

**CASE REPORT**

A Patient with Recurrent Dyskinesia and Hyperpyrexia Syndrome

Min Seok Baek, Hyung Woo Lee, Chul Hyung Lyoo

Department of Neurology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

ABSTRACT

Dyskinesia hyperpyrexia syndrome is a rare medical emergency in Parkinson's disease. It is characterized by continuous dyskinesia associated with hyperthermia, rhabdomyolysis, and alteration of the mental state. We present the case of a 74-year-old woman who presented with recurrent dyskinesia hyperpyrexia syndrome. Although some provocation factors and clinical manifestations seem to be shared with parkinsonism hyperpyrexia syndrome, a clear distinction in management should be considered.

Key Words Parkinson's disease; dyskinesia; hyperpyrexia.

Dyskinesia hyperpyrexia syndrome is a rare movement disorder emergency in Parkinson's disease (PD). It is characterized by severe continuous dyskinesia associated with rhabdomyolysis, hyperthermia, and subsequent alteration of the mental state.¹ We report a PD patient who presented with recurrent dyskinesia and hyperpyrexia syndrome.

CASE REPORT

A 74-year-old woman who first presented with a resting tremor in her left hand at age 51 and had been treated with levodopa since age 53 visited an emergency center for continuous generalized choreiform dyskinesia and high fever during the last 24 hours. Six days before the onset of continuous dyskinesia, she had fractures of ribs after falling. The season was spring. She had been taking acetaminophen since the rib fracture, and no other medication was prescribed. She was alert, but visual hallucination and disorientation were noted. Dyskinesia was too severe for her to lie on a bed safely, and body temperature was 40.3°C. She had not eaten well for a few days because of appetite loss. Blood tests showed mild leukocytosis [white blood cell (WBC) 12,100/mm³], elevated creatine kinase (CK; 1,023 IU/mg), and urine myoglobin (58,611 µg/L). Blood urea nitrogen (BUN)

was 35 mg/dL, and creatinine rose to 1.6 mg/dL. Sputum bacterial culture was sterile, but chest computerized tomography (CT) showed consolidation in both lower lobes, indicating aspiration pneumonia. Intravenous ampicillin and sulbactam were prescribed empirically. She had been taking amantadine (200 mg/day), an extended release (ER) form of pramipexole (1.075 mg/day), and levodopa (375 mg/day) with benserazide for three years. On admission, amantadine and pramipexol were discontinued, and she was sedated with intravenous midazolam infusion in an intensive care unit. When she awakened after four days of sedation, the continuous dyskinesia disappeared. Fever subsided on the 1st day, and the serum CK level was normalized on the 6th day of admission.

During the 19 months after the first attack of serious dyskinesia, she remained stable taking amantadine (300 mg/day), pramipexole ER (1.075 mg/day), and levodopa (500 mg/day) with benserazide. She felt mild peak dose dyskinesia for 30 mins after taking each dose. Seven days before the second attack, she had fallen and experienced trauma to her left flank. She started to show fever and sweating two days before visiting the emergency center for the second attack of continuous dyskinesia after an evening dose. The season was spring. She had been taking acetaminophen for three days, prescribed for flank pain.

Received: April 19, 2017 Revised: May 6, 2017 Accepted: May 12, 2017

Corresponding author: Chul Hyung Lyoo, MD, PhD, Department of Neurology, Gangnam Severance Hospital, Yonsei University College of Medicine, Research Center for Future Medicine, 20 Eonju-ro 63-gil, Gangnam-gu, Seoul 06273, Korea / Tel: +82-2-2019-3326 / Fax: +82-2-3462-5904 / E-mail: lyoochel@yuhs.ac

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

No other nephrotoxic medication was prescribed. Her mental status was alert without confusion at the time of arrival, but after several hours, her dyskinesia grew worse and she became confused. Body temperature was 39.2°C. Her blood test showed mild leukocytosis (WBC 10,090/mm³). Renal function was decreased with elevated BUN (50.3 mg/dL) and serum creatinine (1.17 mg/dL). Serum CK (661 IU/L) and urine myoglobin (27,259 µg/L) levels were elevated (Figure 1). Although there were limitations due to motion artifacts, a chest CT scan showed ill-defined ground-glass opacity in both lower lobes. No space-occupying inflammatory lesion was observed. Since low C-reactive protein (1.7 mg/L), bacterial culture of sputum and a rapid influenza diagnostic test were negative, pneumonia was not considered as a fever source. Antibiotics were not prescribed. We discontinued pramipexole and reduced the levodopa dose to 300 mg/day. After conservative treatment with intravenous hydration and antipyretics, her continuous generalized dyskinesia disappeared 20 hours after the initial onset of dyskinesia. Mental status and body temperature returned to normal. Six days after the onset of dyskinesia, the serum CK level was normalized.

