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LETTERS TO THE EDITOR

Pharmacological Parkinsonism vs. Dementia with Lewy Bodies

Parkinsonismo farmacológico frente a demencia con cuerpos de Lewy

Dear Editor,

Lewy-body dementia (LBD) is a degenerative brain disease characterised clinically by cognitive decline, parkinsonism, psychotic features and cognitive fluctuations.[1] The main pathological finding is the presence of numerous Lewy bodies in the cortex, brainstem and other subcortical nuclei.[1,2] There are consensus criteria for the clinical diagnosis of LBD[3,4] but in spite of them, the differential diagnosis can be difficult, especially in the initial phases. This is relevant due to its therapeutic and prognostic implications.

We present the case of a 74-year-old woman whose most important relevant history includes an anxiety-depression disorder treated with paroxetine, as well as dyspepsia treated with cinitapride. The patient presented clinical signs of various weeks of duration, consisting of tremor during rest in the left upper limb, bradykinesia, generalised rigidity, postural instability and parkinsonian gait (Hoehn and Yahr scale, 4), along with predominantly nocturnal cramps in the lower extremities, which were relieved by leg movement and prevented her from sleeping. Finally, she came to the emergency service suffering confusion and psychomotor agitation. An initial diagnosis of parkinsonism, confusion and restless legs syndrome was established, with suspicion of a possible drug-induced origin (paroxetine and cinitapride). The diagnosis was reinforced when the confusion, psychomotor agitation and restless legs symptoms disappeared after the withdrawal of these drugs. Cranial magnetic resonance imaging (MRI) was performed, among other complementary tests (fig. 1). However, months after the withdrawal of medication, parkinsonian symptoms persisted and, 8 months after onset, the patient developed apathy, anhedonia, social inhibition and anxiety; subsequently, poor language, disorientation and visual hallucinations also appeared. It was decided to conduct a DaTSCAN, which resulted pathological (fig. 2), and a formal neuropsychological assessment, which showed severe cognitive impairment, meeting the criteria for dementia (GDS 6; Schwab and England scale, 40%). At this stage, the diagnosis of probable Lewy-body dementia was established.

This case is that of a patient who developed, in less than 1 year, parkinsonism in relation to dementia and visual hallucinations, with a very pathological DaTSCAN (fig. 2) and a cranial MRI showing cortical atrophy with relative preservation of the temporal cortex.[2,4] All this leads to the diagnosis of probable LBD.[3,4]

This initial misdiagnosis of drug-induced parkinsonism was established due to the close relationship between parkinsonism and the use of potentially parkinsonism-inducing drugs with antidopaminergic effect, such as cinitapride[5] and paroxetine.[6,7] This diagnosis was reinforced by other concomitant symptoms that improved after drug withdrawal.

In this context, this case highlights the complexity of the diagnostic approach to a parkinsonian syndrome in its early

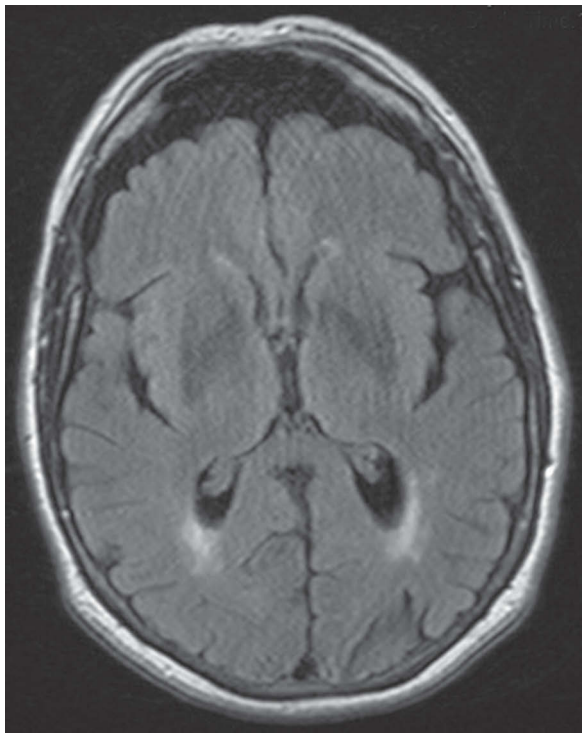

Figure 1 Cranial magnetic resonance, enhanced in T1, in which a significant cortical atrophy of both frontal lobes can be observed. In contrast, the cerebral cortex in the temporal lobes is normal.

