Case Report

Elevated Creatine Phosphokinase in a Patient on a Long-Acting Antipsychotic:

A Challenging Presentation Similar to Neuroleptic Malignant Syndrome

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euroleptic malignant syndrome (NMS) is infamously associated with antipsychotic medications.¹ High fever (>104°F), generalized muscular rigidity (often referred to as "lead pipe"), altered mental status (coma, delirium), and dysautonomia are recognized as the main symptoms of NMS in the DSM-5-TR. Diaphoresis, unstable vital signs, leukocytosis, and an increase in creatine phosphokinase (CPK) are also linked to NMS, as has been shown in most cases, but elevated CPK is not unique to NMS.^{2,3} Differentiation between the diseases that elevate CPK is crucial. Lack of consideration for alternative illnesses due to late diagnosis or presumed bias may result in delayed therapy and higher morbidity.

Case Report

A 59-year-old woman with a history significant for schizophrenia, myasthenia gravis, thyroid surgery, diabetes mellitus, and Crohn's disease presented to our hospital on July 27, 2022, with the chief complaints of generalized weakness, frequent falls, and an inability to walk. She was on long-acting paliperidone palmitate 234 mg/1.5 mL syringe (injectable suspension) for schizophrenia during the past 3 months. She was taking pyridostigmine for myasthenia gravis. Her spouse also noted that she had been falling more frequently over the previous 2 days. At admission, she was hypertensive with blood pressure of 142/75 mm Hg and a heart rate of 111 bpm, and laboratory results showed an increased CPK level, initially attributed to the antipsychotic.

We performed a thorough evaluation to rule out all possibilities of cardiovascular and neurologic causes. Due to an increased CPK level in the presence of long-acting injectable use, the treatment team suspected this to be a case of NMS. She was started on benztropine, while all other drugs were withheld. However, the patient developed respiratory distress with no improvement in CPK levels and was subsequently placed on a ventilator. On August 10th, she underwent a tracheostomy due to failure to wean off the ventilator. We suspected the patient of having exacerbated symptoms consistent with post-thyroid surgery myasthenia, keeping her past medical history in mind. She was treated with 4/5 doses of plasma exchange, with the final dose scheduled for August 17th. Her CPK level stabilized without renal failure. On the last physical examination, her blood pressure remained high at 157/67 mm Hg, but her heart rate stabilized at 80 bpm. Her respiratory rate was 27 breaths/minute, and she was partially oriented and seemed to respond to commands while intubated. The team informed the patient and her family of the evaluation findings, disposition, and treatment plan. The patient acknowledged her understanding by nodding. She was told of the emergency procedures and advised to get medical assistance if her symptoms worsened.

Discussion

NMS is a side effect resulting in the discontinuation of the antipsychotic or replacement with another medication. Research shows that elevated CPK levels in patients on antipsychotic medications resolved in most cases after discontinuation of the drug.⁴ Myoglobinuria has been treated more aggressively.⁴ In a systematic review of published cases of elevated creatinine kinase in patients on antipsychotics, 81% of subjects reported the discontinuation of the antipsychotic.⁴ In 36% of cases, forced diuresis was additionally used.⁴

In addition to a classic presentation of NMS, massive asymptomatic creatine kinase elevation was reported in 3 cases of youth on second-generation antipsychotics.⁵ No intervention is needed, but further investigation should be made into flu-like syndrome, fever, weakness, alteration of consciousness, muscle rigidity, tachycardia, hypertension/hypotension, and dark urine that requires discontinuation of the medication.⁵

Due to the incidence of high CPK levels in patients receiving antipsychotic therapy, providers start treatment for NMS, which is a life-threatening condition. In our case, the underlying cause of elevated CPK in a patient on antipsychotics was not NMS but instead was due to exacerbation of post-surgery myasthenia gravis. This case highlights that elevated CPK should not be presumed to be NMS in patients taking antipsychotics, especially if the treatment for NMS does not work. One should review the patient's history and symptoms in detail for other neuromuscular disorders that could result in elevated CPK. The elevated CPK levels could indicate conditions other than NMS, and timely workup

to identify other possible causes should be done simultaneously if rapid improvement is not seen after medication withdrawal and treatment for NMS. This identification of other causes can prevent the withdrawal of effective medication and some irreversible damage to the patient.

This case indicates that providers who treat patients taking antipsychotic medications with elevated CPK levels and muscle weakness should investigate other causes of this presentation, especially in the case of a history of neuromuscular disease.

Article Information

Published Online: September 21, 2023. https://doi.org/10.4088/PCC.22cr03442 © 2023 Physicians Postgraduate Press, Inc. *Prim Care Companion CNS Disord 2023;25(5):22cr03442* Submitted: November 1, 2022; accepted April 7, 2023. To Cite: Ashraf S, Kochhar H, Jenson C, et al. Elevated creatine phosphokinase in a patient on a long-acting antipsychotic: a challenging presentation similar to neuroleptic malignant syndrome. *Prim Care Companion CNS Disord*. 2023;25(5):22cr03442.

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Relevant Financial Relationships: None.

Funding/Support: None.

Additional Information: Information, including dates, has been de-identified to protect anonymity.

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