consequence of ureterosigmoidostomy alone: ammonia concentrations as high as these have never been observed in patients with hyperammonaemia following ureterosigmoidostomy. The patient had been treated a few weeks before for urosepsis following constipation, which theoretically can lead to very high ammonia concentrations. However, during the final episode, he was not constipated. Therefore, in our patient, pre-existing episodic hyperammonaemia with encephalopathy and seizures was obviously severely aggravated by valproate induced hyperammonaemia and depletion of carnitine. Patients with valproate induced encephalopathy have been repeatedly described, the pathophysiology of which seems to be heterogeneous.[2] In some patients, previously subclinical urea cycle defects have become manifest after treatment with valproate.[3] However, these disorders could be ruled out in our patient. Hyperammonaemia is a frequent side effect of valproate treatment and is often asymptomatic.[2] It seems to occur more frequently in children but is also common in adults, particularly in the presence of other antiepileptic drugs, as was the case in our patient. The exact mechanism of valproate induced hyperammonaemia is unknown but it may appear independently of hepatotoxicity.[4] Valproate has repeatedly been shown to reduce serum and liver carnitine concentrations, both with and without being associated with hyperammonaemia.[5] While most of these patients were children, some cases in adults have been described.[6] Valproate may reduce carnitine concentrations by forming an ester with carnitine, which is co-excreted with organic acids into the urine, or by altering renal reabsorption of acylcarnitine and free carnitine.[7]

In conclusion, our case shows that valproate may greatly aggravate pre-existing, mild hyperammonaemia. We suggest that valproate should be avoided in patients with even slight hyperammonaemia and normal liver function. Equally, we advise the close monitoring of ammonia and carnitine concentrations in patients with ureterosigmoidostomy, such as the one described here, if valproate cannot be avoided.

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References

1 **Fichtner J**. Follow-up after urinary diversion. *Urol Int* 1999;**63**:40–5.
2 **Duarte J**, Macias S, Coria F, *et al*. Valproate-induced coma: case report and literature review. *Ann Pharmacother* 1993;**27**:582–3.
3 **Brusilow SW**, Horwich AL. Urea cycle enzymes. In: Scriver CL, Beaudet AL, Sly WS, *et al*, eds. *The metabolic and molecular causes of inherited disease*, 7th edn. New York: McGraw-Hill, 1995:1187–231.
4 **Zaret BS**, Beckner RR, Marini AM, *et al*. Sodium valproate-induced hyperammonemia without clinical hepatic dysfunction. *Neurology* 1982;**32**:206–8.
5 **Camina MF**, Rozas I, Gomez M, *et al*. Short-term effects of administration of anticonvulsant drugs on free carnitine and acylcarnitine in mouse serum and tissues. *Br J Pharmacol* 1991;**103**:1179–83.
6 **Beversdorf D**, Allen C, Nordgren R. Valproate induced encephalopathy treated with carnitine in an adult. *J Neurol Neurosurg Psychiatry* 1996;**61**:211.
7 **De Vivo DC**, Bohan TP, Coulter DL, *et al*. L-carnitine supplementation in childhood epilepsy: current perspectives. *Epilepsia* 1998;**39**:1216–25.

Palatal tremor and cognitive decline in neuroferritinopathy

Neuroferritinopathy is a recently described autosomal dominant, adult onset, neurodegenerative disorder associated with iron accumulation, particularly in the basal ganglia.[1] All patients found to date have a single adenine insertion between nucleotides 460 and 461 in exon 4 of the ferritin light chain gene. This results in a frame shift and is predicted to cause structural alteration of the polypeptide carboxy terminus. Magnetic resonance imaging of the brain shows iron accumulation, and this has been confirmed pathologically with the detection of numerous iron positive inclusions particularly in the globus pallidus. In spite of this, serum ferritin levels are found to be abnormally low or at the low end of the normal range. Patients tend to present in mid-life with a movement disorder, characterised by chorea, dystonia, and rigidity. In contrast with Hallervorden-Spatz syndrome, which is also associated with accumulation of brain iron, visual and cognitive function is preserved.

Here, we report a patient with genetically proven neuroferritinopathy in which the clinical features included cognitive decline and palatal tremor. These features extend the phenotype of this condition from those previously reported.

The patient was a 49 year old man who developed lingual and oral dyskinetic movements and a slurring dysarthria at the age of 37. Initially, the movement disorder was partially controlled with high dose anticholinergics but then progressed to involve his limbs. Over the next 10 years, he developed dysphagia, unsteadiness, and cognitive decline, particularly of frontal lobe function. His father, paternal uncle, and paternal grandmother had all developed a movement disorder in middle age. A diagnosis of Huntingdon's disease was made at that time and was assumed in the patient until disproved by a negative genetic test result. The family continued to seek diagnostic clarification to enable life planning for the patient's children.

