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CASE REPORT Open Access

Neuroleptic malignant syndrome: a diagnostic dilemma in an unconscious patient—a case report

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Abstract

Background: Neuroleptic malignant syndrome is a clinical condition which has been studied and described well. But history of the patient and the medications he is on are very important to make this diagnosis.

Case presentation: We report the case of a young male who presented with the typical features but lacked the history of medication, hence delaying our diagnosis formation. In-depth history taking is very important in patients who present with unusual symptoms.

Conclusions: Patients on long-term medications, who may develop some side effects due to medication, should always carry a medical card stating their medical history and medication being taken.

Keywords: Neuroleptic malignant syndrome, Neuroleptic agents, Antipsychotics

Background

The neuroleptic malignant syndrome (NMS) is a rare idiosyncratic reaction to antipsychotic medication characterised by hyperthermia, autonomic dysregulation, rigidity, altered consciousness, elevated serum creatinine phosphokinase (CPK) levels and leucocytosis (Caroff 1980). It may lead to multi-organ dysfunction and is potentially fatal.

In absence of a history of neuroleptic intake, it is extremely difficult to make a diagnosis of NMS. This case emphasises that one should keep a high degree of suspicion of NMS in patients presenting with fever and rigidity and effort should be made to actively seek history of any antipsychotic intake.

Case presentation

A 22-year-old unconscious (Glasgow coma scale six) male was brought in the emergency department of our hospital by his friends. On examination, his temperature was 103.5° F, pulse rate (PR) was 136–140 per minute, blood pressure (BP) was 86/34 mm Hg, and respiratory rate was 38–42 per minute with SpO_2 of 89% on room air. Chest auscultation revealed decreased air entry at the base of both lungs with crepitations in the right upper zone. The attendants were unable to provide any significant previous medical history.

He was intubated using fentanyl and etomidate. The chest X-ray revealed a large consolidation at the right upper zone. Routine investigations and cultures of blood, trachea and urine were sent. Patient was then started on piperacillin-tazobactam and azithromycin and transferred to the intensive care unit (ICU) for further management.

During the next 2 days, his vital signs showed marked fluctuations with PR varying from 80 to 120 beats/minute and BP from 100/70 to 150/110 mm of Hg. Patient continued to have high-grade fever (103–104°F) despite on being one gram iv paracetamol six hourly. Cardiovascular examination was normal and the abdomen was soft. On neurologic examination, he was sedated with pupils of normal size and reaction. Reflexes were normal. There was symmetrical rigidity in all four extremities. He had

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mild neck rigidity with negative Kernig and Brudzinski sign. Investigations revealed a white blood cell count of 32,000 with a procalcitonin level of 0.2. Tracheal culture showed *Streptococcus pneumoniae* while urine and blood cultures were sterile. Other investigations like liver and renal function tests, serum electrolytes, blood gas analysis and ECG were within normal limits. He was continued on the same treatment.

On the third day, the patient continued to have a high-grade fever with autonomic dysregulation. He was agitated and sweating. He now had bilateral equal air entry in the lungs and a repeat chest X-ray showed clear lung fields. Repeat cultures of blood, trachea and urine were sterile.

Due to his high-grade fever, agitation and rigidity, his CPK levels were sent and were reported to be 1600 U/L (normal range, 39 to 308 U/L). Toxicological screening test on blood and urine was clean, autoimmune encephalitis panel on serum and CSF was negative for any antibodies, computed tomography of the brain and CSF examination was normal.

On the fourth day, the patient's parents arrived and revealed that the patient was a chronic drug and alcohol abuser since the last 8 years and previously had multiple admissions at a rehabilitation centre. Since the last 1 year, he had developed a schizoaffective disorder characterised by paranoia, hallucinations and delusions of grandeur. He was on irregular medication (lithium and haloperidol) for the same. Recently, he had changed his treating physician who increased his dosage of haloperidol.

In view of the above, a diagnosis of NMS was suspected. The patient was started on tablet bromocriptine 5 mg every 8 hourly and lorazepam 2 mg every six hourly. Urine examination for myoglobinuria was negative. Over the next 3–4 days, he became alert and afebrile, his vital signs stabilised, and with a resolution of rigidity and catatonia. There was a gradual decrease in CPK levels and WBC count. The patient was successfully extubated on day 12. Bromocriptine was gradually tapered off and the patient was transferred to the psychiatry ward on day 18th on lorazepam 2 mg twice a day.

