OMCR

Oxford Medical Case Reports, 2018;11, 382–386

doi: 10.1093/omcr/omy089
Case Report

CASE REPORT

Accidental hypothermia in Parkinson's disease

Hiroshi Kataoka*, Nobuyuki Eura, Takao Kiriyama, Yuto Uchihara and Kazuma Sugie

Department of Neurology, Nara Medical University, Kashihara, Nara, Japan

*Correspondence address. Department of Neurology, Nara Medical University, 840 Shijo-cho, Kashihara, Nara 634-8522, Japan. Tel: +81-744-29-8860; Fax: +81-744-24-6065; E-mail: hk55@naramed-u.ac.jp

Abstract

We describe two patients with Parkinson's disease who presented with accidental hypothermia and review seven patients to delineate the characteristics of hypothermia. All cases of hypothermia occurred in the winter. As clinical symptoms preceding the onset of hypothermia, deterioration of bradykinesia or limb coldness was evident. Most cases of hypothermia were accompanied by impaired consciousness and deterioration of parkinsonian features. After warming the body, the hypothermia improved in a relatively short period. Levodopa, dopamine agonists or anticholinergic agents were given to five patients, three patients and three patients, respectively. Bradykinesia developed in most patients a short time before the onset of hypothermia. In various neurological diseases, deterioration of the disease can occur on the background of metabolic/electrolyte disturbance. However, the fact that the bradykinesia developed a short time prior to the onset of hypothermia warrants close observation for signs of temperature dysregulation in patients with substantial neurologic deterioration, especially in the winter.

INTRODUCTION

Accidental hypothermia is often serious in neurodegenerative diseases. Because five cases of accidental hypothermia have been reported in patients with Parkinson's disease (PD) [1–4], the characteristics of the hypothermia associated with PD remain uncertain. We describe two patients with PD who presented with accidental hypothermia.

CASE REPORTS

Patient 1

In 2010, a 68-year-old man presented with the slowness in his right leg and resting tremor in his left hand. At that time, the early (1.48) and delayed H/M ratios (1.41) on myocardial ^{123}I-MIBG uptake testing was decreased. In 2012, he consulted our hospital, and parkinsonian features such as bradykinesia, left-dominant rigidity and left-hand resting tremor were evident. These features responded to levodopa (300 mg/d) and trihexyphenidyl (2 mg/d). Schellong test did not show a drop in systolic and diastolic blood pressures of >20 and >10 mmHg, respectively, with change in position from sitting to standing. By 2016, the severity of PD had slowly progressed to Hoehn–Yahr stage 4, and trunk flexion was also evident. In early February 2017, bradykinesia developed over the course of 1 week, and the patient required considerable assistance to perform activities of daily living. Finally, he was admitted to our hospital because of impaired consciousness, severe bradykinesia, and coldness of the body. On the day of admission, his consciousness was mildly impaired, the body temperature was 33°C, and rigidity in all four limbs had markedly increased. Motor paresis was absent. Cranial CT was normal. Electrocardiography showed bradycardia without Osborn waves. WBC (2900/μL) and the serum CRP (0.2 mg/dL) were not elevated,

Received: June 4, 2018. **Revised:** July 25, 2018. **Accepted:** August 31, 2018

and the thyroid function was normal. Twelve hours after warming his body with an electric blanket in addition to providing volume resuscitation, the hypothermia improved. On Day 2, brain MRI showed an acute cerebral lacunar infarction in the right corona radiate. On Day 5, the patient resumed an alert level of consciousness. One month after admission, the patient had regained his former clinical state.