On examination, he was alert and orientated. He scored 7/10 on a mini mental state examination. Detailed cognitive testing showed particular impairment of non-verbal abstract reasoning, with some word retrieval difficulties. He tended to perseverate, and his cognitive estimates were poor. He exhibited pout, palmomental, and grasp reflexes. He manifested appreciable oral, lingual, and facial dyskinesias. Eye movements were abnormal, with saccadic intrusion into pursuit and use of head thrust to initiate saccades. He had apraxia of eyelid opening. There was no evidence of a pigmentary retinopathy or Kayser-Fleischer rings, and the optic discs were normal. There was a palatal tremor at a frequency of 1 Hz. Examination of the limbs showed pronounced choreiform movements and dystonic posturing. There was no evidence of a peripheral neuropathy or myoclonus.

The following blood tests were normal or negative; full blood count and film, copper studies, creatine kinase levels, ferritin levels (60 μg/l, normal range 25–350 μg/l), liver function tests, and genetic tests for Huntington's disease (HD), dentatorubral pallidoluysian atrophy, and spinocerebellar ataxia 1–3, 6, and 7. Nerve conduction studies were normal. A muscle biopsy was normal. Cerebrospinal fluid analysis was normal, with no evidence of xanthochromia. Magnetic resonance imaging of the brain (fig 1) showed considerable hyperintensity, with a band of surrounding hypointensity on T2 weighting involving the putamen, pallidum, thalamus, substantia nigra, and dentate nucleus. The cerebral cortex was atrophic. A computed tomography scan showed no evidence of cerebral calcification.

Mindful of the clinical features, ferritin deposits, dominant inheritance, and family origin reported in neuroferritinopathy,[1] further genetic testing confirmed the presence of the same A insertion at position 460–461 of the ferritin light chain gene. Investigation of genotypes at six polymorphic microsatellite markers close to the gene location on chromosome 19 showed sharing of one allele at each marker. Thus, it is likely that the patient potentially shares the disease associated haplotype with all affected individuals of the originally described families and is another example of inheritance of an initial founder event. Additional evidence comes from the northwest geographical origin of his family.

The differential diagnosis in this case initially included HD, neuroacanthocytosis, and Wilson's disease, but these conditions were excluded by appropriate investigations. Atypical Hallervorden-Spatz syndrome was also considered, particularly in the light of the appearances on brain imaging, but this condition is recessively inherited and associated with a defective pantothenate kinase gene

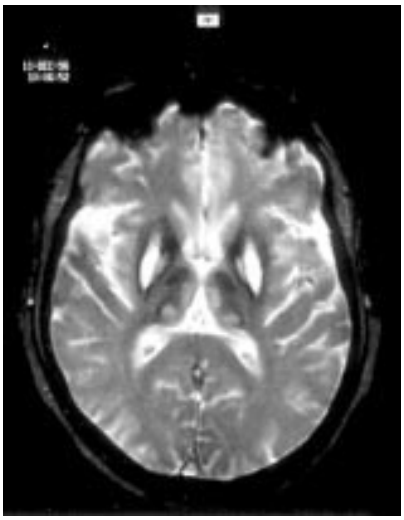

Figure 1 Magnetic resonance image of the brain showing hyperintensity with surrounding hypointensity on T2 weighting affecting the putamen, pallidum, and thalamus.

(PANK2).[2] Interestingly, our patient had significant cognitive impairment and palatal tremor in addition to the movement disorders so far described in patients with neuroferritinopathy. In other neurodegenerative disorders, particularly HD, the causative proteins may be involved in iron metabolism.[3] Thus, cognitive impairment may be predicted to occur in neuroferritinopathy, especially in the presence of a pre-existing hyperkinetic movement disorder.[4]

The development of palatal tremor in our patient deserves further explanation. Palatal tremor (previously known as palatal myoclonus) may be classified as essential or symptomatic.[5] It is thought that palatal tremor arises because of functional disruption in "Mollaret's triangle", which consists of the inferior olivary nucleus, red and dentate nuclei. The symptomatic form is usually associated with hypertrophy of the inferior olivary nucleus and may arise from vascular lesions, particularly in the cerebellum.[6] Further evidence for this hypothesis comes from a positron emission tomography study, which showed hypermetabolism in the inferior olivary nucleus.[7] Most patients also have cerebellar ataxia. However, palatal tremor may also occur in other conditions including multiple system atrophy, progressive supranuclear palsy, and Alexander's disease.[5] As in our case, symptomatic palatal tremor is not usually associated with ear clicking. Presumably, in our patient, iron deposition in the dentate nuclei was responsible for disruption of rubral and olivary pathways.

Ferritin is an iron storage protein and alteration in structure of the carboxy terminus could lead to the release of free iron and excessive oxidative stress.[8] In other conditions, such as haemosiderosis, the use of iron chelators has been advocated as a potentially useful treatment. Results, in the main, have been disappointing. Whether free radical scavengers, such as idebenone,[9] have useful therapeutic value in neuroferritinopathy remains to be seen.

Neuroferritinopathy should be considered in all patients with a hyperkinetic movement disorder, imaging evidence of iron deposition within the brain, and an autosomal dominant family history.

