Recurrent Sinus Arrest in Association with Neuroleptic Malignant Syndrome

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We report a case of neuroleptic malignant syndrome where the catatonia clearly followed the administration of neuroleptics and where the neurovegetative disturbance was remarkably severe, including episodes of tracheal spasm, apnoea and episodes of bradycardia, and sinus arrest requiring insertion of a temporary external pacing wire. To our knowledge, such severe disturbance has not previously been reported.
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Neuroleptic malignant syndrome (NMS) is a fulminant, life-threatening and distinctive side-effect of neuroleptic drugs, characterised by a diffuse and severe muscle rigidity, often with extrapyramidal side-effects: alteration of consciousness; hyperpyrexia and autonomic dysfunction including sweating; tachycardia; and lability of blood pressure. There is often an associated leucocytosis and the serum creatinine kinase is characteristically elevated. The pathogenesis is not unknown. One theory is that there is dopamine depletion and/or dopamine receptor blockade by the neuroleptic medication.

Supportive measures are vital in the management of NMS and most patients will require treatment on the medical intensive care unit. Neuroleptic drugs must be discontinued immediately. The efficacy of specific treatments for NMS remains unclear. Bromocriptine and dantrolene have been used. Electroconvulsive therapy (ECT) and benzodiazepines have also been found helpful in some cases. Rosebush *et al* (1991) suggest that bromocriptine and dantrolene may prolong the course of NMS.

There has been speculation over the association between catatonia and NMS (Fleischhacker *et al* 1990; Arya, 1992; Otani *et al*, 1992; Weller, 1992). Kellam (1987) reviewed the literature relating to NMS and similar conditions, and Castillo *et al* (1989) drew attention to the differences in the mode of onset, signs, symptoms and outcome of lethal catatonia and NMS, which they argue differentiate the two clinically. White (1992), describing episodes of catatonia and NMS in the same patient, suggests that it is misleading to view the conditions as separate entities, and that NMS is but a neuroleptic-aggravated form of the catatonic state that preceded it and should be incorporated into the catatonic disorders.

Case report

A 22-year-old woman of previously good physical and mental health was admitted with an acute schizophrenic psychosis characterised by auditory hallucinations, somatic delusions, and passivity phenomena. On admission, she was in clear consciousness, physically well, and her neurological examination was normal. Her white cell count was $8.6 \times 109/l$, her biochemical profile and thyroid function tests normal and urine drug-screening was negative. She was treated with chlorpromazine, 100 mg, increasing to 150 mg four times daily after 24 hours, and changing to 10 mg haloperidol four times daily after a further 36 hours. She was also given an intramuscular injection of 100 mg zuclopenthixol acetate 24 hours after admission.

Four days after admission, she developed extrapyramidal side-effects which were treated with anti-Parkinsonian medication. Six days after admission, she became catatonic with periods of stupor and excitement and intermittent waxy flexibility. Her temperature rose to 37.5°C per axilla, her blood pressure varied between 170/130 and 120/180 mmHg, she had pronounced diaphoresis and sialorrhoea and, over the next eight hours, her level of consciousness fluctuated and deteriorated. Her white cell count was $12 \times 109/l$ and her serum creatinine kinase was 1261 IU/l (normal range less than 250 IU/l).

Twelve hours after the development of the catatonia our patient was pale, clammy, mumbling incoherently, apparently choking on her profuse saliva and displaying epileptiform phenomena, in the form of twitching facial muscles. She remained hypertonic with waxy flexibility. She developed periods of apnoea lasting for up to 30 seconds and it was decided to transfer her to the medical intensive care unit.

Shortly after her arrival there, she had an episode of bradycardia and sinus arrest lasting 14 seconds. She was subsequently found to be having 10 to 15 episodes per hour, with some sinus arrests lasting as long as 50 seconds (Fig. 1(a) and (b)). In response to this, a temporary pacemaker wire was inserted. Possible mechanisms for the bradycardia and sinus arrest include vagal stimulation, perhaps via the intense pharyngeal spasm resulting in carotid sinus pressure or a Valsalva manoeuvre-type phenomenon. Some of the bradycardiac episodes may have been secondary to intermittent hyperpyrexia and apnoea (Hurst, 1986).

For the next three weeks the patient remained on the intensive care unit. Her condition was very unstable. Her temperature varied between 36.5°C and 38.4°C, and her blood pressure from 100/55 to 180/115 mmHg. Despite repositioning of the pacing wire, the pacemaker did not always capture and the patient continued to have frequent episodes of bradycardia and sinus arrest (Fig. 1(c) and (d)). Some of these episodes were associated with apnoea, when the oxygen saturation dropped as low as 80%. Some were

