Wellcome Trust Clinical Research Unit, Centre for Tropical Diseases, 190 Ben Ham Tu, District 5, Ho Chi Minh City, Vietnam

R KNEEN
J J FARRAR
Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, University of Oxford, UK

Correspondence to: Dr J J Farrar, Wellcome Trust Clinical Research Unit, Centre for Tropical Diseases, 190 Ben Ham Tu, District 5, Ho Chi Minh City, Vietnam

1 Warrell MJ, Warrell DA. Rhabdoviruses: rabies and rabies related viruses. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. 3rd ed. Oxford: Oxford University Press, 1996:394–405.
2 Fishbein DB, Bernard KW. Rabies virus. In: Mandel GL, Douglas RG, Bennett JE, eds. *Principle and practice of infectious diseases*. 4th ed. New York: Churchill Livingstone, 1995:1527–43.
3 Swaddiwudhipong W,Prayoonwiwat N, Kunasol P, *et al*. A high incidence of neurological complications following Semple anti-rabies vaccine. *Southeast Asian J Trop Med Public Health* 1987;**18**:526–3.
4 Toro G; Vergara I; Roman G. Neuroparalytic accidents of antirabies vaccination with suckling mouse brain vaccine. Clinical and pathologic study of 21 cases. *Arch Neurol* 1977;**34**: 694–700.
5 Warrell MJ, Nicholson KG, Warrell DA, *et al*. Economical multiple-site intradermal immunisation with human diploid cell strain vaccine is effective for post-exposure rabies prophylaxis. *Lancet* 1985;i:1059–62.

Leukoencephalopathy associated with khat misuse

The leaves of the tree *Catha edulis*, or khat (also qat and kat) are chewed by a large proportion of the adult population of the Yemen, and throughout Saharan and sub-Saharan Africa. The leaves are also chewed by members of the Yemeni and Somali community in the United Kingdom.[1] The psychoactive constituents of khat are cathin (*d*-norisoephedrine), cathidine, and cathinone (an alkaloid with a structure resembling ephedrine and amphetamine) and users report a mild euphoria similar to that of amphetamine.[1] Khat is acknowledged as a precipitant of psychosis and has also been reported to cause cognitive impairment.[2] We report a case in which khat chewing has been associated with a severe and disabling neurological illness.

A 56 year old Somali living in the United Kingdom for the past 18 years was admitted to a psychiatric hospital with a 5 week history of progressive confusion and agitation. His family reported that he had been chewing khat, in their opinion to excess, every day during that time but had stopped 2 days before admission. There was one previous admission to hospital 9 months previously with khat induced psychosis, from which he recovered without complications within 24 hours. On this occasion, shortly after admission, his conscious level deteriorated abruptly and he was referred for neurological opinion. He was apyrexial and general medical examination was normal. He opened his eyes spontaneously but there was no verbal response and he did not obey commands. He withdrew all four limbs to pain. Upper and lower limbs were held in flexion with markedly increased tone. Reflexes were brisk but equal. The right plantar was extensor. There were bilateral palmomental and grasp reflexes.

Full blood count, urea and electrolytes, glucose, liver function tests, thyroid function test, viral serology, and malaria screen all gave normal results. Tests for HIV antibody, serum angiotensin converting enzyme, white cell enzymes, and serum and urinary porphyrins were negative. Erythrocyte sedimentation rate on admission was 58 mm/h.

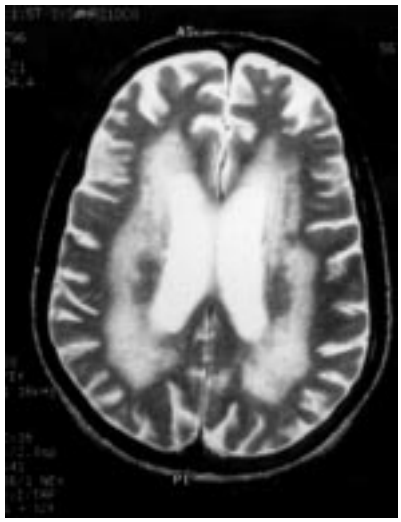
Examination of the CSF showed normal opening pressure, protein 0.27 g/l, glucose 4.3 mmol/l (blood glucose 6.1 mmol/l), and no cells. His initial EEG was abnormal with diffuse slow waves indicative of widespread cerebral dysfunction.

A chest radiograph and ultrasound examination of the abdomen were normal. Cranial MRI, although contaminated by movement artefact, showed diffuse abnormality in the deep cerebral white matter of both cerebral hemispheres. Fourteen days after admission he was witnessed to have a single brief adversive seizure with eye and head deviation to the right.

