A FULMINANT CASE OF NEUROLEPTIC MALIGNANT SYNDROME

S K Teo, K N Sin Fai Lam, W L S Chew

ABSTRACT

We report a fulminant case of Neuroleptic Malignant Syndrome in a 31-year-old male schizophrenic on haloperidol, thioridazine, benzhexol and flurazepam who presented with rigidity, fever, stupor and autonomic instability. He succumbed rapidly over 6 days to rhabdomyolysis, acute renal failure, status epilepticus and disseminated intravascular coagulopathy despite treatment with dantrolene and bromocriptine at the outset.

Keywords: Neuroleptic malignant syndrome, fulminant, rhabdomyolysis, fits, disseminated intravascular coagulopathy.

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INTRODUCTION

Neuroleptic malignant syndrome is a psychiatric complication that is rarely seen in the practice of general medicine. Although it is usually benign if treated early, it can be fatal if complications set in. We report a fulminant case of the syndrome that succumbed to a full range of dreaded complications.

A 31-year-old young man presented with fever, runny nose, sneezing, anorexia and vomiting for two days. This was associated with neckache, backache and 'shivering'. His mother had noted that he had difficulty flexing his neck and was getting more drowsy. He had a past history of schizophrenia 3 years ago and was taking thioridazine 25 mg tds, haloperidol 1.5 mg o.n., benzhexol 2mg o.m. and flurazepam 50 mg o.n. As far as his mother knew, he had not overdosed himself and his psychiatrist reported that there had not been any agitated symptoms or deterioration of his psychiatric condition. There was no travel history and no recent surgery requiring general anaesthesia.

On examination, he was stuporous and febrile. His neck was tonically extended and stiff. His four limbs were also stiff (of lead pipe rigidity) and cogwheel rigidity was elicited in the right wrist. Reflexes were brisk and plantar responses were downgoing. He was tachypnoeic with a respiratory rate of 20/min; heart rate was 98/min and his blood pressure fluctuated between 120/80 and 96/60 mmHg. Other systems were essentially normal.

An urgent computerised tomographic scan of the head was done and reported as normal. Spinal analysis yielded normal results: albumin 0, glucose 52 mg/dl (blood glucose 97 mg/dl), chloride 710 mg/dl, total protein 40 mg/dl, culture results were negative; titres for neurotropic viruses were normal. Blood films for malaria were negative; Widal test showed an O antigen titre of 1:40; sensitised erythrocyte lysis test was negative. His total white count was 4700/ul with polymorphs of 42%, lymphocytes 37%, monocytes 2% and atypical myelocytes 19%. The first specimen of muscle enzymes showed a creatine phosphokinase of 3938 U/l (normal 40-210) and aldolase of 196 U/l (normal 3-12). Dengue serology was negative.

A diagnosis of neuroleptic malignant syndrome was made based on the history of schizophrenia, positive history of taking neuroleptic drugs, fever, rigidity, autonomic instability and raised muscle enzymes. Bromocriptine and intravenous dantrolene was given. The inconsistent lack of leucocytosis and presence of atypical myelocytes was attributed to a preceding viral upper respiratory tract infection.

On the second day of hospitalisation, he started throwing a series of myoclonic fits. Intravenous phenytoin and phenobarbitone was given; the patient was intubated and mechanically ventilated. His low serum calcium (corrected) of 0.91 mmol/l and magnesium of 0.33 mmol/l was corrected. Despite therapeutic levels of anticonvulsants, the fits persisted. Meanwhile the serum creatine phosphokinase climbed to 33780 U/l and urine output trickled to a few millilitres. Serum creatinine rose from 1.9 mg/dl to 7.5 mg/dl. Rhabdomyolysis had caused the tubules to be blocked with myoglobin. Peritoneal dialysis was started but had to be terminated due to persistent hypotension despite maximum inotropic support. Over the next few days, he developed bleeding into his subcutaneous tissues and nose; his coagulation profile was markedly deranged and platelets were 30000/ul. He finally expired on the sixth day of hospitalisation.

DISCUSSION

Neuroleptic malignant syndrome is one of the differentials in a patient presenting with rigidity. In a patient on neuroleptics, drug-induced parkinsonism is a possible cause but the clinical picture would be that of a relatively well patient with some signs of cogwheel rigidity and bradykinesia. Lethal catatonia has been reported in patients with psychiatric illness but these patients are classically described to have waxy flexibility and preceding symptoms of agitation or anxiety prior to the onset of catatonic rigidity[1]. A serotonin syndrome should also be considered. This is believed to be due to activation of serotonin 1a receptors in the brainstem and spinal cord secondary to monoamine oxidase (MAO) inhibitors or serotoninergic drugs. These patients present with mental confusion, restlessness, myoclonic jerks, tremor and tachypnoea.

Meningitis is certainly a condition to be considered when there is fever and nuchal rigidity. Tetanus is another infective

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cause of generalised rigidity and reflex spasms but the patient's consciousness is usually clear and the main complications are related to laryngeal spasms and respiratory failure. Acute demyelinating encephalomyclitis can present with fever, stiffness, paraparesis but it is usually preceded by a viral exanthematous illness (eg rubella, measles) or vaccination. The cerebrospinal fluid in this case would show an increase in proteins and lymphocytes.

Neuroleptic malignant syndrome is an uncommon complication of psychotropic medication. It has been reported to occur in 0.5 – 1.4% of patients on neuroleptics[2]. Various diagnostic criteria have been proposed[3] but the most widely accepted probably comes from Levinson[4,5]. He divided the criteria into 3 major (ie fever, rigidity, elevated creatine phosphokinase) and 6 minor (ie tachycardia, abnormal blood pressure, tachypnoea, altered consciousness, diaphoresis, leucocytosis). He suggested that a diagnosis could be made when 3 major criteria were present or when 2 major and 4 minor criteria were present. This patient met all 3 major criteria.

Various neuroleptics have been associated with this condition but the commonest ones are haloperidol, thioridazine and thioxanthine[2]. Even tricyclic antidepressants, MAO-A inhibitors and metoclopramide have been linked with this illness. Sudden withdrawal of anti-parkinsonian drugs in patients with Parkinson's Disease is also known to precipitate this syndrome[6]. The association with neuroleptics is not dose-related nor time-related. It can occur after being on the drug for months but is said to be precipitated by a rapid increase in dosage[7,8]. This pathophysiologic mechanism is unclear but it is believed to be due to an imbalance in the dynamic status of dopamine in the hypothalamus.

It occurs more commonly in young males. The bad prognostic factors include a history of schizophrenia, presence of rhabdomyolysis and acute renal failure[2]. Mortality ranges from 15 to 30% and increases to 50% if myoglobinuria and acute renal failure is present[2,9,10]. Documented complications include acute respiratory failure, acute myocardial infarction, hepatic failure, disseminated intravascular coagulopathy[7] and myoclonic fits[11]. Treatment is with bromocriptine (which restores the dopamine status) and dantrolene (which acts at a muscular level) to reduce rhabdomyolysis and fever which is believed to be of muscular origin.

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