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CASE REPORT Open Access

Parkinsonism-hyperpyrexia syndrome after withdrawal of antiparkinsonian drugs and deep brain stimulation surgery

Chun-Lei Han[1], Yan Ge[2], Da-Wei Meng[3], Jian-Guo Zhang[3] and Fan-Gang Meng[1*]

Abstract

Background: Parkinsonism-hyperpyrexia syndrome (PHS) is a rare but potentially fatal condition in patients with Parkinson's disease. Deep brain stimulation (DBS) is a widely used and efficacious treatment for advanced Parkinson's disease.

Case presentation: Here, we report a case of PHS in a patient who first underwent withdrawal of antiparkinsonian medications and then bilateral subthalamic nucleus DBS.

Conclusions: Patients should be advised to gradually decrease rather than suddenly stop antiparkinsonian medications when they must stop taking a medication and antiparkinsonian medications should be reintroduced as soon as possible after surgery.

Keywords: Parkinson's disease, Deep brain stimulation, Parkinsonism-hyperpyrexia syndrome

Background

Parkinsonism-hyperpyrexia syndrome (PHS) is a rare but potentially fatal condition in patients with Parkinson's disease (PD) and is manifested by pyrexia, muscle rigidity, a reduced level of consciousness, and autonomic instability. It is generally believed that rapid withdrawal of antiparkinsonian drugs or abrupt changes in medication regimens is the primary cause of this syndrome [1, 2]. Deep brain stimulation (DBS) is a widely used and efficacious treatment for advanced Parkinson's disease. Antiparkinsonian drugs are transiently stopped before the procedure to check the patient's response during the procedure when the patient is in the "off" state. However, sudden discontinuation of medications before or after DBS surgery had been reported to provoke PHS [3, 4]. In addition, the surgery itself may also provoke the condition. Here, we reported a case of PHS in a patient who firstly underwent withdrawal of antiparkinsonian medications and then bilateral subthalamic nucleus (STN) DBS.

Case presentation

A 69-year-old woman with a 24-year history of Parkinson's disease and the use of a variety of antiparkinsonian drugs was admitted on February 27, 2014. Her disease had gradually progressed, and the drugs were less effective, despite increased dosages and changes in drug families. Before admission, she had been experiencing serious motor complications, including wearing-off and dyskinesia, and she was taking levodopa/benserazide 500 mg/day, carbidopa/levodopa 500 mg/day, selegiline 12.5 mg/day, trastal 150 mg/day and amantadine 100 mg/day. After admission, the drugs were gradually discontinued in order to alleviate the dyskinesia (Fig. 1). However, it had no effect. A levodopa test, which compared the Unified Parkinson Disease Rating Scale Part III (motor score) before and after oral intake of levodopa, showed a more than 30% improvement, which indicated that the patient was a suitable candidate for STN-DBS. Bilateral STN stimulation was commenced 5 days after admission. Eight hours before surgery, all PD medications were stopped. Bilateral STN-DBS was performed as described in the literature [4]. During the procedure, the patient was cooperative but exhausted. After recovering from the general anesthesia, the patient was unable to communicate properly. During the night, the patient developed severe muscle rigidity, tremors, continuous

* Correspondence: fgmeng@ccmu.edu.cn
[1]Beijing Neurosurgical Institute, Capital Medical University, No. 6 Tiantan Xili, Dongcheng District, Beijing 100050, China
Full list of author information is available at the end of the article

