Letters


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Neuroleptic malignant syndrome in a patient with Wilson’s disease

Sir: The neuroleptic malignant syndrome (NMS) is a rare but potentially lethal complication of treatment with neuroleptic drugs. It is manifested by Parkinsonian symptoms accompanied by fever and signs of autonomic instability. Most of the reports of NMS concern patients with schizophrenia or major affective disorders.1,2 We here describe a case of NMS in a patient suffering from Wilson’s disease who was taking neuroleptics. To our knowledge this is the first such report.

The patient is an 18 year old man who was well until August 1984. Pregnancy and birth were normal and no serious illness during childhood was reported. He has an older sister who is healthy. His parents are also healthy and not consanguineous. In September 1984 he showed evidence of mental disturbance. He became agitated and began to experience delusions (mainly of a persecutory and homosexual content) and visual and auditory hallucinations. He slept poorly and had anorexia and weight loss. In April 1985, 4 mg haloperidol, 90 mg thioridazine and 6 mg biperiden daily were started. His mental state improved but he developed marked Parkinsonian features and medication was discontinued 10 days later. Until August 1985, the patient was drug free but the Parkinsonian signs, mainly a left hand rest tremor, persisted. During this drug free period he again became agitated, deluded and hallucinated. He was then given 300 mg chlorpromazine, 25 mg loxapine, 4 mg trifluoperazine and 150 mg orphenadrine daily. A few days later his mental state was improved, but the Parkinsonian signs worsened. These drugs were therefore stopped. In November 1985, the patient was receiving only 20 mg diazepam and 150 mg orphenadrine daily. Just before admission to Egiption Hospital (8 January 1986) there was an exacerbation of his psychiatric symptoms. 30 mg haloperidol, 300 mg chlorpromazine and 15 mg trihexyphenidyl daily were restarted. On admission he was sweating profusely, dysarthric with marked sialorrhea, rigidity, choreiform movements, opisthotonic posturing and fever (39.3°C). He required help to be fed, while his conscious level fluctuated. The respiratory rate was 29/min and the pulse 130/min. Blood pressure was 145/80 mm Hg. From time to time he developed oculogyric crises accompanied by retrocollis and elevation in blood pressure (to 180/120 mm Hg) of about 10 min duration. The following day all neuroleptic drugs were discontinued. On 15 January he received only 15 mg diazepam and 80 mg propranolol daily. On neurological examination he was cooperative. He showed fixity of facial expression. His fundi and pupils were normal. Tongue movements were very limited. Both arms were very rigid. Power was normal but discrete finger movements were very poorly performed. The tendon reflexes were sluggish, abdominal reflexes symmetrical, and both plantar responses flexor. There was no detectable sensory deficit and general examination was normal. A detailed investigation of the blood, liver, and thyroid function was performed. Other investigation included: anti-nuclear, anti-DNA and antiviral antibodies, C-reactive protein, α antistreptolysin-O, ECG, EEG, muscle biopsy, motor and sensory conduction velocity. Wright, Widal, Weil-Felix, Paul-Bunnel, VDRL, ELISA test were also performed and urine, blood and CSF cultured. All these tests and laboratory data were normal except an elevation of serum CK (340 U/l, normal up to 76) and aldolase (9.8 U/l, normal up to 7-6). Computed tomography of the brain showed moderate ventricular enlargement without changes in the region of the basal ganglia. The serum caeruloplasmin level was severely reduced at 0.06 g/l (normal 0.2-0.4) and the serum copper level was also reduced at 5-7 μmol/l (normal 11-0-22-0). Urinary copper excretion over 24 h was abnormal at 4-4 and 5-1 μmol/l (normal 0-1-0). Liver biopsy showed evidence of cirrhosis with deposition of copper and copper associated protein. Kayser-Fleischer rings were readily detectable with a slit lamp. The diagnosis of Wilson’s disease was therefore clearly confirmed during the next 20 days his condition deteriorated. Tone was greatly increased in all muscle groups and his temperature rose to 39-5°C. Finally he became mute, withdrawn and unresponsive. Because of his elevated serum CK, high fever, extrapyramidal signs and autonomic dysfunction the diagnosis of NMS was made. Bromocriptine up to 40 mg/day, dantrolene 200 mg/day and amantadine 200 mg/day were given. Shortly afterwards the patient’s condition, including conscious level, muscular rigidity and fever improved considerably. On 5 March, the temperature was normal and remained so afterwards. He was able to feed himself and he could also stand up and walk with support. In contrast his mental condition deteriorated. On 12 March ECT was started and gradually the drug doses were reduced. By 5 April, after 12 ECT treatments he was receiving no drugs except for 80 mg/day propranolol. He was able to speak and communicate. The elevated serum enzymes (CK and aldolase) fell to normal. His psychotic condition was improved with the exception of his impulsive behaviour.

