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Neuroleptic Malignant Syndrome during Perphenazine Treatment

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Abstract: A 50-year old woman developed symptoms of a neuroleptic malignant syndrome with myoglobinuric renal failure during treatment with perphenazine. After discontinuation of perphenazine and repetitive haemodialysis, the patient recovered. Clinical characteristics of the syndrome, differential diagnosis and various therapeutic possibilities are shortly reviewed.

Neuroleptic malignant syndrome (NMS) is a rare and often unrecognized complication of neuroleptic therapy. Characteristic features include altered consciuosness, extrapyramidal dysfunction, hyperthermia and muscle rigidity (Caroff 1980; Smego & Durack 1982; Downey *et al.* 1984). The pathogenesis of the syndrome is unknown, but similarities to malignant hyperthermia of anaesthesia have been found (Gronert 1980; Gronert *et al.* 1980), suggesting common mechanisms underlying both disorders.

Early recognition of NMS is of immediate concern to the clinician, as NMS is a potentially lethal disorder, which is fully reversible when adequately treated.

We report the case of a patient, who developed NMS and myoglobinuric renal failure during perphenazine treatment. After discontinuation of perphenazine and haemodialysis for 12 days, the patient recovered completely.

Materials and Results

A 50-year old woman suffering from psychosis during 3 years had been treated for several months with a daily oral dose of perphenazine 64 mg and 15 mg of biperidin. The medication had been discontinued for two weeks because of inadequate clinical effect. However, as increasing stupor developed, both perphenazine and biperidine were reinstituted. Twenty mg of perphenazine was given intramuscularly together with 10 mg biperidin. Later the same day the patient developed a temperature of 39.2°, a pulse rate of 130 beats per minute, a systolic blood pressure of 90 mmHg and increasing muscular rigidity. The creatinine level in serum increased to 440 μmol/l during the next 24 hours, and the patient became oliguric. She was transferred to our nephrological department on the second day in a condition of anuria, lethargy and hyperthermia. Physical examination revealed: blood pressure 110/80 mmHg, pulse 120 beats per minute, a temperature of 38.2° and universal muscular rigidity.

Immediately prior to the first dialysis on the second day we found the following laboratory values: serum-creatinine: 776 μmol/l (ref. range: 55–115 μmol/l), serum creatine phosphokinase: 44,980 U/l (100 per cent MM-band) (ref. range: < 150 U/l), serum aspartate aminotransferase: 790 U/l (ref. range: 10–40 U/l), serum lactate dehydrogenase: 1,773 U/l (ref. range: < 469 U/l) and serum myoglobin 2,000 nmol/l (ref. range: < 4.5 nmol/l). The serum concentration of calcium was 1.9 mmol/l (ref. range: 2.25–2.50 mmol/l).

Daily haemodialysis was instituted. Body temperature normalized after the first haemodialysis and muscular rigidity diminished. After oliguria for 12 days renal function was gradually regained, and all laboratory values normalized during her recovery. The decrease in serum creatine phosphokinase and serum myoglobin during haemodialysis is shown in fig. 1.

Discussion

The diagnosis of NMS in our patient was based on the presence of hyperthermia, extrapyramidal symptoms, altered consciousness and muscle rigidity with concomitant rhabdomyolysis and myoglobinuric renal failure. Haemodialysis had already been initiated, when the presumptive diagnosis of NMS was made. At this point of time the body temperature had normalized, and the muscular rigidity had decreased, for which reason therapy aimed against NMS was not instituted. Succeeding controls of the serum levels of creatine phosphokinase and myoglobin indicated no further lysis of muscle tissue in the patient.

The differential diagnosis of NMS include drug-induced malignant hyperthermia secondary to muscular rigidity as known from anaesthesia, status epilepticus and delirium. NMS carries a mortality of 20% (Mueller *et al.* 1983), but is often undiagnosed owing to a low overall incidence, and because each of the symptoms constituing the syndrome is commonly seen in psychiatric patients.

The butyrophenones, the thioxanthenes and the phenothiazines, which all exert a dopaminergic blocking effect on the central nervous system, have been associated with the syndrome (Henderson & Wooten 1981). This has lead to the proposal of an alteration of central neuroregulatory mechanisms as the cause of NMS (Caroff *et al.* 1983) and to therapies directed at central dopaminergic receptor sites (Mueller *et al.* 1983). However, similarities between the clinical picture of NMS and malignant hyperthermia have lately lead to new therapeutic strategies with early institution of dantrolene, an inhibitor of intrasarcoplasmatic calcium release. In several case reports (Delacour *et al.* 1981; Coons *et al.* 1982) dantrolene has been shown to induce rapid decrease in body temperature and to inhibit further lysis of skeletal muscle cells.

In patients with a history of NMS, Downey *et al.* (1984) found abnormal reaction to halothane. Smego & Durack

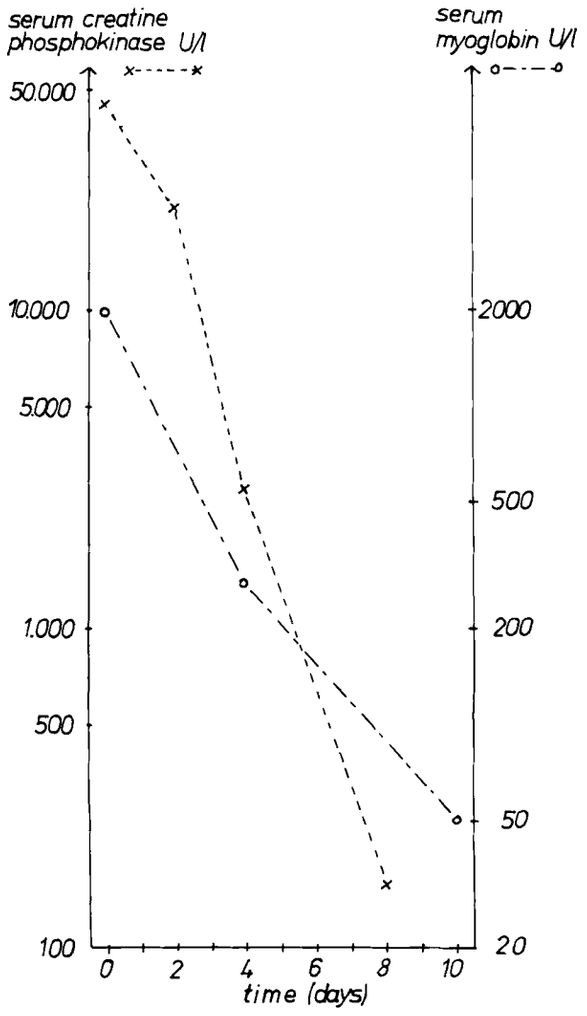

Fig. 1. Serum creatine phosphokinase and serum myoglobin related to time. Day 0 = day of admission = day of the first haemodialysis.

(1982) considered subsequent exposure to halothane in such patients at future anaesthesia to be associated with a risk of developing malignant hyperthermia, irrespective of previous safe exposures. Cross reactivity among the various neuroleptics with respect to development of abnormal muscle contracture response in muscle biopsy specimens from patients with NMS has been found by Downey *et al.* (1984). Halothane and neuroleptics should consequently be used with extreme care in patients with previous symptoms compatible with NMS.

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