Parkinsonism-Hyperpyrexia Syndrome: A Case Report Emphasizing Early Recognition and Management in Parkinson's Disease

Nguyen, DD[1,2], Rader, H[1,2], Coe, B[1,2], Bell, M[1,2], Qureshi, H[1,2], Olejniczak, M[1,2], McCarron, RE[1,2]
[1]Department of Internal Medicine, LSU Health, New Orleans, LA
[2]Ochsner Medical Center, Kenner, LA

Abstract

Parkinsonism-hyperpyrexia syndrome is an uncommon but severe clinical entity with diverse symptoms, including muscular stiffness, hyperthermia, autonomic dysfunction, respiratory distress, and altered consciousness. PHS can be triggered by the abrupt cessation of dopaminergic agents in Parkinson's disease patients. We present a case of a 67-year-old man with Parkinson's disease who developed PHS due to nonadherence to dopaminergic medications. The patient's condition rapidly deteriorated upon arrival at the Emergency Department, leading to admission and intensive care unit transfer. Supportive measures including intravenous fluids, cooling, and antipyretics were administered, along with reinstating dopaminergic agents and dantrolene for muscle rigidity. Gradual improvement was observed with reintroduced medications, and the patient was eventually discharged in a stable condition. PHS requires prompt recognition and management to prevent serious complications. Health education plays a crucial role in preventing PHS by emphasizing medication adherence and awareness of early symptoms.

Introduction

Parkinsonism-hyperpyrexia syndrome (PHS), also known as neuroleptic malignant-like syndrome (NMLS), akinetic crisis, and malignant syndrome, is a rare but severe clinical entity characterized by a diverse array of symptoms, including hyperthermia, respiratory distress, muscular rigidity, autonomic instability, altered mental status, and involuntary muscle movements. Despite sharing certain clinical features with neuroleptic malignant syndrome (NMS), PHS exhibits distinct underlying pathophysiological mechanisms. NMS primarily results from dopamine D2 receptor antagonism caused by neuroleptic medication use, while PHS is associated with the abrupt cessation of dopaminergic agents.

PHS is an infrequently reported complication of Parkinson's disease (PD), with an incidence of 0.3% and a mortality rate ranging between 4% and 30% [1, 2, 3, 4]. Previous case reports have indicated that the discontinuation of dopaminergic agents or deep brain stimulation in patients with Parkinson's disease can potentially trigger PHS [5, 6]. In this context, we present a compelling case report detailing the hospitalization of an individual who arrived at the Emergency Department (ED) with a new diagnosis of PHS after the sudden withdrawal of dopaminergic agents.

Case Report

A 67-year-old man with a medical history of Parkinson's disease, hyperlipidemia, gastroesophageal reflux disease, and depression, presented to the ED with complaints of confusion and generalized weakness persisting for the past two days and dark urine after an unwitnessed fall that occurred the previous day. The patient was currently on multiple medications, including Symmetrel, Sinemet, Mirapex, Lipitor, Protonix, Centrum Silver multivitamin, and Tylenol. The patient's wife reported that the patient had not been taking his Parkinson's medications as prescribed for the last three days.

Upon arrival at the ED, the patient presented with the following vital signs: heart rate of 93 bpm, blood pressure reading 117/68 mmHg, a body temperature of 102.1℉, respiratory rate of 16 breaths per minute, and oxygen saturation (SpO2) of 94% on room air. The comprehensive metabolic panel revealed several abnormal findings, including hyponatremia, metabolic acidosis, and significantly elevated creatine phosphokinase (CPK) levels. Additionally, the patient's lactate, partial pressure of carbon dioxide (PCO2), and pH were outside the normal range. Notably, troponin levels were within the normal limits, and the electrocardiogram (EKG) displayed a normal sinus rhythm. Chest radiography revealed no signs of acute chest disease, and a head CT scan without contrast showed no evidence of vascular distribution infarct, hemorrhage, mass effect, or midline shift. The patient received 0.9% normal saline in the ED and was subsequently admitted to the LSU Internal Medicine service for further evaluation and management.

Shortly after admission, the patient's clinical condition deteriorated, leading to the development of hypertension and worsening altered mental status, accompanied by temperatures peaking at 103℉ (**Figure 1**). As a result, the patient was transferred to the intensive care unit (ICU), and blood cultures were drawn for analysis. Empiric treatment was initiated with acyclovir, vancomycin, ceftriaxone, and ampicillin as well as labetalol and lorazepam. Supportive measures, including intravenous fluids, cooling blankets, and antipyretics, were implemented. Additionally, all home dopaminergic agents (Symmetrel, Sinemet, and Mirapex) were promptly reinstated. Subsequently, the patient developed chills and substantial muscle rigidity, which prompted the administration of dantrolene.