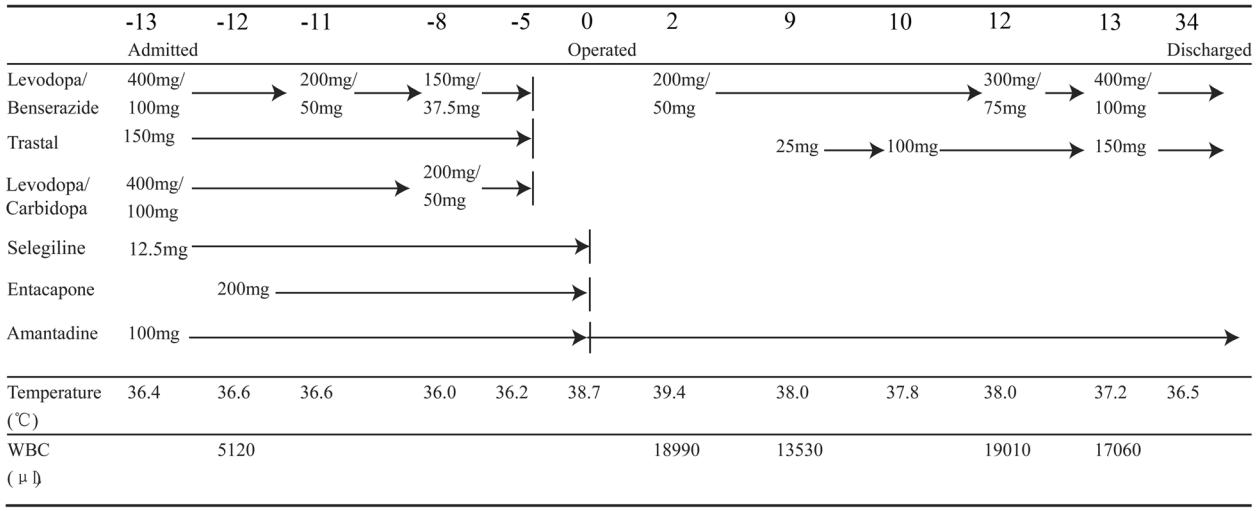

Fig. 1 The antiparkinsonian medication adjustment process of a 69-year-old woman diagnosed with Parkinson's disease and treated with DBS of the STN. WBC, white blood cells. Row 1 indicates the date in "day/month" format

limb shaking, head tremor and trismus. She was febrile, with a temperature of 39.8°C, and had diaphoresis, a pulse rate of 132 beats/min, a respiratory rate of 24 breaths/min, and sustained increasing in blood pressure up to 178/117 mmHg. Her consciousness gradually declined approximately 11 h after DBS. Laboratory tests were normal with the exception of an elevated white blood cell count (18.0×10^9/L). A computed tomography (CT) scan of the brain showed correct placement of the electrodes without evidence of blood or other abnormalities. The next day, the patient was admitted to the intensive care unit. Intravenous fluid replacement and cooling of the body were initiated, and complications were managed. In the next 7 days, a series of tests were run to determine the cause of her condition. An evaluation to determine potential sources of infection was unrevealing. The evaluation of her febrile condition included a chest x-ray, thyroid function tests, routine stool tests, routine urine tests and a bacterial culture analysis; however, causative factors were not identified. A cerebrospinal fluid (CSF) examination was also normal. On the day of surgery and on postoperative days 1, 2, 3, 6, and 12, brain CT showed normal postoperative changes; however, a left frontal cerebral infarction occurred on the 2nd day after the operation (Fig. 2). On day 7 postoperatively, when infection, cerebral infarction and intracerebral hemorrhage were all excluded, the diagnosis of PHS was made. Antiparkinsonian medications were immediately reinstated, and the patient's symptoms began to improve. Levodopa/benserazide was initiated at 250 mg/day and increased to 500 mg/day, trastal was initiated at 25 mg/day and increased to 150 mg/day, and amantadine 100 mg/day per day was initiated (Fig. 1). By the 28th day after surgery, the patient's condition had gradually returned to her preoperative status. Her consciousness recovered, and her vital signs and laboratory tests returned to baseline levels (Fig. 3).

