Missed neuroleptic malignant syndrome

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The neuroleptic malignant syndrome should be considered early in patients with any feverish illness when taking neuroleptic drugs

The neuroleptic malignant syndrome is a rare reaction to neuroleptic drugs characterised by fever, rigidity, alteration in consciousness, and autonomic dysfunction.¹ Early recognition of the diagnosis is essential to allow appropriate treatment and improve outcome. We present a case of the syndrome in which diagnosis was obscured by the presence of a proved infection.

Case report

A 67 year old woman was brought to the accident and emergency department having been found on the floor by a neighbour. She had a history of chronic obstructive airways disease and cardiac failure secondary to valvular heart disease. She had had depressive psychosis for many years and had been treated intermittently with oral trifluoperazine. Her other current drugs included dothiepin, temazepam, digoxin, diuretics, and inhaled bronchodilators.

On admission she was confused and dehydrated, with a temperature of 38°C. She had a tachycardia, normal blood pressure, and the murmurs of mitral regurgitation and mixed aortic valve disease. There were no signs of endocarditis; muscle tone in her limbs was symmetrically increased, with cogwheel rigidity; reflexes, including the plantar reflex, were normal. She had no neck stiffness. Initial investigations found leucocytosis ($19.8 \times 10^9/l$) and renal impairment (urea concentration 15.9 mmol/l; creatinine concentration 238 mmol/l). Chest radiography and electrocardiography gave normal results. Her urine was infected and contained blood, protein, and ketones on dipstick testing.

Urinary tract infection, dehydration, and Parkinsonism (possibly drug induced) were diagnosed. Apart from the bronchodilators, all of her drugs were discontinued and she received intravenous fluids and antibiotics. Despite this treatment her temperature rose to 40°C over the next 24 hours. Her tachycardia persisted but blood pressure remained within normal limits. Her conscious level deteriorated, but examination of her nervous system showed no new features. Urine culture confirmed infection with *Escherichia coli*, sensitive to most antibiotics; blood cultures were repeatedly negative. After 48 hours of intravenous antibiotic her fever remained, so treatment was changed to a combination of broad spectrum drugs. At this point the neuroleptic malignant syndrome was first considered and serum creatine kinase and urine myoglobin concentrations were measured.

On the third day of her admission, further investigations showed persisting leucocytosis, moderate hypoxia, and progressively deteriorating renal function. An echocardiogram showed no evidence of endocarditis. Lumbar puncture and cranial computed tomography gave normal results. Her creatine kinase concentration was high at 30 700 U/l (normal <120 U/l); no myoglobin was detected in the urine.

Treatment with intravenous dantrolene was started, which reduced her creatine kinase concentration but gave no clinical improvement. Her fever remained and she developed increasing respiratory and renal failure. Four days after admission she had respiratory arrest

and was transferred to the intensive care unit. Despite haemodialysis and ventilatory support her condition continued to deteriorate and she died the next day.

Discussion

The neuroleptic malignant syndrome is rare, affecting 0.4–1.4% of people taking neuroleptic drugs.² It is not always associated with the introduction of new drugs or a change in dose but may be precipitated by other factors, including dehydration, infection, or physical exhaustion.³ The condition may be caused by blockade of dopamine receptors in the basal ganglia and hypothalamus.⁴

Because of the clinical similarity between the neuroleptic malignant syndrome and malignant hyperthermia, an inherited condition which predisposes to prolonged muscle contraction and high temperature after exposure to inhalational anaesthetics, the same underlying muscle abnormality has been suggested to be present in both diseases. In vitro testing of muscle samples has produced conflicting results.^{5,6} However, the two conditions can be distinguished in vivo by the response to muscle relaxants—for example, pancuronium—which produce flaccid paralysis in the neuroleptic malignant syndrome but not in malignant hyperthermia. Consequently paralysis and ventilation can be used as a therapeutic manoeuvre in the neuroleptic malignant syndrome but not in malignant hyperthermia.

The neuroleptic malignant syndrome is associated with considerable mortality, reported rates varying from 16% to 24%.² The most common causes of death are respiratory failure, secondary to decreased chest wall compliance and aspiration pneumonia, and acute renal failure, secondary to rhabdomyolysis and myoglobinuria.⁷ Treatment with drugs that act either centrally or peripherally to decrease the excess muscle contraction has been shown to be more successful than supportive therapy alone.⁸ The drugs most often used are the dopamine agonist bromocriptine and dantrolene, a peripherally acting muscle relaxant. Both of these drugs produce improvement in some cases but neither is universally successful. Supportive therapy is therefore important to reduce mortality from renal and respiratory failure, especially as the syndrome seems to be self limiting, with fever usually remitting spontaneously within 10–12 days.

In our case the fever was initially thought to be due to the proved urinary tract infection. Once the syndrome was correctly diagnosed the patient's transfer to the intensive care unit was delayed, despite evidence of increasing respiratory and renal failure, because of the misconception that paralysis and ventilation would be unsuccessful, as they are in malignant hypertension. Intensive care should be considered for any patient with the neuroleptic malignant syndrome and evidence of respiratory failure. Serum creatine kinase should be measured early in patients with any feverish illness who are taking neuroleptic drugs, whether or not there is evidence of infection. Greater awareness of this condition among physicians dealing with patients taking neuroleptic drugs may improve outcome and reduce mortality.

