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Dyskinesia-Hyperpyrexia Syndrome in Parkinson's disease with Deep Brain Stimulation and high-dose levodopa/carbidopa and entacapone

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Dyskinesia-Hyperpyrexia Syndrome (DHS) is a rare hyperkinetic emergency, defined by the presence of severe, continuous, generalized, acute onset dyskinesias associated with increased creatine kinase (CK), hyperpyrexia and altered mental state, which affects patients with advanced Parkinson's disease (PD). It typically occurs in patients with long disease duration, undergoing high dopaminergic daily dose, and can be triggered by therapeutic changes, infections, hot weather, dehydration, or trauma. It is a potentially life-threatening condition, mainly due to the risk of massive rhabdomyolysis and acute renal failure [1].

DHS has been first described in 2010 [2], afterwards only in few case reports and recently in a small case series [3], for a total of eight cases reported, four of which in patients treated with levodopa-carbidopa intestinal gel.

A 62-year-old man, with a 34-year-history of PD and implanted with bilateral Deep Brain Stimulation (DBS) of subthalamic nucleus (STN-DBS) for 19 years, came to the movement disorder clinic of Careggi General Hospital (Florence, Italy) in a hot July afternoon, complaining of severe, disabling, involuntary movements, which appeared acutely three hours before.

He was undergoing subthalamic bilateral bipolar voltage-constant stimulation with amplitude at 3.0 V on the right STN and 2.6 V on the left STN, pulse width at 60 μsec and frequency at 160 Hz bilaterally. His oral therapy included levodopa/carbidopa 250/25 mg and entacapone 200 mg in eight daily doses; except for PD, his past medical history was unremarkable and he did not take other chronic medications. The patient did not suffer from relevant dyskinesia or motor fluctuations. He reported only a recent lower urinary tract infection that was being treated with antibiotic therapy.

On neurological examination, he presented severe, generalized choreo-ballistic movements; he was confused and disoriented; his skin appeared dehydrated; his body temperature was 40.7 °C and his heart rate 130 beats per minute.

We immediately lowered the stimulation amplitude to 2.0 V bilaterally. The patient was hospitalized and monitored for vital signs. Blood tests revealed elevation of serum CK (up to 4891 U/L), moderate hyponatremia (127 mEq/L) and elevation of procalcitonine (1.0 ng/mL). A chest X-ray and a brain CT were negative. Oral medications were temporary suspended and a treatment with acetaminophen, intravenous rehydration and wide-spectrum antibiotic was urgently initiated.

The next morning, serious dyskinesia persisted, so we reduced the stimulation amplitude to 1.0 V bilaterally and to avoid abrupt prolonged withdrawal of dopaminergic therapy, we partially reintroduced oral medications, with levodopa/carbidopa 250/25 mg half a tablet plus entacapone 200 mg a tablet for six daily doses. After this therapeutic changes, the patient showed a remarkable improvement within few hours, with clear reduction of involuntary movements and recovery from confusion. Dyskinesia disappeared completely in two days, and parkinsonism re-emerged, so the third day we increased again stimulation amplitude at 2.0 V on the right STN and 1.8 V on the left STN, keeping oral therapy unchanged.

The patient was discharged four days after the admission, apyretic, in good general and neurological condition; blood and urine cultures resulted negative; blood-work normalized.

This is the first case of DHS described in a patient with DBS. The pathophysiology of DHS is poorly understood; it has been supposed that high dopaminergic stimulation, high external temperature and impaired thermoregulation are the main pathogenetic factors, resulting in an excessive dopaminergic activity in the striatum [3,4].

In our case, the patient underwent an elevated stimulation on the basal ganglia output, both for high daily dose of dopaminergic medications, and for STN electrical stimulation.

It is difficult to establish whether DBS could have played a pathogenic role in this case of DHS, since our patient presented many of the known pathogenic or precipitating factors associated to DHS, such as high-dose levodopa/carbidopa and entacapone, long disease duration,

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hot weather, dehydration and a recent urinary infection. However, it is well known that STN-DBS can cause several types of dyskinesias, in some cases resembling those induced by levodopa [5], and the temporal connection between DBS voltage reduction and clinical outcome in this particular case, may suggest that electrical stimulation has provided a possible adjunctive feature for the development of DHS, or at least in the maintenance of the dyskinetic status.

The treatment of DHS is empirical, consisting in reduction of dopaminergic load, support of vital functions and treatment of trigger factors [1]. In case of DHS in a patient with DBS, we suggest reducing partly dopaminergic oral therapy and partly DBS stimulation parameters, so as to act on both potentially dyskinetic factors and avoid complications due to abrupt dopaminergic withdrawal.

Declaration of interest

The Authors have no sources of funding and no conflicts of interest to declare.

Ethics

The Authors confirm that they have read the Journal's information pages on “Ethics in publishing” and “Ethical guidelines for journal publication”, and they affirm that this work is consistent with those guidelines.

The Authors guarantee that the patient has given his consent to anonymously report their clinical reports.

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