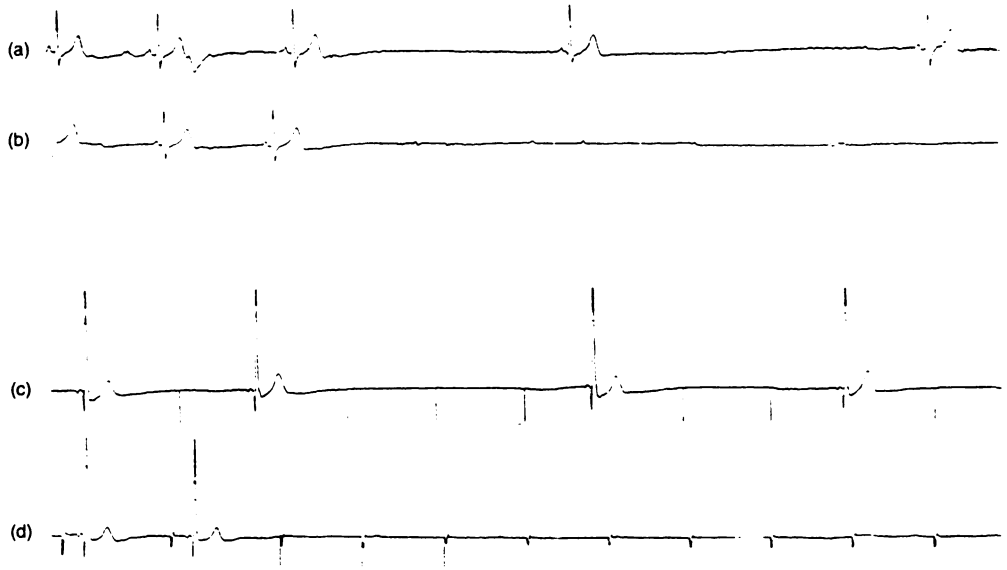

Fig. 1 Electrocardiogram (ECG) traces of patient: (a) and (b), shortly after admission; (c) and (d) three weeks later, with a temporary pacemaker. Pen speed (on this scale) was 11 mm/s.

associated with episodes of stertorous breathing and probably tracheal spasm. Some occurred without any respiratory disturbances. The patient's condition deteriorated steadily during the first week. Treatment centred around supportive care, including intensive monitoring, medical and nursing care, intravenous fluids and nasogastric feeding. Oxygen was given as required to keep the oxygen saturation above 90% (generally 97–99%). The PCO_2 and pH were measured intermittently. PCO_2 levels ranged between 33.4 and 35.9 mmHg and pH levels from 7.41 to 7.48. There was no apparent response to ECT (three treatments) or bromocriptine (2.5 mg three times daily) which made her vomit. There were occasional dramatic responses to intravenous diazepam when the patient was seen to 'wake up', open her eyes, and even speak. The benzodiazepine also seemed to settle her physical condition for short periods. However, overall, her condition worsened. She continued to have frequent episodes of bradycardia, sinus arrest, tracheal spasm and epileptiform twitching around her eyes and mouth. She remained rigid, pyrexial and had heavy sialorrhoea. The periods of responsiveness and excitement gradually became shorter and less frequent, and by the end of the first week she was unresponsive, mute and motionless. Bromocriptine and ECT were discontinued.

During the second week she remained unresponsive but the commencement of dantrolene (25 mg twice daily) reduced the frequency of the tracheal spasms. She continued to have periods of bradycardia and sinus arrest, and also had occasional sinus tachycardias of up to 160 beats per minute. Otherwise her condition was unchanged. During the third week she began to improve. The episodes of stertorous breathing and tracheal spasm stopped completely. She had occasional episodes of apnoea associated with epileptiform phenomena, including facial twitching and tongue biting. She gradually used the pacemaker less and less and, after not being needed for seven days, it was switched off. She remained pyrexial but the sialorrhoea resolved and the rigidity was replaced by intermittent waxy flexibility and occasional spontaneous movement. She gradually became more responsive and there were episodes of laughing, crying and muttering, with occasional comprehensible speech.

Investigations also included: a computerised tomography scan, which was normal apart from a congenital sub-arachnoid cyst in the left posterior fossa; a lumbar puncture, which yielded normal cerebrospinal fluid; an echocardiogram which revealed normal cardiac chambers and valves; several normal chest X-rays and normal electrocardiograms. The creatine kinase fell from 1261 IU/l to 93 IU/l and then fluctuated within the normal range. The white cell count fluctuated from 12 to 20×109/l throughout. Electrolytes were maintained within normal range and the biochemical profile was normal throughout. Blood cultures were persistently negative, as were virology studies. Two catheter urine specimens revealed infection with *Staphylococcus aureus* and *Pseudomonas*. These were treated according to their sensitivities.

Progress

Over the next three months, our patient received 12 ECT applications at weekly intervals, and she made slow progress. Detailed psychometric assessment after three months revealed acquired impairment of intellectual

functioning, including antrograde amnesia, with complete loss of recollection of her initial admission and subsequent treatment.

At the time of reporting, our patient is more or less symptom-free and has been at home for more than three months. Our task will be to control and relieve our patient's psychosis with a limited therapeutic armoury.

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Dysthymia and Mental Handicap

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Two cases of dysthymia in mentally handicapped patients are described. The absence of publications on dysthymia in the mentally handicapped is noted. The importance of early diagnosis and treatment with advanced antidepressants and psychotherapy is emphasised.

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Dysthymia or dysthymic disorder is a hitherto poorly understood protracted dysmorphic state of mood or personality, which burdens the patient not so much because of the intensity but more because of its long duration. Even though the symptoms are sometimes relatively mild, its chronic course causes disability in social life. Clinicians usually meet with frustration in their attempts to treat these patients.

The best-known traditional term for dysthymia is 'chronic neurotic depression'. In the mid-19th century Karl Khalbaum coined the term 'dysthymia' for chronic depression with no history of mania (Jackson, 1986). Dysthymia was first defined in a systematic way in 1980 in the official classification of the American Psychiatric Association, DSM-III. Its successor, DSM-III-R (American Psychiatric Association, 1987), subdivides dysthymia into primary (mood disturbance is not related to pre-existing chronic non-mood axis I or III disorder) versus secondary and early onset (if the disturbance began before the age of 21 years). The ICD-10 classification (World Health Organization, 1992) defines dysthymia as "a chronic depression of mood which does not currently fulfil the criteria for recurrent depressive disorder, mild or moderate severity, in terms of either severity or duration of individual episodes, although the criteria for mild depressive episode may have been fulfilled in the past, particularly at the onset of the disorder". Akiskal (1990) presented the main clinical manifestations of dysthymia as part of a volume of papers arising from a meeting in 1987 (Burton & Akiskal, 1990). We reviewed the case