New-onset impulse control disorders after treatment with levodopa—carbidopa intestinal gel in Parkinson's disease

Trastornos del control del impulso de nueva aparición como complicación del tratamiento con gel intestinal de levodopa-carbidopa en la enfermedad de Parkinson

Dear Editor:

Impulse control disorders (ICDs), are a serious and increasingly recognized complication in Parkinson's disease (PD), occurring in up to 20% of patients.[1] ICDs have been mostly related to the use of dopamine agonists (DAs). However, ICDs have also been reported to occur with levodopa, monoamine oxidase inhibitors, and amantadine treatment, as well after deep brain stimulation.[1,2]

Levodopa treatment has been associated with compulsive behaviors such as punding and dopaminergic dysregulation syndrome.[3,4]

Levodopa—carbidopa intestinal gel (LCIG) is a treatment that has been reported to be beneficial in patients with advanced Parkinson's disease. LCIG treatment can reduce OFF periods and improve motor as well as non-motor symptoms.[5,6]

Switching patients with advanced PD from oral medications to LCIG has been reported to improve IDCs. More stable plasma levels of levodopa and discontinuation of dopamine agonist are thought to underlie the improvement.[2]

We here report our experience regarding two patients with advanced Parkinson's disease who developed a de novo ICD with LCIG.

Case 1. A 70-year-old male with advanced Parkinson's disease that had started ten years ago and that was complicated with motor fluctuations. Treatment with LCIG was initiated, resulting in a reduction in OFF periods of >50%. The initial dose of levodopa was 1340 mg per day (before LCIG the equivalent dose of levodopa was 1500 mg/day). No extra doses were administered and no other concomitant oral medication was necessary. After a month, the patient developed hypersexuality that manifested as an increased sex drive. They had not exhibited this abnormal behavior previously. Initially, quetiapine up to 100 mg/day was added. In later weeks, it became necessary to reduce the levodopa doses. As the patient experienced motor deterioration, the total dose of levodopa was increased again to 1400 mg/day, which resulted in continued hypersexuality. Ultimately, the LICG was withdrawn two years later because the patient developed cognitive impairment.

Case 2. A 58-year-old patient who for the past 12 years had suffered from Parkinson's disease that was complicated with wearing off-type motor fluctuations with more than 15 h of OFF periods. Before LCIG, the equivalent dose of levodopa was 1200 mg/day. LCIG treatment was started and resulted in a good motor response. The initial dose of levodopa was 1246 mg/day and pramipexole was maintained at 0.52 mg/day. One month later, the pramipexole was withdrawn due to choreic dyskinesias. Six months later, the patient developed a pathological gambling behavior and hypersexuality: he started playing Bingo and visiting brothels on a daily basis. Initially, the daily dose of levodopa was reduced. However, as this resulted in motor deterioration, quetiapine was added. At present, after five years of LCIG treatment, the patient still suffer from ICD and finally was institutionalized.

There is experience in the literature of new-onset ICDs after the initiation of LCIG.[7] The ICDs in our cases arose with levodopa monotherapy (>1000 mg in both cases) and with no personal history of previous ICDs. Reductions in the levodopa doses were not possible and quetiapine could only partially control the ICDs.

The high doses of levodopa achieved with LCIG do not fully explain the occurrence of ICDs. It is possible that a personal susceptibility promotes the development of such behaviors, and prospective studies are needed to investigate whether there may be an increased risk of ICDs with LCIG treatment.

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Author contributions

ACC, GVA and MMS have collected the data and written the draft of the manuscript. FGP has reviewed and approved the manuscript. All authors approved the final draft for submission. FGP is the article guarantor.

Conflict of interest

The authors declare no conflict of interest.

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Brain sagging syndrome, a potentially reversible cause of subacute ataxia and dementia. A case report

Brain sagging syndrome, una causa potencialmente reversible de ataxia y demencia. Reporte de un caso

Dear Editor:

Spontaneous hypotension is an infrequent, potentially fatal condition, usually related to a Cerebrospinal Fluid (CSF) leak producing intracranial hypotension (ICH), leading to a downward displacement of the brain known as ''brain sag''.[1]

Brain sagging syndrome (BSS) has recently been described[2,3] as clinically indistinguishable from behavioral variant frontotemporal dementia (Bv-FTD) but with neuroimaging findings suggestive of ICH,[3] and a potentially reversible course.

We report a 53-year-old male, without relevant medical history, who developed progressive bilateral tinnitus and orthostatic headache for six months, and later on: recurrent falls, behavioral changes (irritability, disinhibition, being socially inappropriate), delusional ideation and insomnia, progressively worsening over two months, requiring hospital admission.

On examination, relevant findings were cerebellar syndrome (four-limb dysmetria, gait ataxia with retropulsion, Video-A), kinetic tremor and severe cognitive decline (evaluated with Trail Making Test, Frontal Assessment Battery, Boston Naming Test, Complex Figure of Rey, etc.), consisting in dysexecutive frontal syndrome, severe behavioral impairment with apathy and impulsivity. Blood test resulted normal. CSF study showed low opening pressure (4 cm H_2O), without other alterations. Cranial-CT scan showed bilateral subdural hygromas. During hospital admission clinical condition worsens, presenting urinary incontinence, inability to walk, and severe behavioral impairment (quetiapine 50 mg is started with partial response), being dependent for all activities.

Given the rapidly progressive dementia and ataxia, we proposed the following differential diagnosis: Vascular etiology was ruled out given the progressive course and absence of focal symptoms. The patient did not fulfill 2018 diagnostic criteria for Creutzfeldt—Jakob disease given the absence of cardinal symptoms or radiological findings. Other neurodegenerative diseases were unlikely given the aggressive course and lack of typical radiological findings. Negative serologies (HIV, Whipple) and lack of fever ruled out infectious cause. Autoimmune etiology was also ruled out given the normal blood analysis (including onconeural antibodies) and absence of systemic manifestations.

Brain MRI showed descent of the cerebellar tonsils, transtentorial herniation, distortion of the brainstem structures and descent of the splenium of the corpus callosum (Fig. 1), findings suggestive of ICH. Spinal MRI demonstrated descent of the spinal cord, cisternography showed CSF leak point at D5 level.

Final diagnosis was rapidly progressive dementia (suggestive of Bv-FTD) and cerebellar ataxia, probably secondary to ICH, an entity described as BSS.

We treated ICH with an epidural blood patch, first lumbar (with transient improvement of gait), and later on at dorsal level, achieving progressive significant improvement, both radiologically (resolution of brain sagging, Fig. 1) and clinically, with resolution of ataxia (improvement of SARA scale from a score of 16—0) and recovery of cognitive-behavioral symptoms. Clinical response was maintained six months after discharge (Video-A).

The classic symptoms of ICH include orthostatic headache, tinnitus[4] and, in severe cases, coma and death.[1] In 2002,[5] Hong et al. reported a patient with ICH symp-