Because of the primary diagnosis (Wilson’s disease) at this stage (June 1986) treatment with penicillamine 500 mg/day was initiated. One week later this treatment was discontinued because of leucopenia and thrombocytopenia. In September 1986 treatment with trientine dihydrochloride 1200 mg/day was started. The results of 24 hour copper excretion estimation indicated a reduction to the normal limits. One year later (February 1987) the patient is psychiatrically and neurologically well apart from slight rigidity (mainly of the left hand) and dysarthria. During all this last period (6 months) he received 1200 mg trientine dihydrochloride, 30 mg diazepam and 12 mg benzexol daily and there was no need to give any neuroleptic drug.

The patient fulfilled all the primary criteria for NMS given by Levenson3 (fever, rigidity, increased CK) and five of his six secondary criteria (only leucocytosis exempted). In addition the patient met all the three criteria for the definite diagnosis of NMS given by Pope et al4 (hyperthermia, severe extrapyramidal effects, autonomic dysfunction). To our knowledge no case of NMS in a patient with Wilson’s disease has hitherto been reported though NMS cases in patients with organic brain syndromes, mainly with basal ganglia pathology, such as Huntington’s chorea or Parkinson’s disease, have been described.5,6 Caroff7 has suggested that organic brain diseases might be
Brain death and pinpoint pupils

SIR: Non-reactive pupils are one of the cardinal signs in brain death. Contrary to what was required at one stage it is no longer considered necessary for the pupils to be dilated. In fact they are most often found to be in the mid position.2 3 Pinpoint pupils are not a feature of brain death and may be the result of a bilateral pontine lesion affecting the sympathetic fibres. That pinpoint pupils may be seen in verified brain death is evident from the following case.

The patient was a 69 year old woman with coronary heart disease for 12 years, and one mild ischaemic stroke two months before carotid endarterectomy. The endarterectomy was performed successfully but twenty hours after operation the sutures of the carotid artery ruptured resulting in a profuse bleeding. The huge haematoma in the neck prevented intubation, and an emergency tracheostomy was performed. During about ten minutes the respiration was severely impaired and the situation was further complicated by cardiac arrest. After ten minutes' resuscitation the heart began to beat but the intra-arterially measured blood pressure readings stayed for 80 minutes at the level of 30–50 mm Hg systolic. The patient did not regain consciousness, and six hours later she was deeply comatous with no pupillary reactions, no response to the oculo-cerebral test, and no grimacing during firm compression of the supraorbital nerves.

The patient was ventilated for ten minutes with 100% oxygen and then disconnected from the respirator for 10 minutes. During the disconnection 100% oxygen was infused into the trachea at a rate of 6 l/min. At the time of the disconnection the Paco2 level was 4.5 kPa which, according to a recent study4 results in final Paco2 levels giving a maximal stimulation of the respiratory centre. No spontaneous breathing movements occurred during the test. Because the non-reactive pupils were of pinpoint size and thus not in accordance with the criteria of brain death, the patient was again connected with the respirator. Twenty-four hours later the examination gave the same result, the pupils were still of pinpoint size. The scrutiny of the case history revealed glaucoma treated with pilocarpine eye drops given twice daily in both eyes before and after surgery. The patient was disconnected from the respirator, and two days later a medicolegal necropsy showed a typical respirator brain.

Our case emphasises the importance of a thorough scrutiny of the medication used in case of suspect brain death. In his excellent articles on brain stem death Pallis mentioned as pitfalls in the diagnosis anticholinergic drugs, neuromuscular blockers, and pre-existing eye disease.3 In 1971, Wexler reported of two patients in irreversible coma, with non-mydriatic pupils who had been using miotics for glaucoma. We would like to add pilocarpine to the list of pitfalls in the diagnosis of brain death. It acts as a cholinergic mimetic directly on cholinergic receptors, an effect which is not abolished by denervation. Because glaucoma is common especially among older people, and is often treated with pilocarpine, this possible cause of miotic pupils in suspect brain death must be kept in mind.

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Acute dystonic reaction with asterixis and myoclonus following metoclopramide therapy

SIR: Extrapyramidal side effects are well recognised following medication with metoclopramide, a selective D2 dopamine antagonist.5 6 Some 95% of these effects are of the acute dystonic-dyskinetic type. They occur mostly in younger females, within 24 hours of taking the drug, and disappear without specific treatment. Oculogyric crises, torticollis, opisthotonus, and orofacial dyskinesias are often present. However, the occurrence of asterixis and myoclonus together with acute dystonic reactions has not been reported. We observed such a patient.