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- 1 Levenson JL. Neuroleptic malignant syndrome. *Am J Psychiatry* 1985;142:1137-45.
- 2 Kellam AMP. The neuroleptic malignant syndrome, so-called. A survey of the world literature. *Br J Psychiatry* 1987;150:752-9.
- 3 Guze BH, Baxter LR Jr. Current concepts. Neuroleptic malignant syndrome. *N Engl J Med* 1985;313:163-6.
- 4 Henderson VW, Wooten GF. Neuroleptic malignant syndrome. A pathogenetic role for dopamine receptor blockade? *Neurology* (NY) 1981;31:132-7.
- 5 Caroff SN. Neuroleptic malignant syndrome and malignant hyperthermia. *Lancet* 1983;i:244.
- 6 Adnet PJ, Krivosic-Horber RM, Admantidis MM, Haudecouer G, Adnet-Bonte CA, Saulnier F, et al. The association between the neuroleptic malignant syndrome and malignant hyperthermia. *Acta Scand Anaesthesiol* 1989;33:676-80.
- 7 Ebadi M, Pfeiffer RF, Murrin LC. Pathogenesis and treatment of the neuroleptic malignant syndrome. *Gen Pharmacol* 1990;21:367-86.
- 8 Rosenberg NR, Green M. Neuroleptic malignant syndrome: review of response to therapy. *Arch Intern Med* 1989;149:1927-31.

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Leading for Health

Manpower

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This is the last in a series of articles responding to the questions raised by the BMA's document, "Leading for Health." The document looks well beyond the coming British election and raises questions about health and health care that will be on the agenda of many countries into the next century.

Manpower is accorded just two thirds of a page in *Leading for Health: a BMA Agenda for Health*,¹ yet its importance in the overall strategy of health care provision cannot be overemphasised. Many of the other issues discussed in the document have manpower consequences, not only for doctors but also for nurses, other professional groups, and ancillary staff. The NHS is the largest employer in Europe and some 70% of its budget is spent on salaries and wages. For these reasons alone manpower demands serious consideration by anyone intent on drawing up a blueprint for a health service in the year 2000.

The role of the NHS

In trying to predict the likely manpower requirements of the health services in the next century it is necessary to make an assumption about the role which they will be required to fulfil. The first page of *Leading for Health* recalls the fact that health services are but a part of a broader strategy for improving health, which also includes social services, community and occupational health services, public utilities, local authorities, and bodies concerned with health education.

The magnitude of public spending on health and its distribution between the various responsible bodies are likely to remain matters of controversy for the foreseeable future. The past decade has seen increasing interest in the prevention of illness as opposed to its treatment and in caring for patients in the community rather than in institutions. Unfortunately, both of these shifts are expensive in financial and manpower terms. The flagship of the government's preventive strategy—the United Kingdom breast cancer screening project—has been estimated to cost £4500 per life year saved and has substantially increased the demand on surgical and radiological services for localisation breast biopsy. Community care requires more carers than institutional care, and *Leading for Health* notes the decreasing proportion of informal carers—relatives, friends, and volunteers—relative to the numbers of elderly and mentally ill people. The NHS acts as a safety net for those who can no longer cope in the community and, as the population ages further, this aspect of its task is likely to increase.

There seems little scope for reducing the amount spent on the NHS or for reducing its role in the overall health strategy. The service has been in a state of almost perpetual financial crisis throughout the 1980s, with demand outstripping supply, persistent long waiting lists, and numerous stories reported by the media of apparently scandalous failures of provision. The BMA, most of the general public, and many managers believe that more should be spent on it. Improvements in community care, disease prevention,

and health promotion do not lead to reduced demands on the health service, and they increase the demand for trained health professionals.

The NHS's other role of seminal importance is that of providing training for health professionals, including those who will subsequently work outside it. In the past such training has largely been acquired through service on an apprenticeship model and the numbers trained have been related to service needs. More educationally based programmes are slowly gaining ground in both medicine and nursing, and the role of the NHS as an educational resource must be recognised and supported if sufficient numbers of health professionals are to be available to meet all needs in the future.

Skill mix and changing roles

Concepts of what constitutes appropriate work for doctors, nurses, and other groups of health workers vary from country to country. In countries which have large numbers of doctors relative to the population, doctors may often be found doing work which, in Britain, would be carried out by others, such as those in hospital administration, pharmacy, rehabilitation and physiotherapy, and nurse education. Where doctors are scarce substantial amounts of treatment may be carried out by paramedical practitioners. The correlation between density of doctors and task allocation, however, is not exact. In the United States there are over 25 000 medical assistants, who, on the basis of two years' training, undertake such tasks as patient clerking, investigation, surgical assistance, and postoperative management, utilising written protocols. The accepted roles of doctors, nurses, and others in Britain are largely the result of tradition and bear re-examination.

Both the medical and the nursing professions have proved conservative in their attitudes to changing or extending roles, as evidenced by their opposition to the introduction of nurse prescribing, to the trial appointment of a paramedical surgeon's assistant in cardiothoracic surgery in Oxford, and to the giving of parenteral drugs by nurses. Yet in other areas non-medical staff have proved their value as counsellors, diagnosticians, and therapists. The need to reduce the burden on junior doctors has led to discussions between the BMA's Junior Doctors Committee (JDC) and the Royal College of Nursing on the reallocation of tasks, and the University of London has taken a lead in insisting on the presence of ward clerks and phlebotomists in hospitals whose house jobs it approves.²

Experience in the United States and elsewhere proves that appropriately trained paramedical staff can carry out many medical tasks to a high standard, and

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