Letters

Carbamazepine-induced choreoathetoid dyskinesias

Sir: Choreoathetoid and choreiform dyskinesias have been attributed to antiepileptic drug intoxication, especially with phenytoin.¹⁻⁶ Isolated cases of choreoathetoid movements also have been observed during intoxication with other anticonvulsants, including ethosuximide, methsuximide,⁷⁻¹¹ keto-carbamazepine,¹² phenobarbitone,^{13 14} primidone,¹⁵ and sulthiame.² The dyskinesias caused by simultaneous administration of phenytoin and sulthiame or succinimides may have been provoked by an increase in the serum level of phenytoin. Very few cases of involuntary movements after administration of carbamazepine have been reported so far. One patient of Lefevre and Gablain¹⁶ developed dyskinesias similar to a "flapping tremor" as a symptom of carbamazepine intoxication. Wendland¹⁷ described three patients with myoclonic jerks in connection with carbamazepine intake. A patient of Gruska *et al*¹⁸ taking 20 g of carbamazepine in a suicidal attempt developed "incoordinate ballistic or cramp-like movements of all extremities". Several authors¹⁹⁻²¹ have reported dystonia in patients treated with carbamazepine. Troupin *et al*²² also observed a dyskinetic eye movement disturbance as a symptom of carbamazepine intoxication.

A 71-year-old female patient, without any family history of involuntary movements, was referred because of choreoathetoid dyskinesias. The patient developed generalised epileptic seizures of unknown aetiology (pneumencephalography was normal) at the age of 53 years, and subsequently was treated with 250 mg of primidone daily. Because of the development of partial seizures with elementary symptomatology, additional anticonvulsant therapy with carbamazepine was started four years ago. The daily dose was increased to 800 mg of carbamazepine over four days. Her husband reported the sudden onset of distal choreoathetoid dyskinesias of the upper and lower limbs on the third day of administration of carbamazepine, which also caused an impairment of gait and a confused state of mind with visual and acoustic hallucinations. On neurological examination, there were intermittent distal choreoathetoid dyskinesias of the extremities. The speech was

slurred and the gait ataxic, but nystagmus was not present. The EEG was characterised by a 8-9/s background activity, interspersed with theta and 2-3/s delta waves. Epileptic discharges and focal activity were not observed. Serum levels of the antiepileptic drugs (method: Emit Immunoassay) were: carbamazepine 80.4 µmol/l (19 µg/ml), phenobarbitone 61.6 µmol/l (14.3 µg/ml), and primidone 17 µmol/l (3.7 µg/ml). The carbamazepine value was confirmed by high pressure liquid chromatography. The dose of carbamazepine was gradually reduced and completely withdrawn within 7 days, and the choreoathetoid dyskinesias disappeared. Two months later the patient was re-examined and showed no involuntary movements or psychosis.

K BIMPONG-BUTA

W FROESCHER

Department of Epileptology,
University of Bonn, D-4300 Bonn 1,
Federal Republic of Germany

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Post-traumatic tremor due to vascular injury and its treatment by stereotactic thalamotomy

Sir: We have elsewhere given an account of the development of "peduncular" tremor in patients surviving severe head injuries, and its responses to stereotactic thalamotomy.¹ The clinical and radiological evidence in those cases pointed to a midbrain lesion, probably at the level of the superior cerebellar peduncle, as the cause of the disabling postural and action tremor usually of the upper limb. We have recently had the opportunity to study and treat a patient in whom tremor developed

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after trauma, but in whom the mechanism of production of the lesion, and its siting were fundamentally different. Despite this the tremor was successfully controlled by unilateral thalamotomy.

