LETTERS

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Neuroleptic malignant syndrome from chlorpromazine: case report

Sir,

We would like to draw attention to a case report detailing a condition which can be avoided by careful selection of medication.

A 56-year-old housewife who had suffered depression for several years, was readmitted to a psychiatric ward with symptoms of a relapse of depression including insomnia. Treatment was begun with lofepramine (120 mg), temazepam (10 mg) and piroxicam (20 mg). She had taken thioridazine intermittently in the past without any ill effects but during her recent admission thioridazine was not prescribed and she had last taken thioridazine many months before. During the second night of her stay in hospital she was given chlorpromazine (50 mg) orally as she was unable to sleep. She had never taken chlorpromazine before. She slept well but early in the morning awoke with acute hyperpyrexia, acute rigidity and acute confusion. She was transferred to a medical ward where, three hours later, she became unconscious and did not respond to painful stimuli.

Her past medical history includes appendicectomy, hysterectomy, oophorectomy, non-specific chest pain, episcleritis and osteoarthritis. She is known to be allergic to chlormethiazole.

At the time of admission to the medical ward her temperature was 41.1 °C, her pulse rate 123 per minute and regular, and her blood pressure 150/90 mmHg. She was deeply unconscious, had cogwheel rigidity and lead pipe rigidity in all limbs. Her reflexes were normal, the Babinski sign was negative, there was no meningism, her pupils were small and reacted equally, and her chest was clear. Her cardiovascular system and gastrointestinal systems were normal.

Her haemoglobin at that time was 16.2 g dl^{-1}, white cell count 6.1 × 10 l^{-1}, erythrocyte sedimentation rate 85 mm in the first hour, sodium 146 mM, chloride 112 mM, potassium 3.9 mM, urea 22.1 mM, creatinine 171 mM, alkaline phosphatase 90 IUl^{-1}, alanine aminotransferase 70 IUl^{-1}, calcium 2.23 mM, random blood sugar 10.5 mM, and bilirubin 17 μM. Her serum salicylate and paracetamol levels were negative. She had *Escherichia coli* in her urine with red blood cells, occasional white cells and some proteins. Her blood culture showed skin contaminants of staphylococci. Her creatine phosphokinase was raised to 4877 mM and her T4 level was 94 nM. Her electrogardiogram and chest x-ray were normal. A lumbar puncture or computerized tomography scan were not done. The characteristics of the arterial blood gases are shown in Table 1.

Table 1. Characteristics of the arterial blood gases.

	At admission on air	Two hours later, on 50% oxygen	In 24 hours, on 60% oxygen
pH	7.1	7.5	7.4
$P(O_2)$ (kPa)	5.2	5.9	6.4
$P(CO_2)$ (kPa)	3.4	3.4	4.4
Bicarbonate concentration (mM)	24.0	24.0	22.4

This 56-year-old, obese, heavy smoker had a single dose of chlorpromazine and became unconscious, hyperpyrexial, rigid and uraemic overnight. Highly raised creatine phosphokinase indicated a catabolic state. Having excluded infection, thyroid problems, catatonia and malignant hyperthermia of anaesthesia, she was diagnosed to have developed neuroleptic malignant syndrome, possibly from chlorpromazine therapy.

The patient was treated with supportive measures for hyperthermia and neuroleptics were immediately discontinued.[1] Fluid and electrolytic balance was maintained and appropriate oxygenation was undertaken. Before anticholinergics, dopamine agonists or dantrolene sodium could be introduced she improved remarkably. She regained consciousness on the third day with no residual neurological signs and was transferred back to the psychiatry ward for further psychiatric treatment. She was discharged by them in good health on lofepramine, temazepam and thioridazine.

In the USA in 1985 a survey of 53 patients with neuroleptic malignant syndrome showed pyrexia in 98% and raised creatine phosphokinase in 97% of the patients.[2] Remaining features included tachycardia in 91%, rigidity in 89%, altered consciousness in 84%, leucocytosis in 79%, abnormal blood pressure in 74%, tachypnoea in 73%, profuse diaphoresis in 67%, tremor in 45% and incontinence in 21%. Our patient had six of these 11 criteria.

Neuroleptic malignant syndrome is a potentially lethal reaction following the use of antipsychotic medication.[3] The most notorious drugs are those capable of blocking dopamine receptors in the basal ganglia and hypothalamus.[4] Up to November 1987 the Committee on Safety of Medicines had registered 634 side effects from chlorpromazine, of which nine were neuroleptic malignant syndrome. Three of these proved fatal and the mortality rate is said to be 20–30%. This case is perhaps the tenth in the series, warning us of the need for more selectivity when using chlorpromazine as a hypnotic or even a psychotropic drug. Unfortunately, there are no definite means of determining which patient will develop the syndrome.

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References

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Funds for research

Sir,

As compared with industry, the activities and effectiveness of the NHS are grossly under-researched. Issues of clinical management and policy arise mostly in