Discussion

It has been reported repeatedly that acute withdrawal of antiparkinsonian drugs in PD patients is considered to be the sole cause of PHS. Apart from these medication-related causes, physiological stressors, such as surgery, injury, may also precipitate PHS [5]. Overnight withdrawal of antiparkinsonian drugs in PD patients is widely performed before DBS surgery to aid in the identification of the optimal macrostimulation response site during surgery. Thus, withdrawal of antiparkinsonian drugs combined with further surgery is more likely to cause the complication than either factor alone. Until now, about 5 cases of PHS after DBS surgery have been documented; 3 of these cases occurred due to perioperative drug cessation [4, 6, 7], while, the other 2 cases occurred 6 and 8 days after antiparkinsonian drug dosages were reduced abruptly when the DBS system was activated [3, 8]. In our case, the patient first experienced rapid reduction of antiparkinsonian drugs due to dyskinesia. However, there was no improvement, which eventually made her received DBS surgery. After surgery, PHS happened and a left frontal cerebral infarction occurred on the 2nd day after surgery. However, it is uncertain whether the occurrence of cerebral infarction precipitated PHS or not. PHS occurred eventually and was characterized by hyperthermia, extreme muscle rigidity, autonomic instability, and altered consciousness. At first, the patient's condition was not considered to be PHS because of a lack of experience with this disorder and confounding factors such as the possibility of infection and cerebral infarction. The differential diagnosis included infection, cerebral infarction and intracerebral