DISCUSSION

Dyskinesia hyperpyrexia syndrome is a rare complication of PD. It is characterized by severe continuous dyskinesia associated with rhabdomyolysis, hyperthermia, and subsequent alteration of the mental state. Previously, only three cases had been reported in the English literature since its first description in 2010 (Table 1). In all three previous cases, the patients were characterized by long-duration PD with motor symptom fluctuation on dopaminergic medication.^{1,3,4} In one case, ropinirole medication was added before the attack,⁴ while in the other cases, no medication regimen change before the attack was reported.^{1,3} Two of the three patients suffered fever spiking before the attack.^{1,3} The underlying mechanisms of dyskinesia hyperpyrexia are still not well understood but are probably related to impairment of the dopamine buffering capacity of the striatum,⁴ the administration of D-3 agonist,⁴ and thermostatic deregulation.³ Tapering off of dopaminergic agonist medication and continuous dopaminergic stimulation seemed beneficial, but one case of dyskinesia hyperpyrexia syndrome despite continuous levodopa enteral infusion was also reported.⁴ In our patient, recurrent-onset continuous dyskinesias were reported. CK elevation was remarked in both events. Although

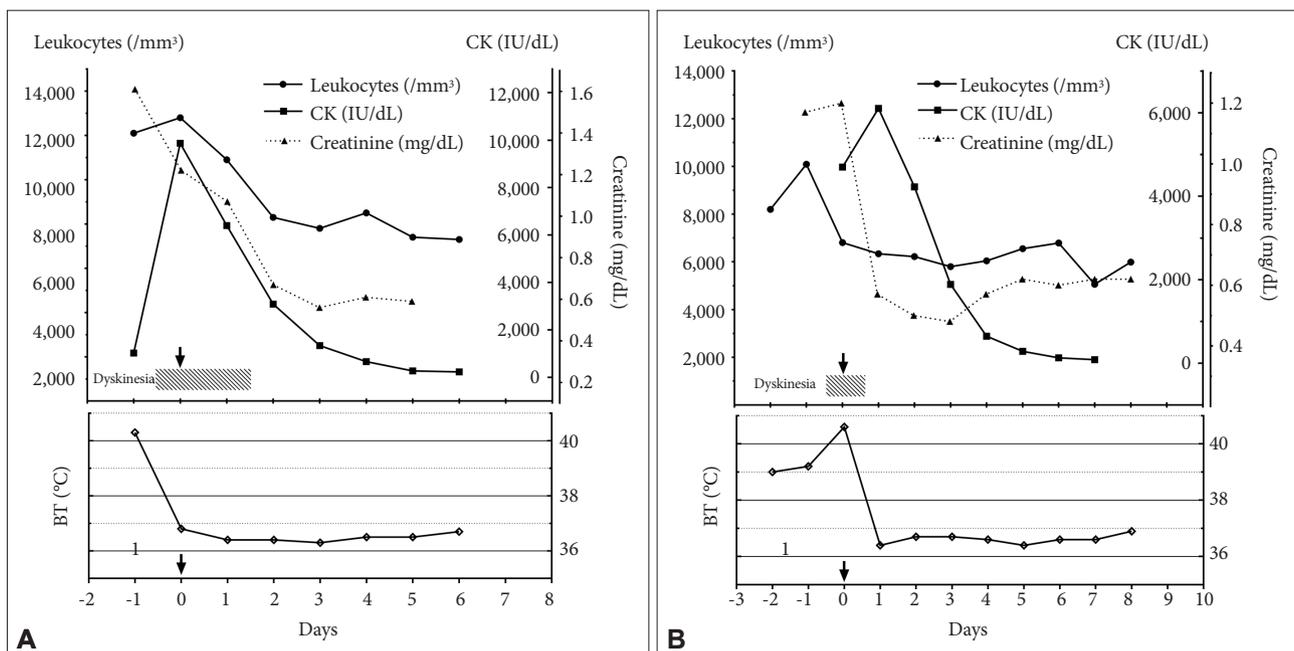


Figure 1. Clinical course and laboratory results. Temporal changes in clinical and laboratory findings during the first (A) and second (B) attacks of dyskinesia-hyperpyrexia syndrome. Arrows indicates first visit to emergency room. Marked areas designate the duration of continuous dyskinesia. CK: creatine kinase, BT: body temperature.

