HTLV-1 infection: the clinical spectrum widens

A neurological condition causing spastic paraparesis has long been recognised in the West Indies but it is only recently that the association between tropical spastic paraparesis (TSP) and human T-cell lymphotropic virus type 1 (HTLV-1) has been confirmed.1,2 Serological tests for HTLV-1 can now support a diagnosis of TSP in patients with atypical clinical features.

Patient 1 was born in Jamaica and came to the United Kingdom at the age of 38 years. At the age of 61 years she presented with pain in her left shoulder, a three year history of difficulty raising her arms above her head, fatigue and inability to walk long distances. On examination there was spasticity of both scapulae with weakness in the deltoids, triceps and biceps, without fasciculations. Distal upper limb musculature was normal. The biceps and supinator jerks were absent and the tendon jerks were brisk. There was a mild spastic paraparesis with increased knee jerks, diminished ankle jerks and extensor plantar responses. Sensory testing was normal. The creatine kinase was mildly raised and muscle histology revealed neurogenic changes. Myelography and CSF examination were normal. There was a polyclonal increase in the serum immunoglobulins.

At first a diagnosis of motor neuron disease was considered but there was no change in her condition during the following four years and reinvestigation revealed serum antibodies against HTLV-1 in a titre of 1 in 6400. In TSP, pain, weakness and or sensory loss is unacceptably long waiting time in both hands. Antibodies against HTLV-1 were detected in the serum in a titre of 1 in 6400. The blood film was normal but there was a polyclonal increase in the serum immunoglobulins.

The initial detection of HTLV-1 antibodies was by gel particle agglutination assay and confirmed by more specific methods (ELISA, indirect immunoelectrophoresis, IgG antibody capture radio-immunoassay and Western blot techniques).3 These patients illustrate many of the recognised features of TSP, however in this, the illness in each of them had been tentatively attributed to another cause: motor neuron disease (patient 1), parasagittal tumour or neurosyphilis (patient 2), neurosarcoidosis or neuromyelitis optica (patient 3).

For more information, see the references cited in the text. Correspondence to: Mrs Wood.

We would be pleased to consider for publication short letters describing similar audit of outpatient practice in other countries.

Ed

Notes
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operator gave an eight year history of attacks of unilateral headache with minimal nausea, lasting for up to two days. These occurred initially at intervals of two or three days but more recently every three days. At first the attacks were preceded by a typical 25 minute visual aura, in which he experienced a coloured rotating diamond and zig zag lines, usually in the lower visual field, since then the visual aura has increased to a momentary feeling that his actual behaviour is unduly familiar, followed by a 20 minute sequence of unpleasant, almost morbid sensations that he felt he had come across before, as if in previous dreams, "in another world". This would be followed by some impairment of memory lasting for three days, and a rather milder, though sometimes more generalised headache with nausea that would last for one day. In addition some attacks were preceded by 15 seconds of quite intense giddiness and there have been several episodes of dizziness. There have never been any lapses of concentration or impairment of consciousness, and he said he was able to carry on speaking and working while the aura was in progress. There is no family history of migraine. He derived some benefit from pizotifen which seemed to shorten his aura, but was not helped much by methysergide.

There were no physical abnormalities on examination. A CT scan was normal and two EEGs showed a generalised excess of slow wave activity.

Visual, sensory and motor symptoms, usually in that order of frequency, are the commonest seen in the aura phase of classical migraine. Occasional patients become dysphasic and some symptoms (for example, ataxia, dysarthria and vertigo) have been attributed to disturbances in the vertebro-basilar circulation. In one series of patients with transient global amnesia, 42% gave a past history of migraine, a figure considered significantly greater than the prevalence in the general population. It seems likely that some such cases, which are only rarely recurrent, are indeed manifestations of migraine while others are ischaemic in origin. Raskin describes a young woman who experienced 15 episodes of transient global amnesia, each lasting up to six hours followed by headache, each after drinking a glass of red wine. While olfactory and auditory hallucinations have been described in the aura phase of classical migraine,14 15 recurrent transient memory disturbances of the type experienced by this patient, which are reminiscent of deja vu phenomena, do not appear to have been reported in detail, though Saul and Sacks16 allude to similar cases.