Throughout the patient's hospitalization, the differential diagnosis included PHS, among other conditions. On hospital day 2, Symmetrel, Mirapex, dantrolene, and all antibiotics were discontinued. The patient remained mildly febrile, with clinical improvements observed in mentation, speech, and muscle rigidity. However, by hospital days 4-6, the patient's mental status and mobility worsened, resulting in somnolence on day 7. By hospital days 9-10, gradual improvement in alertness was noted, along with decreased dysarthria, dysphagia, bradykinesia, and cogwheel rigidity following the reintroduction of Symmetrel and Mirapex. Over the remaining days of admission, the patient's condition improved, leading to a successful step-down from the ICU, and the patient's temperature and CPK levels eventually normalized (**Figure 2**). Ultimately,

the patient was discharged in a stable condition to a long-term acute care facility for continued rehabilitation and physical therapy.

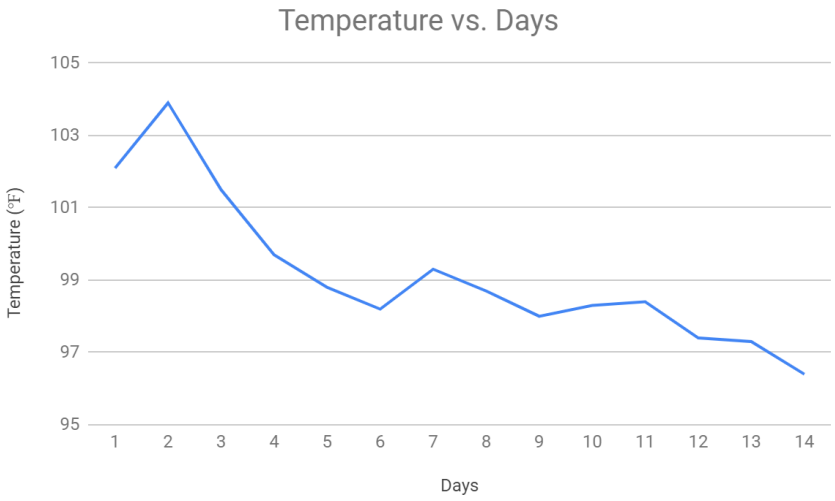

Figure 1. Admission is day 1. Discharge is on day 14.

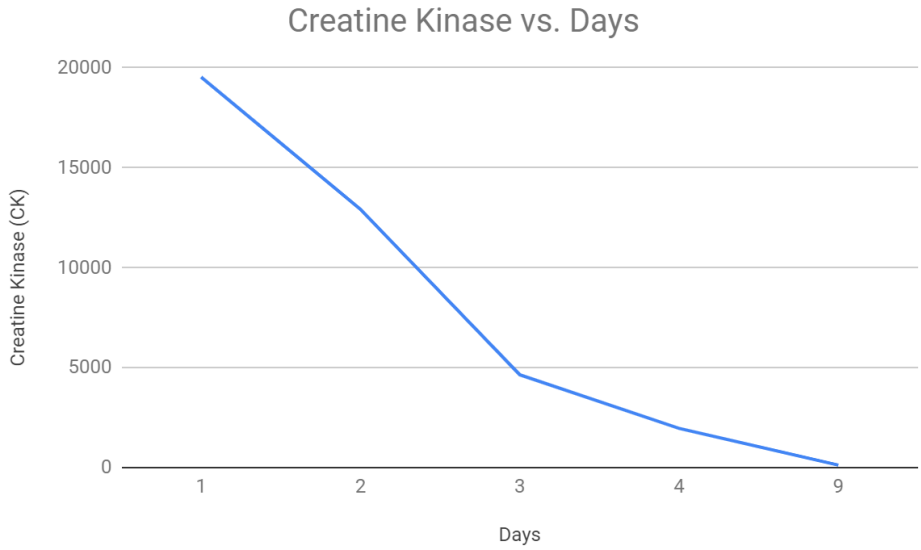

Figure 2. Admission is day 1. CK levels return to baseline by day 9.

Discussion

The clinical presentation of PHS may mimic and overlap with other medical conditions, such as NMS, serotonin syndrome, malignant hyperthermia, cerebrovascular disease, sepsis, meningitis, and encephalitis. Establishing the diagnosis of PHS often requires a comprehensive investigation into the patient's history. Although the exact underlying mechanism remains unclear, dysregulation within the hypothalamus, nigrostriatal system, and the mesocortical

dopaminergic pathways is believed to be involved in PHS development. Left untreated, PHS can lead to serious complications, including acute respiratory and renal failure, aspiration pneumonia, deep venous thrombosis/pulmonary embolism, heart failure, and potentially death [6, 7]. Our patient’s presentation of hyperthermia, altered mental status, and muscular rigidity, combined with recent nonadherence to antiparkinsonian medications, raised our suspicion for PHS.