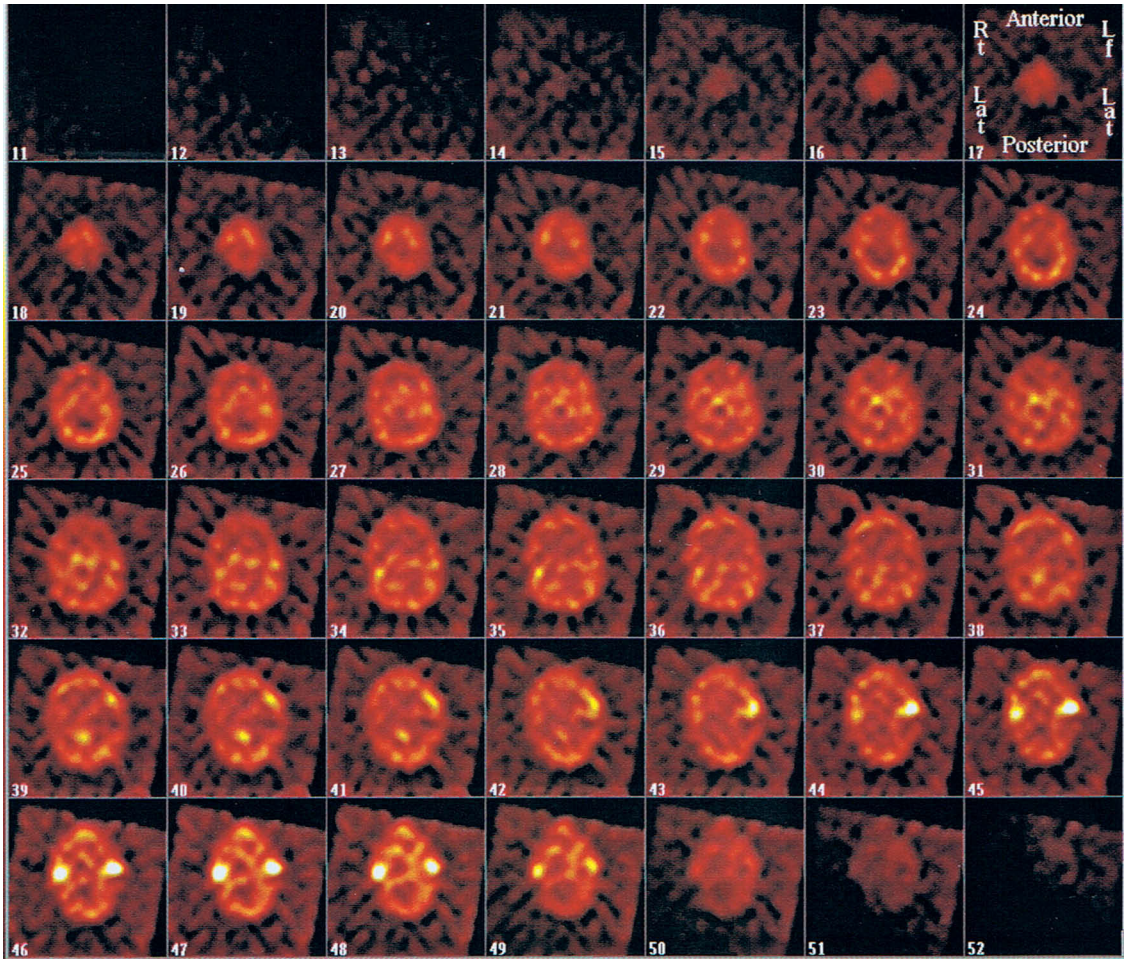

Figure 2 DaTSCAN with ioflupane, showing virtually no uptake in the basal ganglia; uptake can be observed only in the right caudate head. Non-specific extranodal uptake can be seen in other brain areas.

stages. To be useful, clinical diagnostic criteria require time to allow evolution. In addition, the use of common drugs with a potential parkinsonism-inducing effect (such as certain SSRI or prokinetics such as cinitapride) may mask an underlying degenerative parkinsonism. This consequently leads to the frequent diagnosis of drug-induced parkinsonism, with the therapeutic and prognostic implications entailed. The main contribution of our case lies in the usefulness of a DaTSCAN[8] and a formal neuropsychological assessment in the aforementioned diagnostic process. The first established the underlying degenerative parkinsonism and, therefore, a non-pharmacological origin (DaTSCAN is usually normal in pharmacological parkinsonism[8]). The second showed, in the context of a complex case of anxiety, apathy, and anhedonia, which was difficult to categorize, the existence of dementia. All of this contributed decisively to the final diagnosis.

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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