Neuroleptic Malignant Syndrome with Normal Creatine Phosphokinase Levels: An Atypical Presentation

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ABSTRACT

Neuroleptic malignant syndrome (NMS) was initially notified as an adverse effect of an antipsychotic agent called chlorpromazine, in 1956. In the past, several case reports of NMS have been reported, even if they did not meet the proposed diagnostic criteria for it. The diagnostic criteria for NMS include increased muscle stiffness, increased body temperature, elevated creatine phosphokinase (CPK) levels by at least four times the upper limit of normal (ULN), autonomic dysfunction, and an altered mental status.

We present a case of a 25-year gentleman with schizophrenia, who arrived in the Emergency Department, with significant behavioural changes for a month, accompanied by drowsiness and high-grade fever for two weeks. CPK levels done on two occasions were 669 U/L and 710 U/L, respectively. Persistent hyperthermia and autonomic symptoms with further deterioration in mental status, led to a working diagnosis of NMS. The patient, thereafter, received bromocriptine, benzodiazepines and continuous intravenous hydration, but his clinical condition deteriorated and he expired after nine days of hospital stay.

Key Words: *Neuroleptic malignant syndrome, Creatine phosphokinase, Hyperthermia, Muscle stiffness.*

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INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a potentially life-threatening, neuroleptic-induced idiosyncratic reaction, characterised by muscle stiffness, increased body temperature, elevated creatine phosphokinase (CPK) levels, autonomic dysfunction, increased white blood cell (WBC) count, and an altered mental status.[1] Global estimates from a review have shown an overall estimate of 0.991 cases per 1,000 people; whereas, the incidence in Pakistan remains understudied.[2] NMS has been associated with significant death rate or permanent damage, which highlights the need for its early diagnosis and treatment.[3,4]

We, herein, present a case of a 25-year gentleman with schizophrenia, who arrived in the Emergency Department, with significant behavioural changes for a month, accompanied by drowsiness and high-grade fever for two weeks. He was diagnosed with NMS and managed accordingly, but we were not able to save his life.

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CASE REPORT

We present a case of a 25-year gentleman with schizophrenia, who arrived in the Emergency Department, with significant behavioural changes for a month, accompanied by drowsiness and high grade fever for two weeks.

Detailed history revealed that the patient was having a low mood and lack of interest in his work and relationship for the past two years. A month ago, he became aggressive, verbally and physically abusive towards his family members, throwing objects at them and not recognising them. For this change in behaviour, he was started with anti-psychotics and benzodiazepines (haloperidol, olanzapine, and clonazepam). Later, medications were adjusted in accordance with his psychotic episodes. His brother added that he had received anti-psychotics in the injectable form together with electro-convulsive therapy for the control of his psychotic symptoms.

On admission, the vitals were: Temperature 101°F, heart rate 120 beats/minute, respiratory rate 18 breaths/minute, and blood pressure 120/80 mmHg. The patient was lean and thin, drowsy, grimacing on pain; his pupils were 3mm in diameter, and sluggish in reaction. There was an increase in muscle tone all over and remarkable axial rigidity (neck stiffness in all directions). Laboratory workup revealed hemoglobin 15.7 g/dL, total leukocyte count (TLC) 13,500/uL, platelets 264,000/mm^3, urea 51 mmol/L, creatinine 0.99 mg/dL, sodium 146 mmol/L, potassium 3.8 mmol/L, and bicarbonate 26 mmol/L. Furthermore, CPK levels done on two occasions were 669 U/L and 710 U/L, respectively. Magnetic resonance imaging (MRI) brain was unremarkable and electroencephalo-

gram (EEG) showed slow posterior dominant rhythm. Cerebrospinal fluid (CSF) detailed report showed glucose to be 93 mg/dL (normal: 50-80 mg/dL), protein 27 mg/dL (normal: 15-45 mg/dL), and WBC count 4/mm^3 (normal: 0-8/mm^3) and red blood cell (RBC) count 323/mm^3.

The patient on arrival was admitted under the psychiatry services, and was given broad-spectrum antibiotics for a possible central nervous system (CNS) infection. Later, persistent hyperthermia and autonomic symptoms with further deterioration in mental status led to a working diagnosis of NMS.

The patient, thereafter, received bromocriptine, benzodiazepines and continuous intravenous hydration, but his clinical condition deteriorated and he expired nine days after hospital admission.

DISCUSSION

To establish the diagnosis of NMS in a patient, several signs and symptoms have been reported over the years. Among these, some of the widely accepted ones are those suggested by Pope *et al*, DSM-IV-TR, Caroff *et al*.; and in all of these, serum CPK elevation is not included as a major criterion.[5-7]

Additionally, Levenson also put forward a diagnostic criterion that suggests the presence of either three major criteria (elevated CPK levels, increased body temperature, muscle stiffness) or two major with at least four minor manifestations.[8] Our patient fell under the latter. He had elevated body temperature, stiff muscles (major) and also elevated WBC counts, increased sweating, rapid heart rate, rapid breathing and an altered mental state (minor). The patients of NMS normally present with elevated CPK levels, typically more than 1,000 U/L.[9] In our patient, serum CPK titers tested were not that high, on both occasions, which led to the unique finding of this case. The possible cause behind the lack of elevation of CPK levels was the low BMI (body mass index) of our patient, similar to a case previously reported in the literature.[10]

From this case, we also track that the patient was developing mental symptoms like low mood and lack of interest for two years; and his family still did not get any form of help from psychiatrists, until his condition was exacerbated. The lack of confidence in terms of identifying mental illnesses, at an early stage by our community and in terms of seeking help with so much delay, goes to show how such illnesses are still a social stigma and taboo in Pakistan.[11]

Furthermore, clinical practitioners like psychiatrists and physicians should be made aware that the conditions like NMS are a possible complication of antipsychotics, so they are more judicial before prescribing high doses of these drugs in patients with mental illnesses. Perhaps these shortcomings in knowledge and practices of NMS can be attributed to the lack of research in our region and appropriate guidelines for the prompt management of mental conditions without inadvertently bringing about more harm to the patient.

Although diagnostic criteria for NMS have been established, widely accepted and applied, this condition still poses a diagnostic dilemma, as CPK levels may not be as high as expected. Diagnosis of NMS should still be considered in appropriate circumstances.

PATIENT'S CONSENT:
Informed consent was obtained from the patient.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
SZ: Writing, editing, designing, reviewing.
NI, ZK: Writing, designing.

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