Neuroleptic malignant syndrome: a fatal case with unusual features

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Abstract
Neuroleptic malignant syndrome is a rare, but potentially life threatening, idiosyncratic reaction primarily related to use of neuroleptic medications. We report a fatal case of neuroleptic malignant syndrome in a 67 year old female with bipolar affective disorder, triggered by recent change of medications. She had marked elevation of creatinine phosphokinase levels, thrombocytopenia and acute kidney injury but no muscle rigidity. Despite early detection, intensive care support and continuous renal replacement therapy, the patient died of rhabdomyolysis induced acute kidney injury and persistent metabolic acidosis.

Key words: neuroleptic malignant syndrome

Case report

A 67 year old female presented to the emergency treatment unit with a two day history of drowsiness, significant myalgia and one day history of fever. She had been commenced on lithium carbonate and haloperidol for bipolar affective disorder five weeks previously. This treatment had been replaced by olanzapine, aripiprazole and benzhexol one week previously, due to concerns of deterioration of general wellbeing which was attributed to medication. The patient was brought for medical attention by her son, who suspected possible drug overdose or toxicity. There was no other significant history of note. On examination she was febrile with a temperature of 100°F, conscious but disoriented. Her blood pressure was 80/60 mmHg and pulse rate was 116 per minute. There was no neck stiffness or generalized rigidity and the rest of the examination was unremarkable. After initial resuscitation she was admitted to the intensive care unit with the differential diagnoses of NMS or underlying sepsis. All neuroleptics were discontinued. The patient was started on broad spectrum antibiotics, inotropes and bromocriptine 2.5 mg twice daily.

Investigations revealed a markedly elevated creatinine phosphokinase of 55,491 U/I, with low serum calcium (6.9 mg/dl) and high phosphate levels (10 mg/dl); serum potassium levels remained normal. The SGOT level (1301 U/I) was disproportionately higher than the SGPT (396 u/l) level. Serum creatinine was elevated to 658 micromoles/l and urine was positive for myoglobin. Arterial blood gases showed metabolic acidosis. Full blood count showed leukocytosis (15.57u/L) with thrombocytopenia (48u/L). Septic screen, D-dimers and urine toxicology were negative. Echocardiogram and electro cardiogram did not reveal any abnormalities. Ultra sound scan of the abdomen showed only mildly elevated renal echogenicity. Brain imaging and lumbar puncture were withheld due to instability of the patient. In view of the ongoing rhabdomyolysis and resultant acute kidney failure, alkaline diuresis was commenced and later followed by hemodialysis. Post-dialysis creatinine phosphokinase was 46878 U/I and serum creatinine was 521 micromoles/l. She continued to have persistent severe metabolic acidosis and went into supra-ventricular tachyarrhythmia which was successfully cardioverted. Continuous renal replacement therapy was commenced. However the patient eventually went into asystolic cardiac arrest and died after two days of intensive care.

Discussion
Major criteria for diagnosis of NMS includes fever, rigidity and elevated creatinine phosphokinase levels. Minor criteria are tachycardia, abnormal arterial pressure, tachypnoea, altered level of consciousness, diaphoresis and leukocytosis (4). This patient presented with two major and four minor criteria, which fulfilled the diagnostic criteria for neuroleptic malignant syndrome. Importantly, creatinine phosphokinase levels greater than 1000 IU/L

Introduction
Neuroleptic malignant syndrome (NMS) is a rare, but potentially life threatening, idiosyncratic reaction primarily related to the use of neuroleptic medications (1). Exact pathogenesis is unclear but most studies suggest that it is related to central dopaminergic blockade induced by neuroleptics (1, 2). Incidence of NMS ranges from 0.02 to 3% among neuroleptic users, with a male predominance. Mortality rate in patients with NMS is 10% to 20% (3, 4). Both typical and atypical antipsychotics and antiemetics have been implicated (2). Cardinal clinical features are fever, rigidity, change in mental state and dysautonomia (1). Treatment consists of prompt withdrawal of the neuroleptic agent and supportive care of complications. Medical therapy includes dantrolene, bromocriptine and amantadine, while electroconvulsive therapy also has a place in treatment (5).
are documented to be more specific for NMS, and the degree of creatinine phosphokinase elevation correlates with disease severity and prognosis (4).

Lithium, haloperidol and olanzapine all can trigger this syndrome, but one could speculate that changing over to olanzapine and aripiprazole with discontinuation of haloperidol one week before was the immediate contributory factor (2,10). Rigidity, which is one of the main features of NMS, was not observed in this patient. Similar cases have been reported previously in the literature and this lack of rigidity stands out as an important factor which warrants further evaluation (6, 7). Similarly thrombocytopenia has also been observed in some case studies (8, 9). The initial differential diagnosis of sepsis induced shock was ruled out due to negative blood and urine cultures, D dimers and reactive blood picture without evidence of sepsis.

Neuroleptic malignant syndrome carries a significant mortality. Persistent metabolic acidosis and hypoxia in the presence of rhabdomyolysis induced acute kidney injury may have aggravated the myocardial suppression and predisposed to tachyarrhythmia, contributing to the death of the patient. The absence of rigidity, presence of thrombocytopenia and massive elevation of creatinine phosphokinase levels need to be highlighted as uncommon features in this patient. In conclusion, this case report illustrates the high case fatality associated with neuroleptic malignant syndrome and the importance of increased clinician awareness of atypical presentations, in order to facilitate early detection and treatment.

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Declaration of interest

None declared

References