Discussion

NMS is a well-known entity dealt by a psychiatrist, but rarely encountered by an intensivist. In this case, the unavailability of the patient's past history of psychiatric illness and medications led to a delay in diagnosis.

This disorder occurs in 0.4% of newly treated patients and carries a mortality risk of 22% (Shalev and Munitz 1986). It occurs in patients of schizophrenia who are treated with high doses of antipsychotics. Though most neuroleptic medications are associated with the risk of NMS, first-generation antipsychotics such as haloperidol are the most common causative agent (Strawn et al 2007). NMS can occur after the initiation or increase in the dose of neuroleptics and rarely after the sudden discontinuation of the drug therapy (Shalev and Munitz 1986). Differential diagnosis include CNS infections and mass lesions, lethal catatonia, severe extrapyramidal reactions, anti-cholinergic or lithium toxic, heat stroke and malignant hyperthermia (Castillo et al 1989).

Levenson described the presence of either three major criteria (fever, rigidity and raised levels of CPK) or two major and four minor criteria (tachycardia, abnormal blood pressure, tachypnoea, altered consciousness, diaphoresis and leucocytosis) for diagnosis of NMS (Levenson 1985). In the present case, the patient was on haloperidol and fulfilled all major and minor criteria for diagnosis of NMS.

Development of dehydration in a patient on neuroleptics is the most important risk factor for developing NMS because decreased blood volume induces peripheral vasoconstriction and impairs heat dissipation. Other risk factors for NMS include stress, humidity and concomitant use of lithium, anticholinergic agents or some antidepressants (Bhanushali and Tuite 2004). Patient in this case scenario was on lithium along with haloperidol. Though the exact pathophysiology of NMS is not known, sudden and massive down-regulation of dopaminergic transmission by neuroleptics leads to the development of NMS (Shalev and Munitz 1986).

Once NMS is diagnosed, the suspected causative agent should be stopped. The patient should be kept well hydrated to prevent acute renal failure. Antihypertensive agents may be added to manage autonomic instability. Cold sponging is done to reduce hyperthermia. Medications such as Dantrolene, a skeletal muscle relaxing agent, bromocriptine, a dopamine agonist, and lorazepam are given to reduce muscle rigidity and muscle necrosis. These drugs are tapered off slowly to prevent recurrence (Bhanushali and Tuite 2004). Other methods of treatment include electroconvulsive therapy (Davis et al 1991). Our patient responded well to bromocriptine and lorazepam. Bromocriptine was tapered off and lorazepam was continued in low dose in post-NMS period as it has tranquillising properties.

Major complications of NMS include pulmonary aspiration and rhabdomyolysis leading to acute renal failure (Gauze and Baner Jr 1985). Our patient was intubated till he was alert enough to prevent pulmonary aspiration and urine was routinely monitored for myoglobinuria.

NMS is a diagnosis of exclusion and one should have a high degree of suspicion in case a patient on neuroleptics presents with fever and rigidity. In this case, the absence of a history of neuroleptic intake initially led to a delay in the diagnosis of NMS. In view of the high mortality

rate associated with NMS, it would be advisable that such patients should always keep a medical card detailing their medical condition with them.

Conclusions

History taking is an important part of the medical field, but cases like these have emphasised more on this fact. Neuroleptic malignant syndrome should be one of the differential diagnoses of the patient with typical clinical features until it is be proven with history. In case of failure to take history with typical Levenson's criteria and after exclusion of other diagnoses, we may try management with bromocriptine and lorazepam.

Abbreviations

NMS: Neuroleptic malignant syndrome; CPK: Creatinine phosphokinase; BP: Blood pressure; ICU: Intensive care unit; CSF: Cerebro spinal unit; CNS: Central nervous system.

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Authors' contributions

SJ played a key role in managing the case and writing up the manuscript, ShJ played a key role in managing and diagnosing the case and correcting the manuscript, and VT played an essential role in formulating the diagnosis and critically approving the manuscript. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets of this case report are not publicly available as it is not relevant towards the cause of publication of the case, but it is available with the corresponding author.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient to publish the report.

Competing interests

The authors declare that they have no competing interests.

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