Table 1. Overview of four affected individuals with dyskinesia hyperpyrexia syndrome

Authors	Age/sex	Season	PD duration (years)	Suspected provocation factor	Symptoms	Duration of dyskinesia/hyperpyrexia	Medication (mg/day)	Treatment
Gil-Navarro and Grandas ¹	68/F	NA	12	NA	Generalized dyskinesia, confusion, hallucination, drowsiness, hyperpyrexia	Few days	Levodopa 750 Pramipexole 4 Amantadine 200	Pramipexol tapered off quetiapine 25 mg added
Taguchi et al. ²	70/F	Fall	13	Recent medication change (pramipexole IR→ER)	Generalized dyskinesia, hallucination, hyperpyrexia	7 days	Levodopa 600 Pramipexole 3	Reduction of dopaminergic drugs
Herreros-Rodríguez et al. ³	83/F	Summer	25	Seasonal variation	Generalized dyskinesia, hyperpyrexia	Few days (8 recurrent episodes)	Levodopa 150 Amantadine 100	Levodopa enteral infusion
Acebrón Sánchez-Herrera et al. ⁴	66/F	Summer	16	Trauma/recent medication addition (ropinirole due to RLS)	Generalized dyskinesia, confusion, hallucination, hyperpyrexia	4 days	Levodopa 1,450 (enteral infusion) Amantadine 200 Ropinirole 8	Reduction of dopaminergic drugs

IR: immediate release, ER: extended release, RLS: restless leg syndrome, PD: Parkinson's disease.

an underlying infection might have co-existed with hyperpyrexia, the relatively short duration of fever and immediate subsidence after the discontinuation of dyskinesia more strongly implies hyperpyrexia. In this circumstance, a diagnosis of dyskinesia hyperpyrexia syndrome was made.

This case showed a rare movement disorder emergency, which occurred recurrently without recent dopaminergic medication changes. Prior traumas and fever spiking were followed by continuous dyskinesia, with subsequent serum CK and creatinine elevation. The symptoms probably resolved with levodopa tapering and the discontinuation of dopaminergic medication.

The patient shares some clinical characteristics of parkinsonism hyperpyrexia syndrome (PHS), such as hyperthermia and rhabdomyolysis. The provocation factors of PHS include infectious disease, trauma, surgery, or treatment manipulation, especially the withdrawal of levodopa, which were observed in a previous cohort study.⁵ The underlying mechanism is implicated by the sudden suppression of central dopaminergic activity and alteration in the central serotonin metabolism.

Considering the patient's history of a recent fall, appetite loss and fever spiking preceding the attack of continuous dyskinesia in this case, some provocation factors seem to affect both PHS and dyskinesia hyperpyrexia syndrome. In contrast to PHS, dyskinesia hyperpyrexia syndrome is probably due to the excessive stimulation of central dopaminergic activity. Since no dopaminergic medication had been changed in our patient, a reduced buffering capacity for dopaminergic medication could play a role. Trau-

mas, infection and dehydration could be related to alteration of the dopaminergic buffering capacity. Further investigation of the provocation factors of dyskinesia hyperpyrexia syndrome is warranted.

In PHS, treatment is based on intravenous hydration and an addition or increase in the dose of dopaminergic medication. In contrast, dyskinesia hyperpyrexia syndrome should be treated with the reduction of dopaminergic medication. Consequently, rapid recognition and application of a treatment plan are essential in this life-threatening movement disorder emergency.

Conflicts of Interest

The authors have no financial conflicts of interest.

Acknowledgments

This study was financially supported by the "Mirae Medical" Faculty Research Assistance Program of Yonsei University College of Medicine (grant number 6-2016-0162) and Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (2017R1A2B2006694).

REFERENCES

- Gil-Navarro S, Grandas F. Dyskinesia-hyperpyrexia syndrome: another Parkinson's disease emergency. *Mov Disord* 2010;25:2691-2692.
- Taguchi S, Niwa J, Ibi T, Doyu M. Dyskinesia-hyperpyrexia syndrome in a patient with Parkinson's disease: a case report. *Clin Neurol* 2015;55:182-184.
- Herreros-Rodríguez J, Sánchez-Ferro Á. Summertime dyskinesia-hyperpyrexia syndrome: the "dual heat" hypothesis. *Clin Neuropharmacol* 2016;39:210-211.
- Acebrón Sánchez-Herrera F, García-Barragán N, Estévez-Fraga C, Martínez-Castrillo JC, López-Sendón Moreno JL. Dyskinesia-hyperpyrexia syndrome under continuous dopaminergic stimulation. *Parkinsonism Relat Disord* 2017; 36:103-104.

5. Thomas A, Onofrj M. Akinetic crisis, acute akinesia, neuroleptic malignant-like syndrome, Parkinsonism-hyperpyrexia syndrome, and malignant syndrome are the same entity and are often independent of treatment withdrawal. *Mov Disord* 2005;20:1671; author reply 1671-1672.