Letters

Neuroleptic malignant syndrome associated with metoclopramide

Sir: The neuroleptic malignant syndrome is a rare idiosyncratic drug reaction comprising muscular rigidity, altered consciousness and autonomic dysfunction, which has been described following the administration of major tranquillisers such as butyrophenones, thioxanthenes and phenothiazines.^{1,2} It is thought to be due to dopamine receptor blockade in the basal ganglia and hypothalamus.² We describe a patient who developed the neuroleptic malignant syndrome after metoclopramide therapy.

A 53-year-old Jamaican man was given 20 mg of metoclopramide by intramuscular injection for nausea during an acute illness characterised by pyrexia and productive cough. Three days later he noticed stiffness and weakness of his legs; over the next week he became increasingly immobile and tremulous, with difficulties in swallowing, speaking and breathing, and frequent bouts of sweating. On examination on admission to hospital he was agitated and sweaty but afebrile. He had a sinus tachycardia of 120 beats/min and his blood pressure was 190/110 mm Hg. He was dysarthric and could not protrude his tongue. There was moderate bradykinesia and marked axial and limb rigidity, with a tendency to maintain a catotonic posture, and a coarse resting tremor at 6 Hz. A full blood count was normal; serum bilirubin and creatine kinase were elevated at 44 µmol/l and 440 iu/l (normal <200) respectively. Hepatic enzymes, cerebrospinal fluid examination and computed tomography of the brain were normal. No phenothiazine metabolites or other drugs were detected in blood or urine.

Treatment with anticholinergic drugs and levodopa in doses of up to 2 g/day was ineffective. The patient's pulse and blood pressure fell to normal within 10 days of admission, and his neurological signs slowly resolved between two and six weeks after admission.

Metoclopramide is known to produce a number of extrapyramidal syndromes, such as acute, or more rarely chronic, dystonic reactions and mild drug induced parkinsonism.^{3,4} The autonomic and other neurologic features of our patient's illness suggest a diagnosis of the neuroleptic malignant syndrome, as does the lack of response to dopaminergic and anticholinergic drugs.⁵ Abnormal liver function tests and elevation

of serum creatine kinase concentrations often occur in the neuroleptic malignant syndrome.³ Pyrexia, leucocytosis, and stupor have been described in a number of previously reported cases, and there is an overall mortality of 20%, often due to respiratory failure.¹ Although the neuroleptic malignant syndrome has not been reported before in association with metoclopramide administration, its occurrence could be expected in view of the dopaminergic activity possessed by this drug.⁶

MB ROBINSON

RP KENNETT

AE HARDING

NJ LEGG

Department of Neurology, Hammersmith Hospital, Du Cane Road, London, W12 0HS

B CLARKE

Ealing Hospital, Uxbridge Road, Southall, Middlesex, UB1 3HW, UK

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Accepted 12 June 1985

Catamenial exacerbation of action myoclonus: successful treatment with acetazolamide

Sir: Lance and Adams first described action (intention) myoclonus in 1963 as a syndrome following severe hypoxia. This consists of incapacitating lightning-like jerks induced by voluntary movements,¹ and was later shown to be associated with consistently low cerebrospinal fluid (CSF) levels of 5-hydroxyindoleacetic acid (5-HIAA), a metabolite of serotonin.² Successful treatment has been reported using l-5-hydroxytryptophan (5-HTP), valproic acid and clonazepam.²⁻⁶ Each of these drugs raises CSF 5-HIAA levels.

Methysergide, a serotonin receptor blocker, tends to increase the myoclonus.⁴ Hence it is believed that action myoclonus is an effect of serotonin insufficiency, presumably from damage to or dysfunction of the raphe nuclei.

I report a case of postanoxic action myoclonus that was effectively treated with 5-HTP, clonazepam and valproic acid. Premenstrually she suffered severe exacerbations. Acetazolamide produced prompt and marked improvement.

The patient is a 35-year-old woman who suffered prolonged hypoxia when aged 27 years during the excision of a pilonidal cyst. This resulted in a mild cognitive impairment, tonic-clonic and tonic seizures, and severe action myoclonus. While being treated with valproic acid, clonazepam, phenytoin and quinine her seizures were well controlled but her myoclonus was only modestly improved. She was confined to bed or her wheelchair and was unable to transfer herself or perform most self care. Her speech was often unintelligible because of myoclonus. Premenstrually her symptoms regularly worsened. At age 34 years 5-HTP and carbidopa were added to her regimen as phenytoin and quinine were discontinued. This resulted in marked improvement of her myoclonus and thus her functional ability. She was able to dress and feed herself, speak much more clearly, perform transfers, and to walk with assistance. Her seizures continued to be well controlled.

Postmenstrually her speech was quiet, hypernasal and ataxic. She could speak in whole sentences with each breath and was understandable. Saccades were hypometric and symmetric gaze-evoked horizontal nystagmus was present. All limbs showed mild to moderate ataxia with intention tremor and rebound. Myoclonic jerks occurred infrequently in association with volitional movements. Deep tendon reflexes were normal and the plantar responses were downgoing. Her gait was markedly ataxic.

Beginning 2 days premenstrually and lasting for about 3 days she would return to her previous status. During an untreated exacerbation her speech markedly deteriorated. She could speak no more than two words per breath. Opsoclonus was present. At rest multifocal myoclonus occurred every few seconds. Intentional movements were profoundly contaminated by large amplitude myoclonic jerks. This was noted on seven consecutive cycles. Valproic acid levels were unchanged during these exacerbations. She was then placed on acetazolamide 250 mg, four