Sixteen months previously the patient, aged 34 yr, fell from his motorcycle and twisted his neck sharply in order to avoid striking his head on a projecting object. He did not actually injure his head. Two weeks later, his left leg suddenly became weak for a short period, with a recurrence leading to a left hemiparesis the same evening deteriorating over the next three weeks. A CT scan at another hospital, showed a low density lesion in the white matter close to the roof of the body of the right lateral ventricle. This area appeared to have increased in size by a small amount over the next few weeks, but then remained stationary. During the next three months the power began to improve in the left limbs but increasingly severe resting and action tremors of the left arm developed. This considerably increased his disability. Although he had adequate strength in the arm he could not even hold a cup in his left hand. During the few months immediately prior to referral the patient had been treated with clonazepam. He was also receiving baclofen which had improved the spasticity in his left leg. Examination showed an intelligent, right-handed man. There was a coarse resting tremor of the left arm and a very mild left spastic hemiparesis with the usual reflex changes. On lifting the left arm to the horizontal, the rhythmical 4 Hz tremor became much more pronounced and was further exaggerated on finger-nose testing. He had good grip in that hand. The tremor had the character of a red nucleus or "peduncular" tremor. He was found to have a few beats of horizontal nystagmus on gaze to the right. Hearing on tuning fork testing was equal in both ears. Skull radiographs showed no fracture. A CT scan (fig A) confirmed the presence of a lucent area in the white matter above the anterior part of the body of the right lateral ventricle and this seemed to be of the same size and shape as in the previous records at the referring hospital. An EEG showed no focal disturbance and it was concluded that the scan lesion was not progressive. Its nature was not immediately certain. It was thought most likely that it was due to infarction. Since a plaque of demyelination was possible detailed vestibular testing was carried out. This showed enhanced caloric nystagmus in the dark and on electronystagmography eye closure provoked a few

Figure A CT scan showing low density lesion above right lateral ventricle, B right carotid arteriogram showing site of intimal tear (arrow).

beats of first degree nystagmus to the right and second degree to the left. In the dark well marked first degree nystagmus was elicited to either side. Brain stem evoked potentials showed some distortion of the normal wave form. These features were thought compatible with a separate brain stem lesion but when his clonazepam and baclofen were withdrawn these abnormalities disappeared. We concluded therefore that they were due to the effects of medication. His CSF was also examined because of the possibility of demyelination, and revealed no evidence of an oligoclonal pattern. Right carotid angiography showed dissection of the intima of the distal 3 cm of the right common carotid artery (fig B). It was concluded that the low density lesion on the scan was indeed likely to be due to an infarct, produced by embolism from mural thrombus that had developed at the site of the traumatic intimal tear in the carotid vessel.

Staged stereotaxic thalamotomy was performed on the right side, using cell recording and electrical stimulation in order to determine the position of the nucleus ventralis intermedius, where we wished to centre the lesion. A total of three lesions was made, the second and third being anterior and posterior extensions of the nucleus ventralis intermedius lesion. The tremor then disappeared. There was a slight increase in his hemiparesis. The patient was treated with vigorous physiotherapy and discharged from hospital ten days later. When seen 4 months after operation the hemiparesis had almost recovered to its pre-operative state but it

was deemed advisable to prescribe a small dose of baclofen for residual spasticity in the leg. The tremor was greatly reduced, only a few beats of very low amplitude being detectable on using the left hand. Tremor no longer presented any disability to the patient.

Maki *et al*² described a group of cases in whom hemidystonia developed within a few minutes, or up to a few hours following a minor head injury. In their cases there was a linear lucent area on scans extending from the head of the caudate through the anterior limit of the internal capsule to the lentiform nucleus. It was suggested that the lesion was an infarct produced by dislocation of the perforating vessels of the middle cerebral artery through the sudden twisting movement of the head. Injury to the side or back of the head was thought to create a rotational movement of the brain within the skull, thus inflicting damage on the small perforating vessels whose parent trunks would be partly fixed to the meninges. In the present case the source of the vascular occlusion appears most likely to have been an embolus from a mural thrombus in the common carotid artery. The patient had sustained no head injury but a severe rotational stress in the neck appears to have caused an intimal tear as described under such circumstances.^{3,4}

We have reported elsewhere a similar type of tremor developing after head injury in patients in whom there was clinical and

CT scan evidence of a mid-brain lesion. The relationship between this patient's lesion in the white matter, below the sensory motor cortex, and close to the roof of the lateral ventricle, and a "penduncular" tremor is difficult to explain. Cortical lesions may produce a tremor as seen in three personally studied cases where a tremor was associated with a small frontal tumour on or near the surface of the brain. In such cases however the tremor is Parkinsonian in type and there is often associated rigidity.

It is of course well recognised that tremor may respond dramatically to stereotactic thalamotomy whether it is due to Parkinsonism, essential tremor, or the mid-brain lesion of multiple sclerosis or head injury. It is of interest that this patient's tremor associated with a deep hemisphere white matter lesion was equally responsive to thalamotomy.