There is much, admittedly circumstantial, evidence that the cortical disturbances of classical visual field, due to spreading depression moving across the cortical surface, 14 15 Olesen and Jorgensen16 have speculated that transient global amnesia is due to a wave of spreading depression moving across the hippocampal surface. This patient's deja vu phenomena, which have a frequency and duration typical of classical migraine, are probably mediated similarly, and it is speculated that this is due to spreading depression in the temporal lobe. Migraine therefore should be considered among the causes of deja vu phenomena, particularly if prolonged.

Dr R Guilford made helpful comments on this manuscript.

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Subcutaneous apomorphine for Parkinsonian patients with psychiatric side effects on oral treatment

Subcutaneous apomorphine has recently been shown to reduce off periods in patients with Parkinson's disease (PD) who are resistant to conventional management.1 A previous study indicated that neuropsychiatric side effects on oral treatment did not recur when apomorphine was used, but the effects of apomorphine in those for whom these complications were the major dose limiting factor has not been investigated.2 We describe three patients with PD whose optimal control was compromised by severe neuropsychiatric side effects and who responded to treatment with apomorphine.

The first case was a 46 year old woman who had had PD for eight years and was underdosing herself with oral levodopa because of side effects. Bromocriptine had produced psychosis, and levodopa/benserazide (madopar 65 mg) in excess of seven times daily caused hallucinations, paranoid delusions and aggression predominantly in the on periods, which led to two hospital admissions.

Subcutaneous apomorphine infusion was started at 3 mg/hour for 12 hours daily and dramatically reduced her off periods from eight hours daily to one. Tremor was abolished and levodopa dosage could be reduced from 350 mg/day to 200 mg/day. She has now been maintained on this treatment for eight months without psychiatric side effects.

The second case was a 67 year old man who had had PD for 10 years. Eight Madopar 65 mg tablets caused severe dyskinesias and visual hallucinations on and off periods. Bromocriptine 2.5 mg four times daily caused visual hallucinations and confusion and was discontinued. He took seven madopar tablets a day and had nine hours off periods daily. Apomorphine was given initially by a "Penject" system and subsequently by subcutaneous infusion at a dose of 40 mg/day. Off periods for one hour daily and levodopa could be reduced from 400 mg daily to 300 mg daily. She has now been maintained on apomorphine infusion for 14 months with mild involuntary movements but no psychiatric side effects.

Case 3 was a 74 year old man with severe Parkinsonism tremor and bradykinesia who could not tolerate optimal doses of levodopa, bromocriptine or ropinirole. Madopar in access of 62.5 mg four times daily caused nausea and psychosis, both during on and off phases. Bromocriptine 2.5 mg, three times daily caused visual hallucinations with confusion and the same patient then tried benzhexol 2 mg, twice daily. He tolerated subcutaneous apomorphine infusion at 3 mg/hr for 12 hours daily and his tremor grading (modified King's College scoring system) improved from 3 to 1 (4-2-1-0 scale) with improvement in his bradykinesia. Single blind infusion of normal saline in place of apomorphine resulted in a return of the severe Parkinsonism. His levodopa dosage could be reduced from 200 mg to 150 mg daily and he has been maintained on apomorphine for 14 months without any neuropsychiatric problems except for occasional nocturnal confusion.

Over the past two years we have treated 12 non-demented PD patients with refractory on-off oscillations, using subcutaneous apomorphine. Nine have continued treatment parenteral treatment in PD, but neuropsychiatric complications were the major limiting factor in its use.3 It is unclear why apomorphine should be better tolerated than oral therapies. It contains a piperidine moiety which may itself be antipsychotic and it lacks the serotonergic effects of bromocriptine or the ergolides.4 Furthermore, its potent effect on both D1 and D2 receptors may differentially affect the dopaminergic agents. For instance, unlike levodopa and amphetamine, small doses of apomorphine in schizophrenics do not exacerbate the psychotic symptoms.5 Likewise, although it induces stereotyped behaviour in laboratory animals, an emetic dose of apomorphine does not lead to behavioural changes in humans.6

Our experience suggests that PD patients with neuropsychiatric problems with conventional treatment benefit from treatment with apomorphine. Further experience with large numbers of patients may confirm it.