Parkinsonism-hyperpyrexia syndrome-A rare case report

Abstract

Parkinsonism-Hyperpyrexia Syndrome (PHS) though rare, is a catastrophic treatment-related complication of Parkinson's Disease (PD). It is a hypodopaminergic state which occurs due to the abrupt withdrawal of dopaminergic medications in patients with PD. Clinically PHS resembles neuroleptic malignant syndrome (NMS). We report a case of a 66-year-old male who was diagnosed with PD 12 years earlier and was on Levodopa (200 mg)+Carbidopa (50 mg) twice a day and Tablet Selegeline 5 mg once in the morning. He had abruptly stopped taking medications because he went on a trip to his relative's place and presented to us with hyperpyrexia and acute kidney injury. He recovered after the reinstitution of levodopa.

Keywords: parkinsonism, hyperpyrexia, hypodopaminergic state, acute kidney injury

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Introduction

Parkinsonism-Hyperpyrexia Syndrome (PHS) was first described in 1981. If not suspected early it can be life-threatening [1]. Sometimes it is misdiagnosed as a neuroleptic malignant syndrome (NMS), sepsis with multi-organ failure, infection. It is a hypodopaminergic state that results due to the sudden stoppage of levodopa [2]. Clinical manifestations of PHS are very akin to neuroleptic malignant syndrome (NMS) [2,3]. PHS presents with myriads of features ranging from hyperpyrexia, rigidity, altered sensorium, autonomic dysfunction and elevated creatine kinase (CK). Early diagnosis and prompt reinstitution of antiparkinsonian medications are the cornerstones of the treatment of this condition [2].

Case Report

A 66-year-old male presented to us with a history of high-grade fever and altered sensorium for 12 hours. There was no history of headache, vomiting, diplopia or seizures. There was no history of diabetes, hypertension. He was a known case of PD for 12 years and was taking Levodopa (200 mg)+Carbidopa (50 mg) twice a day. He had last visited his treating physician 2 months back before the presentation.

Three days back he went to a relative's place and had forgotten to pack his medications. He had come back to his home after 3 days and presented with the sudden development of symptoms in the form of irrelevant talking, not recognizing relatives and fever for which he was brought to this hospital.

On examination, the Glasgow Coma Scale was 11(E-3/M-5/V-3). Temperature -104.2°F, Pulse -166 beats/min, regular. Blood pressure was 100/70 mmHg. There was no significant lymphadenopathy, JVP was normal and there was no oedema foot. There were no rashes over the body. CVS, RS, and P/A examination were normal. Neurologic examination revealed hypertonia and cogwheel rigidity in all 4 limbs. Plantars were bilateral flexor. The patient did not co-operate for the elicitation of flapping tremors.

On investigations complete blood count was normal. LFT and serum electrolytes were normal. Blood urea was 78 mg/dl and serum creatinine was 3.9 mg/dl. X-ray chest and USG abdomen did not reveal any abnormality. Total CPK was 2800 U/L (normal -39-308 U/L). CT brain revealed cortical atrophy. Malaria antigen test, IgM dengue was negative. ABG revealed metabolic acidosis.

He was treated with antipyretics, IV fluids, empirical antibiotics, external cooling with ice packs, injection soda bicarbonate and two sessions of hemodialysis. In the next 24 hours his fever did not come down and mental obtundation persisted. At this point, the history was re-evaluated and levodopa was reinstituted. Over the next 72 hours his fever subsided, the mental condition improved, creatinine came down to 1.9 mg/dl and total CPK was decreased to 600 U/L. Through the next 5 days, his recovery was significant and he was discharged with normal sensorium, normal temperature, and normal biochemical profile.

Discussion

PHS is a medical emergency that resembles NMS. Diagnosis is usually straight forward if the prior history of PD is known and the history of the sudden stoppage of levodopa is elicitated. Our patient had hyperpyrexia, rigidity, altered sensorium, rhabdomyolysis induced AKI with high CPK levels which required holistic management including dialysis. But dramatic recovery occurred only after the reinstitution of levodopa. Literature suggests if the diagnosis of PHS is delayed, multiple complications like AKI, pulmonary embolism, and DIC can occur, leading to death [2].

The most common cause of PHS is sudden withdrawal or sudden decrease in the doses of levodopa or dopa agonists. Amantadine an antiviral drug used to treat PD also can predispose to PHS after sudden withdrawal. Untreated it is potentially fatal [3].

PHS is also known as Neuroleptic Malignant Like Syndrome (NMLS) [1] because it resembles the clinical presentation of NMS. Diagnosis is straightforward if a careful drug history is elicitated regarding discontinuation of antiparkinsonian medication [4,5]. Our case had features suggestive of NMS and the reinstitution of levodopa improved the clinical picture. If the diagnosis of PHS is delayed then catastrophic complications in the form of AKI, aspiration pneumonitis and DIC may prove to be fatal [6,7].

Medical literature has documented evidence of the occurrence of PHS mostly in the form of case reports and case series [8-15].

The most common etiology of PHS in these cases was abrupt withdrawal/reduction and/or alteration of anti-parkinsonian medication especially levodopa /dopa agonists [4,5]. Two case reports of PHS also describe the failure of deep brain stimulator due to exertion of its battery or withdrawal of DBS. All these cases improved after the reinstitution of therapy, though some cases reported mortality [16-22].

The underlying pathophysiology of PHS is a sudden hypodopaminergic state which occurs by the abrupt cessation of anti-parkinsonian therapy. Muscular rigidity of PHS is due to decreased dopaminergic activity and hyperthermia is due to dysregulation of preoptic, anterior hypothalamic and posterior hypothalamic functions. The affection of mesolimbic and mesocortical pathways through dopamine deletion explains the mental status changes [16,17].

Conclusion

It is important to differentiate PHS from NMS. A careful clinical examination and a drug history resolve the issue in most of the cases. Any patient of Parkinson's disease who presents with a clinical picture of NMS should be entertained as a high index of suspicion for PHS. Supportive measures and reinstitution of anti-parkinsonian drugs are the cornerstone of therapy.

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