergency, with administration of intravenous medication to stem the crises, involves the reduction of this syndrome,[23] which may leave persistent epilepsy and hemiplegia sequelae. The evolution of epilepsy in HHE syndrome is favourable, the crises disappearing in adolescence. Our case brings to the literature the favourable evolution persistent over time, as our patient has spent more than 10 years without epileptic seizures.

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Pseudo-subarachnoid haemorrhage. A need for clinical-radiological diagnostic criteria

Pseudohemorragia subaracnoidea. Necesidad de criterios diagnósticos clínico-radiológicos

Dear Editor,

Subarachnoid haemorrhage (SAH) is a medical emergency, so its early diagnosis and treatment are vital. In cranial computerized tomography (cCT) it appears with an increased density in the basal cisterns and the subarachnoid space. Some neurological diseases have been described (hypoxic encephalopathy, hyperperfusion radical encephalopathy, extensive infarctions, viral meningoencephalitis, purulent meningitis, bilateral subdural haematoma and idiopathic intracranial hypertension)[1-5] that exceptionally present a tomographic pattern typical of SAH, without clinical or pathological haemorrhage data; this entity is known as pseudo-subarachnoid haemorrhage (pSAH).

We report a case of pSAH in the context of an advanced hypoxic-ischemic encephalopathy (HIE). The patient was a 38-year-old male smoker. He was admitted to the intensive care unit under mechanical ventilation after suffering cardiopulmonary arrest outside the hospital. He could not open his eyes or make sounds, but carried out approximation-pronation of the right arm under algesic cranial stimulation; brainstem reflexes were present and there was general spastic hypertonia. The electrocardiogram showed the classic pattern of Brugada syndrome. The initial cCT presented an early bilateral occipitotemporal hypodensity indicative of acute ischemic injury, presumably with an anoxic-haemodynamic origin, and there were no other findings (fig. 1). The electroencephalogram (EEG) showed an alpha-coma pattern. At 72h, his condition worsened, with loss of brainstem reflexes and reactivity; a new cranial CT showed diffuse cerebral oedema (DCE), hypodensity in the territory of the posterior cerebral arteries and symmetric diffuse hyperdensity in the cerebral sulci and cisterns, with an appearance of massive SAH (fig. 1). The incongruity of SAH in the clinical context led to a diagnostic reconsideration, with Hounsfield unit (HU) determination, with a value of at most 42 UH, in hyperdense sulci and cisterns; the final interpretation of the finding was pSAH related to severe diffuse cerebral oedema. A new EEG confirmed brain death.

One of the most common causes of pSAH is diffuse cerebral oedema due to HIE, which can displace the healthy brain areas into areas normally occupied by cerebrospinal fluid (CSF); neuroimaging can show the disappearance of the convexity sulci, poor differentiation between grey and white matter and generalised cerebral hypodensity. Increased intracranial pressure may also cause vascular congestion with dilation of the superficial (pial) venous structures. Consequently, the CSF (hypodense) is displaced from the subarachnoid space, where the meninges and vessels are concentrated (hyperdense). The blood-brain barrier breakdown in relation to hypoxia may contribute to an increase in CSF protein content, although this mechanism