Patient 2

A 73-year-old man noticed bradykinesia in 2004. In 2005, he had some difficulty in walking and visited our hospital. He showed parkinsonian features, including bradykinesia, cogwheel rigidity in all four limbs, stooped posture and frozen gait, and these signs and symptoms responded to treatment with levodopa (300 mg/d). After 2006, treatment with pramipexole followed by subsequent treatment with selegiline was begun because bradykinesia had developed. In 2009, droxidopa was initiated because of dizziness due to hypotension. In June 2011, the early (1.94) and delayed (1.32) H/M ratios decreased on myocardial ^{123}I-MIBG uptake testing. A few months later in November 2011, systolic and diastolic blood pressures dropped from 141 and 68 mmHg (supine position) to 72 and 50 mmHg (sitting position), respectively. Wearing-off developed, and the patient was given daily levodopa (300 mg), pramipexole (2 mg), selegiline (7.5 mg), entacapone (200 mg) and droxidopa (600 mg). In the latter part of February 2012, he noticed dizziness and coldness in all four limbs 3 days before admission and had difficulty in walking. On the night before admission, shouting and unintentional hand movements occurred. On the day of admission, the level of consciousness had decreased in association with increased rigidity and bradycardia. The body temperature was 30°C. Electrocardiography showed bradycardia with Osborn waves. Echocardiography and cranial MRI showed normal findings. The WBC (12 500/μL) and CRP (1.9 mg/dL) were mildly elevated, and the thyroid function was normal. In the evening, myoclonus was evident. Seven days after the admission, intestinal paresis and hypohidrosis had developed. His body was warmed for 1 day with the use of an electric blanket, volume resuscitation was provided, and the hypothermia improved. Three weeks after admission, tilt table testing showed a significant drop in his blood pressure in the supine position from 182/98 to 110/80 mmHg on 5 min after an inclination of 45°. At 5 weeks post-admission, early and delayed H/M ratios on myocardial ^{123}I-MIBG uptake testing was further decreased to 1.82 and 1.17, respectively. Six weeks after admission, a thermal sweat test by means of iodine starch showed lack of sweating on his trunk and on all four limbs except for his palms after 30-min rest at a room temperature of 40°C. Seven weeks after admission, 24-h BP measurements demonstrated a non-dipper pattern during sleep and systolic blood pressures fluctuated between 190 and 95 mmHg. An organic causable abnormality for intestinal paresis was not detected on colonoscopy or abdominal CT. These findings suggest that intestinal paresis and hypohidrosis were features of autonomic failure. Two months after admission, the clinical status was restored to the former clinical state.

H/M ratios on myocardial ^{123}I-MIBG uptake testing were decreased in the two patients. Cranial MRI findings were normal at presentation to our hospital. Neither patient was given neuroleptics. Both patients had not the other common causes of hypothermia such as hypothyroidism, hypoglycemia or diabetic mellitus

REVIEW OF SEVEN PATIENTS WITH HYPOTHERMIA

Most cases of hypothermia occurred in the winter (Table 1). The duration of PD ranged from 1 to 13 years, and the Hoehn–Yahr stage varied from 2 to 4. As clinical symptoms preceding the onset of hypothermia, deterioration of bradykinesia was evident in six patients, limb coldness occurred in two patients and one patient sometimes had a low body temperature. Most cases of hypothermia were accompanied by impaired consciousness and deterioration of parkinsonian features. Electrocardiography showed Osborn waves in four patients. In one patient, subsequent cardiopulmonary arrest occurred transiently. After warming the body, the hypothermia improved in a period ranging from 12 h to several days.

DISCUSSION

Hypothermia occurred in the winter despite a well-heated house. Neurologists sometimes encountered patients with PD who complained of severe skin coldness during the winter, and their skin was actually very cold. A histological study of skin specimens in patients with PD demonstrated decreased autonomic innervation of cutaneous vessels [5]. The hypothalamus has an important role in the maintenance of body temperature. Thermoregulatory central autonomic failure has been shown to be caused by hypothalamic lesions [6]. Pathologically, Lewy bodies were seen in the hypothalamus or skin in addition to other autonomic regulatory regions, such as intermediolateral nucleus of the thoracic cord [7]. The pathological severity of PD might be prerequisite to the development of hypothermia. The reduced H/M ratios on myocardial ^{123}I-MIBG uptake testing has been known to be associated with Lewy body diseases, such as PD. Some studies have reported a greater decrease in the H/M ratios with increasing disease severity [8]. The H/M ratios was highly decreased in two patients and the decrease in the early and delay H/M ratios in patient 2 was developed at the second examination. The loss of cardiac sympathetic activity may be correlated with the development of the autonomic dysfunction in PD.

