NEUROLEPTIC MALIGNANT SYNDROME

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Introduction

Neuroleptic malignant syndrome (NMS) first described by Delay and Deniker in 1968 [1] is a rare but potentially fatal life threatening condition seen in association with antipsychotic medication (dopamine receptor antagonists). Levenson suggested the diagnostic criteria which consisted of three major manifestations viz. pyrexia, muscular rigidity, raised creatine phosphokinase (CPK) and six minor manifestations viz. tachycardia, tachypnoea, altered blood pressure, diaphoresis, altered mental state and leukocytosis. The presence of all three major or two major and four minor manifestations indicate a high probability of NMS [2]. This group of symptoms develops abruptly and may lead to serious complications. The overall mortality rate is between 20 to 30 percent [3]. We report one such case whose outcome had been satisfactory.

Case Report

A 30 year old airman was transferred to our hospital on 7 April 98 for management by neurophysician and psychiatrist. Initially admitted to peripheral hospital on 31 March 98 for acute onset illness of 2-3 days duration. He manifested with low grade fever, focal seizure and behavioural abnormality like tearing of clothes, running naked and shouting incessantly. On examination temperature was 100°F, pulse 96/min, BP 122/78 mm of Hg and respiration 14/min. He had features of early papilloedema and extensor plantar reflex on Rt side. On arrival at this hospital there was no significant change in his physical condition. On mental state examination he was unkempt and not in touch with reality. His speech was irrelevant and incoherent. Perseveration was noted. He had clouded sensorium and gross disorientation to time, place and person, poor retention and recall memory impairment for recent events, fleeting paranoid delusions, marked emotional lability, impaired judgement and lack of insight. Routine haemogram, biochemical and metabolic parameters carried out at both the hospitals were normal, Blood for malaria parasite was repeatedly negative. CSF studies including antibody titre for herpes simplex virus, CT scan and MRI of brain were all normal. EEG showed non-specific changes. With the diagnosis of transient organic psychotic condition secondary to cerebral malaria he was managed empirically with parenteral quinine and antibiotics, alongwith dexamethasone, intravenous fluids and nutritional supplements.

To control his organic psychotic condition high potency neuroleptic drug haloperidol 10 mg per day in divided doses was orally given. On the third day his condition worsened for he developed hyperpyrexia (105°F), dehydration, tachycardia (130-140/min), variable blood pressure (fluctuating between 110/70 and 180/110 mm of Hg), confusion and agitation, tremors and profound muscular rigidity of all four limbs.

Serum creatine phosphokinase (CPK) was elevated to 2090 IU/L. Liver function tests (serum bilirubin 0.6 mg percent, AST 496 IU/L, ALT 726 IU/L and serum alkaline phosphatase are 175 IU/L) and renal function tests (blood urea 87 mg percent and serum creatinine 2.2 mg percent) were impaired. Urine for myoglobin was negative.

He was diagnosed as a case of neuroleptic malignant syndrome (NMS) and the offending drug haloperidol was immediately stopped. He was treated with electro convulsive therapy (ECT) which had to be discontinued after two treatments as his mental condition further worsened. Within 10-12 days of therapy with tablet bromocriptine 7.5 mg to 10 mg and tablet lorazepam 4-6 mg per day in divided doses there was a definite improvement in his physical condition. However, his mental condition remained unchanged. In intensive care unit (ICU) he was a management problem and hence transferred to psychiatric ward. Complete recovery occurred within four weeks with mood stabiliser carbamazepine 200 mg bid and low potency neuroleptic chlorpromazine 25 mg tid/qid which were further continued during four weeks sick leave. Prior to his discharge all laboratory parameters came to base line and psychometric test did not reveal any residual features of organicity.

Discussion

The incidence rate of neuroleptic malignant syndrome is 0.1 to 1% of all psychiatric patients receiving neuroleptics. It is more likely to be present in young patients, men being affected twice as compared to women [3]. The patient in our case report is a male aged 30 years who developed features of NMS with haloperidol, a high potency drug of butyrophenones class despite being prescribed in a therapeutic dosage. Sharma et al [4] reported three psychiatric cases, two of affective psychosis and one of schizophrenia who developed features of NMS as early as 7-9 days of antipsychotic medication, however our patient had florid manifestations within just two days of therapy. Many authors like us have noted existence of organic

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brain syndrome as predisposing factor for the illness [5]. Sachdev et al [6] identified dehydration before the onset of illness, need for restraint or seclusion, large dosage of neuroleptic over short period in the management of psychosis and previous treatment with ECT as potential risk factors for the occurrence of NMS.

The most common serious complication of NMS is acute renal failure (ARF). Rhabdomyolysis, an acute diffuse breakdown of muscle tissue results in myoglobinuria, myoglobinuria and elevation in muscle related CPK which eventually lead to acute renal insufficiency [2]. Early detection and prompt correction of fluid and electrolyte balance in this case made the condition reversible within 5-7 days, thus averting the need for haemodialysis. The other complication noted in our patient was abnormal liver function tests reflecting cholestatic hepatitis which returned to normal level within 4-6 weeks.

Recent studies indicate that either dantrolene or bromocriptine [2,3], combination of bromocriptine and dantrolene [2] or bromocriptine and ECT [4] can be successfully used in cases of functional psychosis developing NMS following antipsychotic medication. However, in our experience we consider ECT as relatively unsafe but recommend a combination of bromocriptine and benzodiazepine in cases of organic psychotic condition developing NMS following antipsychotic medication. Once his physical condition had stabilised, a combination of carbamazepine and low

potency neuroleptic chlorpromazine in low dosage was used though there are conflicting reports about the ability to tolerate antipsychotic medication once again [3]. The outcome was rewarding. Thomas et al [7] in their report of two cases found a cause-effect relationship between carbamazepine administration and NMS relief. During six monthly follow up he remained asymptomatic without any medication.

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