The patient was admitted to a rehabilitation unit. His mini mental state examination score and Barthel scores were zero. Feeding by percutaneous gastrostomy was started. A trial of intravenous methylprednisolone (1 g on 3 consecutive days) gave no benefit. Repeated EEGs (on four occasions) showed diffuse slow waves only. A second MRI (figure) 3 months after onset of symptom showed the presence of a continuing diffuse extensive abnormal signal in the deep white matter of both cerebral hemispheres with marked cortical atrophy. Brain biopsy (via right frontal craniotomy) was performed 3 months after the onset of his illness. There was no evidence of acute inflammation, vasculitis, or infarction.

While undergoing rehabilitation there has been slow improvement in his cognitive and locomotor function. After 1 year he is able to open and close his eyes, occasionally verbalise, localise pain, and obey simple commands. His plantars are flexor but he has persistent grasp and palmomental reflexes. His nutrition is maintained by gastrostomy and he has an indwelling catheter.

The clinical presentation, EEG, and MRI findings suggest a rapidly progressive leukoencephalopathy. There are no previous reports of leukoencephalopathy in association with khat or amphetamine misuse; it has, however, been reported in association with other recreational drugs taken by mouth or inhalation.[3 4] An alternative for this man's presentation is a necrotising vasculitis, a well described complication of oral amphetamine misuse.[5] The clinical features, MRI appearance, brain biopsy, absence of haemorrhage, and lack of response to steroids make this unlikely.



Cranial MRI 3 months after onset of symptoms showing diffuse signal abnormality in the deep white matter of both cerebral hemispheres. There is also marked cortical atrophy.

The likely precipitant of this man's illness seems to be his use of khat. A drug screen on admission was negative, and his family denied misuse of other drugs. It remains possible that the sample of khat chewed by this man was contaminated. We are unaware of any previous reports of khat misuse with severe neurological deterioration; previous cases may not have been investigated or reported. In reporting this case our intention is to alert others to a possible complication of the misuse of this drug. Evidence of other cases would provide a powerful argument for the restriction of import and sale of khat.

P K MORRISH
N NICOLAOU
P BRAKKENBERG
P E M SMITH
Department of Neurology, University Hospital of Wales, Heath Park, Cardiff CF4 4XN, UK

Correspondence to: Dr PK Morrish, Department of Neurology, University Hospital of Wales, Heath Park, Cardiff CF4 4XN, UK. Telephone 0044 1222 747747; fax 004 1222 744166; email: morrishpk@cardiff.ac.uk

1 Pantelis C, Hindler CG, Taylor JC. Use and abuse of khat *(Catha edulis)*: a review of the distribution, pharmacology, side effects and a description of psychosis attributed to khat chewing. *Psychol Med* 1989;**19**:657–68.
2 Khattab NY, Galal A. Undetected neuropsychological sequelae of khat chewing in standard aviation medical examination. *Aviat Space Environ Med* 1995;**66**:739–44.
3 Celius EG, Andersson S. Leucoencephalopathy after inhalation of heroin: a case report. *J Neurol Neurosurg Psychiatry* 1996;**60**:694.
4 Walters EC, van Wijngaarden GK, Stam FC, *et al*. Leucoencephalopathy after inhaling "heroin" pyrolysate. *Lancet* 1982;ii:1233–7.
5 Salanova V, Taubner R. Intracerebral haemorrhage and vasculitis secondary to amphetamine use. *Postgrad Med J* 1984;**60**:429–30.

Necrotising vasculitis with conduction block in mononeuropathy multiplex with cold agglutinins

Cold agglutinins are cold reactive autoantibodies that have haemolytic effects on red blood cells mediated via complement fixation. Neuropathy associated with cold agglutinins has been described,[1–5] however, details of its pathomechanism are unclear. Here, we report the clinical, electrophysiological, and pathological findings of a mononeuropathy multiplex in a patient with cold agglutinins, who responded very well to plasmapheresis.

A 72 year old man was admitted with a 1 month history of progressing dysaesthesia and weakness of the limbs. He had no anaemia, jaundice, hepatosplenomegaly, or lymphadenopathy. Cranial nerves and the cerebellum were not involved. There was severe weakness and atrophy of bilateral thenar, interossei, and plantar muscles with severe dysaesthesia of both palms and plantaris. Pin prick and light touch were reduced as well as position and vibratory sensation in both hands and feet. Deep tendon reflexes were hypoactive. Babinski's sign was negative.

Laboratory investigation showed a raised erythrocyte sedimentation rate: 52 mm/hour (normal <10) and serum C reactive protein: 1.8 mg/dl (normal; < 0.5). Blood cell counts were within normal limits. The following were normal or negative; IgG, IgA, IgE, IgM,