Another interesting possible cause of hypothermia has been proposed. Hama *et al.* [2] speculated that a dopamine D2 agonist can affect thermal homeostasis mechanisms. An experimental animal study using dopamine D2 agonists such as pramipexole showed that dopamine D2-receptor stimulation induced hypothermia in a cold environment by reducing heat production [9]. In our series, dopamine agonists were used in three patients, and two patients were receiving pramipexole. However, the patient 1 was not received this type of medication. The confirmation of this speculation will be needed for a larger study of PD with hypothermia.

Patient 1 had an acute cerebral lacunar infarction in the right corona radiate, and this may have accelerated the worsening of his PD condition.

Patient 2 had orthostatic hypotension and severe loss of sweating, suggesting a diagnosis of multiple system atrophy. However, these autonomic dysfunctions were evident 5 years after the initial motor symptom of PD. Patient 1 had no evidence of autonomic failure expect for constipation. Moreover, H/M ratios on myocardial ^{123}I-MIBG uptake testing was decreased in both patients. Patient 1 experienced temporary hallucinations 3 years after the onset of PD, whereas Patient 2 did not experience any hallucinations during the course of the disease. We believe both patients were not derived from PD with autonomic dysfunction rather than multiple systemic atrophy or dementia with Lewy bodies.

Table 1: Clinical characteristics of patients with Parkinson's disease who showed hypothermia

	Patient 1	Patient 2	Patient 3 [1]	Patient 4 [2]	Patient 5 [3]	Patient 6 [4]	Patient 7 [4]
Age/Sex	68/M	71/M	80/F	58/M	89/F	73/F	61/F
Disease duration (years)	6.5	7.5	3	13	10	4	1
Hoehn–Yahr stage[a]	4	3 (on periods), 4 (off periods)	3	3 (on periods), 5 (off periods)	2	3 (on periods), 5 (off periods)	NA
Motor fluctuations[a]	–	+	–	+	+	NA	NA
Dementia[a]	–	–	–	+	NA	+	+
Autonomic symptoms[a]	Constipation	Constipation, orthostatic hypotension	NA	NA	NA	NA	NA
Hypothermia							
Onset time	Winter	Winter	Winter	Winter	NA	NA	Winter, very cold weather
House room conditions	Well-heated house	Well-heated house	Well-heated house	NA	Keeping room temperature around 20°C	NA	Extremely cold room
Symptoms preceding the onset of hypothermia	Progressing bradykinesia in 1 week	3 Days before, dizziness, progressing bradykinesia and coldness in four limbs, 1 day before, shouting or unintentional hand movements	Lethargy and bradykinesia in a few days	Low body temperature below 35°C in the weeks	Prominent deterioration of motor slowness (Hoehn–Yahr stage IV) in recent 2 months, new onset of mutism 1 day before	1 week before, retired to bed, and felt very cold	Few weeks before, became slow and unsteady on her feet
Symptoms just before the onset of hypothermia	Impairment of consciousness, coldness in four limbs	Impairment of consciousness	After breakfast, movement gradually became impaired	Impairment of consciousness	Slight response to outside stimuli	Stuporous condition, responded only to painful stimulation	Become drowsy, mute and staring into space unresponsively
Body temperature (°C)	33	30	29.7 (Core temperature)	33.1 (Rectal temperature)	30.9	32.8 (Rectal temperature)	35.9
Blood pressure (mmHg)	90/62	98/70	87/52	107/68	112/67	120/80	120/80
Heart rate (/min)	45	44	38	45	50	100	70
Glasgow coma scale	14	10	12	Coma status with his eyes opening spontaneously	8	ND	Confused
Rigidity	Markedly worsened	Markedly worsened	Mild	Markedly worsened	Markedly worsened	Marked worsened	Markedly worsened
Involuntary movements	–	–	Tremor in four limbs	–	Myoclonus in the hands	Flapping tremor in the hands	Flapping tremor in the hands