The management of PHS is mainly centered around supportive measures, including body cooling, administration of intravenous fluids, and antipyretics. Additionally, antiparkinsonian drugs are restarted at their previous dosages, as prescribed before the onset of PHS [8]. In cases where patients experience muscle spasms and do not respond well to standard dopaminergic dosing, adjunctive treatments like dantrolene and bromocriptine have been employed effectively to address PHS symptoms [6, 9].

Conclusion

Parkinsonism-hyperpyrexia syndrome represents an under-reported yet preventable complication of Parkinson's disease. This case report underscores the significance of health education in managing this condition effectively. It is imperative for physicians to consistently remind patients with Parkinson's disease about the importance of adhering to their prescribed medications and being vigilant regarding the initial signs and symptoms of PHS. By emphasizing the need for timely medical attention if any concerning symptoms arise, healthcare providers can play a pivotal role in preventing the development of PHS and ensuring the well-being of their patients with Parkinson's disease.

References

1. Simonet C, Tolosa E, Camara A, Valldeoriola F. Emergencies and critical issues in Parkinson's disease. Pract Neurol. 2020 Feb;20(1):15-25. doi: 10.1136/practneurol-2018-002075. Epub 2019 Aug 19. PMID: 31427383; PMCID: PMC7029239.
2. Capasso M, De Angelis MV, Di Muzio A, Anzellotti F, Bonanni L, Thomas A, Onofrj M. Critical Illness Neuromyopathy Complicating Akinetic Crisis in Parkinsonism: Report of 3 Cases. Medicine (Baltimore). 2015 Jul;94(28):e1118. doi: 10.1097/MD.0000000000001118. PMID: 26181547; PMCID: PMC4617089.
3. Kaasinen V, Joutsa J, Noponen T, Päivärinta M. Akinetic crisis in Parkinson's disease is associated with a severe loss of striatal dopamine transporter function: a report of two cases. Case Rep Neurol. 2014 Nov 26;6(3):275-80. doi: 10.1159/000369448. PMID: 25566059; PMCID: PMC4280458.
4. Wei L, Chen Y. Neuroleptic malignant-like syndrome with a slight elevation of creatine-kinase levels and respiratory failure in a patient with Parkinson's disease. Patient Prefer Adherence. 2014 Feb 27;8:271-3. doi: 10.2147/PPA.S59150. PMID: 24600209; PMCID: PMC3942214.
5. Grover S, Sathpathy A, Reddy SC, Mehta S, Sharma N. Parkinsonism-hyperpyrexia syndrome: A case report and review of literature. Indian J Psychiatry. 2018 Oct-Dec;60(4):499-503. doi: 10.4103/psychiatry.IndianJPsychiatry_113_18. PMID: 30581218; PMCID: PMC6278220.
6. Azar J, Jaber Y, Ayyad M, Abu Alia W, Owda F, Sharabati H, Zeid H, Khreshi S, AlBandak M, Sayyed Ahmad D. Parkinsonism-Hyperpyrexia Syndrome: A Case Series and Literature Review. Cureus. 2022 Sep 27;14(9):e29646. doi: 10.7759/cureus.29646. PMID: 36320988; PMCID: PMC9616322.
7. Newman EJ, Grosset DG, Kennedy PG. The parkinsonism-hyperpyrexia syndrome. Neurocrit Care. 2009;10(1):136-40. doi: 10.1007/s12028-008-9125-4. Epub 2008 Aug 20. PMID: 18712508.
8. Wang JY, Huang JF, Zhu SG, Huang SS, Liu RP, Hu BL, Zhu JH, Zhang X. Parkinsonism-Hyperpyrexia Syndrome and Dyskinesia-Hyperpyrexia Syndrome in Parkinson's Disease: Two Cases and Literature Review. J Parkinsons Dis. 2022;12(6):1727-1735. doi: 10.3233/JPD-223362. PMID: 35811538; PMCID: PMC9535593.
9. Mizuno Y, Takubo H, Mizuta E, Kuno S. Malignant syndrome in Parkinson's disease: concept and review of the literature. Parkinsonism Relat Disord. 2003 Apr;9 Suppl 1:S3-9. doi: 10.1016/s1353-8020(02)00125-6. PMID: 12735909.