

Neuroleptic malignant syndrome in a patient with newly diagnosed schizoaffective disorder

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Citation

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Abstract

Neuroleptic malignant syndrome is a rare but fatal complication when using neuroleptic drugs. We report a case involving a 47-year-old woman with newly diagnosed schizoaffective disorder who presented with neuroleptic malignant syndrome after an increase in her neuroleptic dose.

INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a potentially fatal, although rare, complication of treatment with class of medications labeled neuroleptic medications (e.g., antipsychotics, sedatives and antinauseants). NMS is characterised by hyperthermia, muscle rigidity, an elevated creatinine kinase level and autonomic instability. The incidence of NMS falls in the range of 0.2-3.23% of patients exposed to neuroleptics (1,2,3). The syndrome often develops after a sudden increase in the dosage of the neuroleptic medication or in states of dehydration (4). Treatment is mainly supportive and includes withdrawal of the neuroleptic medication and administration of drugs such as dantrolene and bromocriptine.

We report about a 47-year-old woman with a history of schizoaffective disorder who presented with acute onset of hyperthermia, altered mental status, rigidity and tremor 10 days after treatment with haloperidol and risperidone.

CASE REPORT

A 47-year-old woman was sent to the emergency room after suddenly developing symptoms of high fever, tremor, muscular rigidity and altered mental status. The patient's past medical history revealed that 10 days prior admission, she presented to another hospital with increasing auditory hallucinations and persecutory delusions and was given haloperidol (10 mg every morning, 10 mg every evening) and risperidone (1 mg every morning and 1 mg every evening). 5 days later, the haloperidol dose was increased to 20 mg twice daily, respectively. Initial assessment on arrival at the emergency department revealed that the patient was

obtunded and disorientated. Her body temperature was 39.5 °C, pulse rate was 125 bpm, respiratory rate was 30/min and blood pressure was 147/98 mmHg. Neurologic examination showed mild neck stiffness without meningism, tremor, normal deep tendon reflexes and cogwheel rigidity.

Biochemical measures were normal except for increased serum creatine kinase (CK) (350 U/L; normal, 30-150 U/L). White blood cell (WBC) count was $4.55 \times 10^9/L$. Brain computed tomography revealed no abnormalities. Lumbar puncture showed normal intracranial pressure without presence of pleocytosis.

Despite receiving fluid hydration (0.9% sodium chloride) and i.v paracetamol infusion her temperature elevated to 40.0 °C. NMS was diagnosed and haloperidol and risperidone was discontinued. Bromocriptine 2.5 mg twice a day was given. She was then admitted to the intensive care unit (ICU) for further care.

After ICU admission, fluid hydration, bromocriptin medication and other supportive treatments were given. Within a few days, the patient's NMS symptoms improved and his CK level and temperature returned to normal. The septic workup yielded negative results. In order to control her ongoing psychotic symptoms, the patient was prescribed olanzapine (2.5 mg once daily). She was transferred to a medical ward and was free of symptoms at discharge 15 days later.

DISCUSSION

NMS is a serious complication of neuroleptic medications. It was first described in 1967 as akinetic hypertonic syndrome

(₁). The frequency of the syndrome ranges from 0.2 to 3.23% among patients receiving neuroleptic medications (_{2,3}). The mortality is 10%-30% (₄).

NMS likely results from a complex interaction between the neuroleptic medication and susceptible host. The pathophysiological mechanism of NMS is unclear. Two theories have been proposed to explain this syndrome: central dopamine receptor blockade and skeletal muscle defect (_{5,6,7}).

Most neuroleptic medications have some risk of NMS. Typical neuroleptics such as haloperidol, chlorpromazine, fluphenazine, loxapine and levomepromazine have much more risk than atypical neuroleptics. Even atypical neuroleptics (clozapine, olanzapine, quetiapine and risperidone), previously thought to have less risk, have been associated with reported cases of NMS (_{8,9}).

NMS most often occurs after the initiation or increase in the dose of neuroleptics, sudden discontinuing neuroleptic therapy or a rapid change in neuroleptic dose. Also dehydration, stress, humidity, concomitant use of lithium, anticholinergic agents and some antidepressants are the risk factors (₁₀).

Many diagnostic criteria have been proposed for NMS, but because of its variable presentation, no single set of criteria is used universally. Physical findings (abnormal blood pressure usually hypertension, altered level of consciousness, chorea, diaphoresis, fever, generalized tonic-clonic seizures, muscle rigidity, mutism, opisthotonus, positive Babinski's sign, tachycardia, tachypnea and trismus) and laboratory findings (increase in creatinine kinase level, leukocytosis with shift to the left, myoglobinuria and increase in transaminase levels) can be seen. The symptoms usually develop over 24 to 72 hours and can last from 1 to 44 days (₁₁).

The diagnosis of NMS can be difficult, for differential diagnosis acute lethal catatonia, anticholinergic syndrome, central nervous system infection, heat illness, heavy metal poisoning, lithium toxicity, malignant hyperthermia, neuroleptic-related heat stroke, sepsis, serotonin syndrome, tetanus and withdrawal states must be considered (₁₁).

A thorough history taking, physical examination and laboratory investigations, including leukocyte count, renal function tests, electrolyte measurement, serum CK and lithium measurement should be performed. An

electroencephalogram, CT scan of the head and lumbar puncture should be performed for differentiation.

The treatment of NMS depends on early recognition. General treatment, including hydration, nutrition and reduction of fever is essential and secondary complications (e.g. hypoxia, acidosis, renal failure, rhabdomyolysis, acute respiratory failure, seizures, brain damage, myocardial infarction, disseminated intravascular coagulation, hepatic failure and sepsis) must be treated aggressively. Withdrawal of the neuroleptic agent is crucial. Dopamine agonists such as bromocriptine and amantidine hydrochloride have been used successfully to treat NMS(_{3,4,5,6,7,8,9,10,11,12}).

After an episode of NMS, neuroleptic therapy is still required to control the patient's psychiatric symptoms. Starting with an atypical neuroleptic at a low dose and slowly increasing the dose while monitoring for signs of NMS is the safest option (₁₃).

CONCLUSION

NMS is a potentially fatal complication of neuroleptic therapy. In light of the fact that primary care physicians use neuroleptics for a variety of medical and psychiatric conditions, physicians must be aware of NMS. The mortality and morbidity associated with NMS can be decreased with early recognition, early discontinuation of the neuroleptics and aggressive treatment.

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