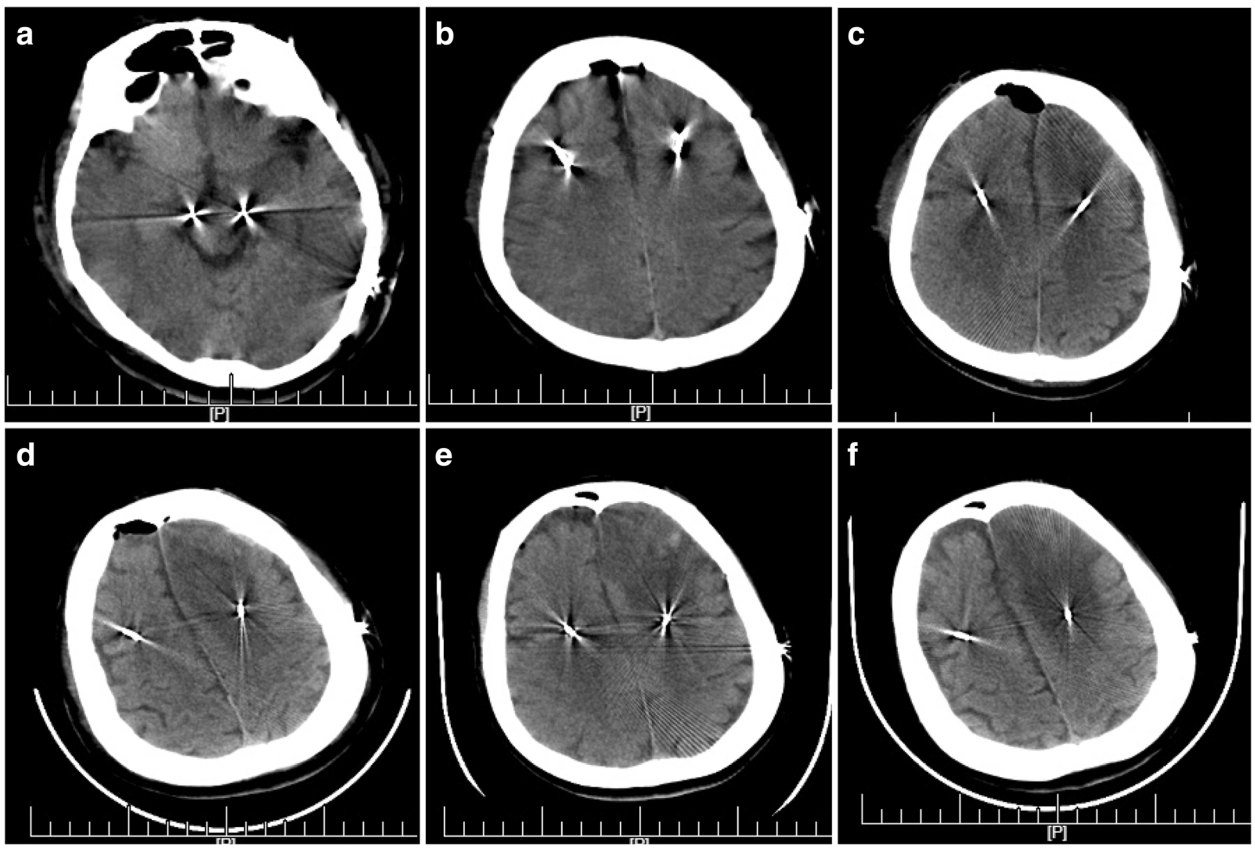

Fig. 2 Postoperative CT showed correct placement of the electrodes (**a**-**b**) and a suspicious left frontal cerebral infarction on the 2nd, 3rd, 6th and 12th days after operation (**c**-**f**)

hemorrhage. Infection was excluded based on CSF analysis, an x-ray, routine stool tests, routine urine tests and bacterial culture analysis. CT of the brain revealed no intracerebral hemorrhage but showed a left frontal cerebral infarction. Thus, in the first 7 days after surgery, only symptomatic treatment was administered. Finally, when infection, cerebral infarction and intracerebral hemorrhage were all excluded, the diagnosis of PHS was made, and antiparkinsonian medications were gradually prescribed. The patient' condition returned to her preoperative status with clear consciousness and stable vital signs when discharged.

Conclusions

In summary, patients should be advised to gradually reduce rather than suddenly stop antiparkinsonian medications when they must stop taking a medication due to significant side effects. Once a patient is seen to have very high fever, extreme muscle rigidity, autonomic instability,

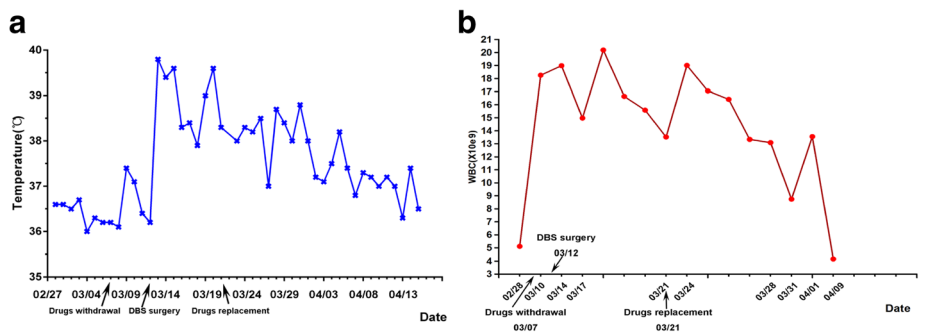

Fig. 3 The patient's temperature (**a**) and white blood cell (WBC) counts during treatment (**b**). Her temperature and WBC counts increased after the withdrawal of antiparkinsonian drugs and deep brain stimulation surgery but returned to normal after reinstatement of the medication

and altered consciousness, PHS should be considered. Moreover, antiparkinsonian medications should be reintroduced as soon as possible after surgery. In the event that a patient develops PHS, it should be treated as a neurological emergency. The key to success is early diagnosis and initiation of treatment. Finally, we should consider the possibility that DBS surgery itself, as a physiological stressor, may precipitate PHS.

Abbreviations
CT: Computed tomography; DBS: Deep brain stimulation; PD: Parkinson's disease; PHS: Parkinsonism-hyperpyrexia syndrome; STN: Subthalamic nucleus

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Availability of data and materials
Not applicable.

Authors' contributions
CH contributed to the data collection and writing. YG and DM were involved in the surgery and participated the data collection. JZ and FM were the surgeons who performed the surgery. FM conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Ethics approval and consent to participate
Written, informed consent was obtained from the patient for publication of this case report and accompanying images.

Author details
[1]Beijing Neurosurgical Institute, Capital Medical University, No. 6 Tiantan Xili, Dongcheng District, Beijing 100050, China. [2]Department of Neurosurgery, Beijing Fengtai Hospital, Beijing 100071, China. [3]Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China.

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