Continued

Table 1: Continued

	Patient 1	Patient 2	Patient 3 [1]	Patient 4 [2]	Patient 5 [3]	Patient 6 [4]	Patient 7 [4]
Electrocardiogram	Bradycardia	Osborn waves, bradycardia, atrioventricular block	Osborn waves, bradycardia, QT prolongation	Osborn waves, bradycardia	Osborn waves, bradycardia	Normal	Normal
Subsequent complications	Cerebral lucunar infarction	Myoclonus, intestinal paresis, hypohidrosis	–	Cardiopulmonary arrest, but it soon resolved	–	–	–
Daily treatment when development of hypothermia (dose/d)							
Carbidopa-levodopa (mg)	500	300 (benserazide)	400	550	700	–	–
Pramipexole (mg)	–	2	4.5	–	–	–	–
Cabergoline (mg)	–	–	–	2	–	–	–
Selegiline	–	7.5	5		–	–	–
Trihexyphenidyl (mg)	2	–	–	–	Benzhexol	Benzhexol	
Entacapone	–	200	–	–	–	–	–
Droxidopa	–	600	–	–	–	–	–
Neuroleptics	–	–	–	Quetiapine (50 mg/d)	–	–	Nortriptyline (50 mg/d)
Outcome							
Warming with an electric blanket or pad	+	+	+	+	+	+	-
Intravenous warm saline	–	–	–	+	–	–	–
Period to resolution of hypothermia	12 h	1 day	12 h	Slowly improved	Several days	12 h	48 h
Clinical state	Regained his former clinical state	Regained his former clinical state	Regained her former clinical state	No sequelae	ND	Regained her former clinical state	Regained her former clinical state[b]
Recurrence	None	None	None	None	ND	ND	ND

[a]Before the onset of hypothermia; [b]spontaneously improved; NA, not available.

CONCLUSION

In various neurological diseases, deterioration of the disease can occur on the background of metabolic/electrolyte disturbance. Bradykinesia frequently occurs in the general population among persons who present with moderate hypothermia (32–35°C) as well as apathy or confusion [10]. Our observation that the severity of PD was worsen along with hypothermia is not a novel one. However, the fact that the bradykinesia developed a short time prior to the onset of hypothermia in most patients warrants close observation for signs of temperature dysregulation in patients with substantial neurologic deterioration, especially in the winter.

CONFLICT OF INTEREST

The authors report no conflicts of interest related with our article.

FUNDING

There was no financial disclosure related with our article.

ETHICS STATEMENT

No investigations or interventions were performed outside of routine clinical care for this patient. As this is a case report, without experimental intervention into routine care, no formal research ethics approval was required. Written, fully informed consent was obtained from the patient. This case study describes routine clinical care provided for a patient only.

REFERENCES

1. Sehara Y. Hypothermia with Osborn waves in Parkinson's disease. *Intern Med* 2009;**48**:615–8.
2. Hama K, Miwa H, Kondo T. Life-threatening hypothermia in Parkinson's disease. *Mov Disord* 2009;**24**:945–6.
3. Li BY, Lou M. Severe hypothermia in Parkinson's disease. *CNS Neurosci Ther* 2012;**18**:864–6.
4. Gubbay SS, Barwick DD. Two cases of accidental hypothermia in Parkinson's disease with unusual E.E.G. findings. *J Neurol Neurosurg Psychiatry* 1996;**29**:459–66.
5. Dabby R, Djaldetti R, Shahmurov M, Treves TA, Gabai B, Melamed E, *et al*. Skin biopsy for assessment of autonomic denervation in Parkinson's disease. *J Neural Transm* 2006;**113**:1169–76.
6. De Marinis M, Stocchi F, Testa SR, De Pandis F, Agnoli A. Alterations of thermoregulation in Parkinson's disease. *Funct Neurol* 1991;**6**:279–83.
7. Micieli G, Tosi P, Marcheselli S, Cavallini A. Autonomic dysfunction in Parkinson's disease. *Neurol Sci* 2003;**24**:S32–4.
8. Rascol O, Schelosky L. 123I-metaiodobenzylguanidine scintigraphy in Parkinson's disease and related disorders. *Mov Disord* 2009;**24**:S732–41.
9. Collins GT, Newman AH, Grundt P, Rice KC, Husbands SM, Chauvignac C, *et al*. Yawing and hypothermia in rats: effects of dopamine D3 and D2 agonists and antagonists. *Psychopharmacology (Berl)* 2007;**193**:159–70.
10. Aalam AF, Aslam AK, Vasavada BC, Khan IA. Hypothermia: evaluation, electrocardiographic manifestation, and management. *Am J Med* 2006;**119**:297–31.