CASE REPORT

Neuroleptic malignant syndrome masked by cerebral malaria

Kumar Muniandy Rajesh,¹ Vellan Sinnathamby,² Arul N Sakthi³¹Medicine Based Department, School of Medicine, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia²Department of Anaesthesiology and Intensive Care, Kulim Hospital, Kulim, Kedah, Malaysia³Department of Anaesthesiology and Intensive Care, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia**Correspondence to**
Dr Rajesh Kumar Muniandy,
farbe63@hotmail.com**SUMMARY**

A 38-year-old man with an underlying psychiatric illness presented with altered sensorium and abnormal behaviour. He was febrile at 38°C and weak looking; otherwise no other abnormalities were detected. A blood film conducted for malarial parasite (BFMP) revealed *Plasmodium falciparum*; hence a diagnosis of cerebral malaria was made. He was treated with antimalarial drugs for 2 days prior to being transferred out to the ward following clinical improvement. He subsequently developed episodes of stupor and refusal of feeding. Following an evaluation by the psychiatrist, a diagnosis of catatonic schizophrenia was made and he was started on oral sulpiride and benhexol. Unfortunately, he developed high-grade fever at 40°C with muscle rigidity and fasciculation. The diagnosis of neuroleptic malignant syndrome (NMS) was clinched and the antipsychotics were discontinued. However he succumbed to NMS several days later due to multiorgan failure.

BACKGROUND

Neuroleptic malignant syndrome (NMS) is a life-threatening, idiosyncratic reaction to both typical and atypical antipsychotics which is characterised by severe muscle rigidity, autonomic dysregulation (tachycardia, labile blood pressure or diaphoresis), altered thermoregulation (hyperthermia) and altered sensorium (delirium, stupor or coma). These manifestations are due to dopaminergic transmission block in the hypothalamus and basal ganglia following dopamine antagonistic therapy.¹

The risk of NMS has been shown to correlate with the dose, potency, rate and route of administration and abrupt withdrawal of dopamine antagonists.² It has been shown that the decrease in both incidence and mortality of NMS was attributed to increased awareness, preventive strategies, early detection and treatment. However, the diagnostic dilemma arises when patients manifest atypical symptoms in the absence of pathognomonic criteria such as muscle rigidity or elevated creatine kinase (CK) which is predominantly seen in atypical antipsychotics such as risperidone, ziprasidone, quetiapine, amisulpiride, olanzapine and clozapine.^{2,3}

CASE PRESENTATION

A 38-year-old man with a history of psychiatric illness presented to the casualty with altered sensorium. His Glasgow Coma Scale was only 12 of 15 (eye: 4, verbal: 2, motor: 6). No further history regarding his psychiatric illness was obtained, as he was staying with his friends who were not aware of his past medical problems. He also had an

abnormal behaviour with irrelevant speech. He was febrile at 38°C and weak looking; otherwise no other abnormalities were detected. His blood pressure was 138/79, with a pulse rate of 110/min and respiratory rate of 18/min. A blood film conducted for malarial parasite (BFMP) revealed *Plasmodium falciparum*; hence, a diagnosis of cerebral malaria was made. Other blood parameters were within the normal range. He was treated in the intensive care unit (ICU) with oral antimalaria drugs (Chloroquine combined with Fansidar) until the repeated BFMP on day 4 of the treatment was negative.

However, he subsequently developed episodes of stupor; refusal of feeding and waxy flexibility. Following an evaluation by the psychiatrist, a diagnosis of catatonic schizophrenia was made and he was transferred out to the psychiatric ward and started on oral sulpiride 200 mg thrice a day and benzhexol hydrochloride 1 mg thrice a day. He responded to the treatment until day 5 of the antipsychotic where he developed another bout of high-grade fever at 40°C with leucocytosis, thready pulse and was toxic looking. His blood pressure at the time was 108/60, with a pulse rate of 124/min. There was no muscle rigidity or other positive clinical findings. The clinical impression then was sepsis, secondary to nosocomial infection and a probability of residual cerebral malaria requiring more time for clearance. Hence the antipsychotic was continued. The following day he developed a blank stare and was not communicative (E2V1M5) and had muscle rigidity; reduced reflexes and mask-like facies.

INVESTIGATIONS

A blood creatine kinase (CK) conducted was elevated at 40 800 IU/l and as the hours passed the CK further raised to 97 640 IU/l. There was reducing urine output; urea was elevated to 25.1 mg/dl, creatine 692 mg/dl, sodium 152 mg/dl and potassium 4.5 mg/dl. Liver enzymes were deranged and myoglobin was detected in the urine.

DIFFERENTIAL DIAGNOSIS

- Neuroleptic malignant syndrome
- Cerebral malaria

TREATMENT

A diagnosis of NMS was made and the antipsychotic was withheld. He was generously hydrated to balance the intake and output and was placed on regular oral paracetamol 1 g thrice a day and tapid sponging. He was intubated and

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transferred to ICU where he underwent an urgent haemodialysis and was started on intravenous Dantrolene 75 mg thrice a day. For the next few days in ICU, he further deteriorated into a vegetative and oliguric state necessitating regular haemodialysis and inotropic support.

OUTCOME AND FOLLOW-UP

After almost 10 days of treatment, he succumbed to the illness.

DISCUSSION

Studies have shown 96% of patients who developed NMS had this problem within the first month of initiating neuroleptic therapy. From these patients, 16% developed NMS within 24 h and 66% by 1 week after starting therapy. Only 4% of patients developed NMS beyond that.¹ In this case, the initial clinical presentation lacked core extrapyramidal symptoms such as muscle rigidity, catatonia, sialorrhoea; tremors and dystonia which are considered the harbingers of typical NMS.⁴

The usage of atypical neuroleptic agent in this patient could have attributed to the initial atypical presentation as reported in other literatures.⁵ Laboratory investigations that aids in the diagnosis of NMS include elevated serum CK activity, leucocytosis; deranged liver enzymes, myoglobinuria and electrolyte abnormalities which were present in this patient.⁶ Extraordinary levels of CK in NMS reflect massive rhabdomyolysis which precipitates renal failure and other sequelae of the illness that leads to mortality as seen in this case. Studies have shown that plasma exchange coupled with continuous haemodiafiltration facilitates excretion of myoglobinuria thus increasing the survival rate of patients compared with that when haemodialysis alone is used.^{6,7}

Risk factors of NMS shown in this patient include his gender, dehydration, concurrent brain pathology due to cerebral malaria and psychomotor agitation. Other documented risk factor for developing NMS include previous history of NMS; intramuscular/parenteral delivery or abrupt dosage increase of neuroleptic agent, concurrent usage of other psychotropic agent and alcohol abuse.⁸

NMS contains features of catatonia which is paradoxically precipitated by a neuroleptic drug which would otherwise

resolve a catatonic state secondary to mental psychosis as depicted in this case although an astute observation of clinical deterioration of the patient following the neuroleptic therapy should have differentiated psychotic catatonia from NMS.^{8,9} In addition, the presence of a prior psychiatric history and concomitant cerebral malaria further delayed an accurate diagnosis.

Learning points

- ▶ Delayed recognition of neuroleptic malignant syndrome (NMS) results in numerous complications and is associated with a high mortality.
- ▶ Heightened clinical vigilance and index of suspicion are crucial to facilitate recognition of NMS.
- ▶ Neuroleptic drugs should be used cautiously.

Competing interests None.

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