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J ANDREW
CJ FOWLER
MJG HARRISON
BE KENDALL

*The Departments of Neurosurgery
and of Neurological Studies,
The Middlesex Hospital Medical School,
Mortimer Street, London W1*

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Heroin myelopathy

Sir: Varied neurological complications of heroin abuse have been reported, including transverse myelitis, polyneuropathy, and rhabdomyolysis.¹⁻⁵ A young woman is

described, who made an uneventful recovery from such complications.

A 20-year-old Caucasian female had been abusing drugs, including cannabis, barbiturates, amphetamines and morphine, for 4 years, and heroin intermittently for 14 months. For a short period she used intravenous heroin daily, and suffered withdrawal symptoms when forced to abstain for 3 months before her illness. She relapsed, however, and injected herself with 60 mg "BS" heroin, purified using lemon juice and a cotton-wool filter, the night before and on the evening of her collapse. She lost consciousness within 5 minutes of the injection. Six hours later she woke to find herself lying on the floor, with excruciating cramp-like pains, and weakness of her legs. There was sensory disturbance to the level of the groins, including the buttocks, with loss of touch and postural sensibility, such that she had no perception of the floor. There was no disturbance of sphincter function, but later that morning she passed deep red-brown urine. On examination a few hours later, her doctor found her in severe pain, with contraction spasms in her legs, marked reduction in power, and absent reflexes, including unresponsive plantars. Sensory loss was confirmed to a level of T12, including gross loss of proprioception. She was treated at home with analgesics and baclofen, the latter having no effect on the muscle spasm. After 2 days she began to show improvement, and there was progressive recovery over the following week, with resolution of the spasm and weakness, but persistence of numbness in the legs. She was admitted to the Midland Centre for Neurosurgery and Neurology a week later. Examination revealed sensory impairment in the lateral aspect of the right thigh, and below the calves. Power and reflexes were now normal. All blood tests were normal, including serological tests for syphilis, viral and auto-immune antibody screen, and serum creatine kinase. Myelogram was normal, as was the cerebrospinal fluid (CSF) cell count and total protein content; the gamma globulin was raised to 15% of the total protein, and contained a faint abnormal band on electrophoresis. Visual and auditory evoked potentials, and nerve conduction studies, were normal. Myoglobin was not detected in the urine. She made a complete recovery.

Since the first reported cases of transverse myelitis associated with heroin abuse,¹ several others have been reported, mainly in American negroes who had been chronic addicts, and resumed the habit after

a period of abstinence.² In Britain, neurological complications of drug addiction have been encountered only rarely,⁴ but recently three white Caucasian patients were described, who developed myelopathy during uninterrupted chronic abuse of heroin.³ The clinical picture consists of an initial flaccid paraparesis, or paraplegia of sudden onset, with sensory loss in the legs and lower thoracic dermatomes, with urinary sphincter disturbance; occasionally the sensory (and motor) levels extend to the cervical region.¹⁻³ The prognosis is often poor, with residual spastic paraparesis and sensory deficit, and in several patients, death.¹⁻³ Extensive necrosis of the cervical and thoracic cord has been described in some.¹ Full recovery has been reported occasionally,² and this was the case in the present patient. Investigations are normal, including CSF and myelography. Our patient developed symptoms of a low thoracic cord lesion on resuming heroin abuse after abstinence for 3 months, suggesting that a hypersensitivity reaction to heroin or an adulterant might have provoked a sudden hypotensive episode, during which the thoracic cord suffered relative ischaemia; alternatively, a direct toxic effect of the drug on the cord may have been responsible for the myelitis, but such action would not easily explain the loss of consciousness. Although acute demyelination (multiple sclerosis) may have been responsible for the clinical picture and the abnormal CSF gamma globulin, no corroborative evidence was found. In addition, the patient had shown clinical features of rhabdomyolysis (muscle spasm, pain, red-brown urine), which has been reported previously in association with heroin abuse.⁵ This patient illustrates the more benign end of the spectrum of complications of heroin abuse. It is possible that similar cases are seen and managed at home, either by the patients' doctors, or their friends and relatives, without referral to hospital.

LC GOODHART

LA LOIZOU

MILNE ANDERSON

*The Midland Centre for Neurosurgery and
Neurology,
Holly Lane,
Smethwick,
Warley,
West Midlands
B67 7JX, UK*

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