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References

1 **Curtis AR**, Fey C, Morris CM, *et al*. Mutation in the gene encoding ferritin light polypeptide causes dominant adult-onset basal ganglia disease. *Nat Genet* 2001;**28**:350–4.
2 **Zhou B**, Westaway SK, Levinson B, *et al*. A novel pantothenate kinase gene (PANK2) is defective in Hallervorden-Spatz syndrome. *Nat Genet* 2001;**28**:345–9.
3 **Hilditch-Maguire P**, Trettel F, Passani LA, *et al*. Huntingtin: an iron-regulated protein essential for normal nuclear and perinuclear organelles. *Hum Mol Genet* 2000;**9**:2789–97.
4 **Olanow CW**, Arendash GW. Metals and free radicals in neurodegeneration. *Curr Opin Neurol* 1994;**7**:548–58.
5 **Kulkarni PK**, Muthane UB, Taly AB, *et al*. Palatal tremor, progressive multiple cranial nerve palsies, and cerebellar ataxia: a case report and review of literature of palatal tremors in neurodegenerative disease. *Mov Disord* 1999;**14**:689–93.
6 **Gasparini M**, Spinnler H, Sterzi R. CAT findings in a cerebellar stroke resulting in palatal myoclonus. *Med J Aust* 1977;**1**:462.
7 **Dubinsky RM**, Hallett M, Di Chiro G, *et al*. Increased glucose metabolism in the medulla of patients with palatal myoclonus. *Neurology* 1991;**41**:557–62.
8 **Rouault TA**. Iron on the brain. *Nat Genet* 2001;**28**:299–300.
9 **Schols L**, Vorgerd M, Schillings M, *et al*. Idebenone in patients with Friedreich ataxia. *Neurosci Lett* 2001;**306**:169–72.

Cocaine induced hypokalaemic periodic paralysis

The use of cocaine has been associated with a number of psychiatric, medical, and neurological complications. This is the second reported case of a patient who suffered three distinct episodes of paralysis after engaging in a cocaine binge.

Case report

A 33 year old male horse breeder with no significant medical history was evaluated at the Texas Tech Health Sciences Center after the abrupt onset of ascending generalised weakness. He reported not being able to walk or lift his arms or legs, much less climb up or get down the stairs of his home. He reported no bowel or bladder incontinence, loss of sensation, headache, nausea, or vomiting. The patient did report mild chest pain at the time. Ten days before his initial evaluation he had suffered a very similar episode but had not sought medical attention. At the time of his evaluation the patient stated that he would be better in 24–48 hours. A very similar event had occurred five years earlier, for which he was seen in an urgent care facility and discharged home; symptoms resolved after 2–3 days. Records of this first episode were not available, although he reported that potassium supplements were provided at that time.

Physical examination found an uncomfortable appearing, slightly dishevelled, unshaven man with no spontaneous motor activity. Vitals signs were a pulse of 88 beats/min, respiration 16 breaths/min, and blood pressure 132/94 mm Hg. Neurological evaluation found an awake, alert, and oriented person. Speech and language were normal. Cranial nerves were intact. Motor examination found normal bulk with a reduction in tone. Strength was 2/5 in all major muscle groups with a very mild left upper limb predominance. Neck extensors and flexors were 5/5. Bulbar muscles were spared. No myoedema, myotonia, fasciculations, or other abnormalities were noted. The sensory examination was normal and reflexes were symmetric with no Babinski signs. A complete blood count and comprehensive metabolic panel, including thyroid studies, urine drug screen, blood alcohol concentration, and erythrosedimentation rate, were performed. Cardiac enzymes were normal. Neuroimaging of the brain and spinal cord were normal. Forced vital capacity and negative inspiratory fraction were normal. Laboratory investigations showed a blood glucose concentration of 6.6 mmol/l, sodium 141 mmol/l, calcium 2.27 mmol/l, and creatine kinase (CK) 395 IU/l. Acetylcholine receptor antibodies were drawn at the time of admission and subsequently shown to be in the normal range. Two laboratory investigations were of particular interest. The patient's potassium concentration was 1.9 mmol/l and urine toxicology screen found the presence of cocaine, cannabinoids, and benzodiazepines.

The patient had initially denied any illicit drug use but later admitted to having engaged in a cocaine binge the previous night and before the previous two episodes of weakness. There was no family history of periodic paralysis or other neuromuscular disorders. Supplemental potassium was provided and the patient's strength gradually improved with rising concentrations of serum potassium. Nerve conduction studies and electromyography were normal at 48 hours after the onset of symptoms. He was discharged home to an outpatient substance abuse program three days later with almost complete resolution of symptoms. At the time of discharge, the serum potassium concentration was 4.5 mmol/l and the CK concentration declined to 133 IU/l.

It is not clear why the use of cocaine led to such severe generalised weakness and hypokalaemia in this patient. Nalluri *et al*[1] reported a similar case and suggested that the hypokalaemia was caused by an intracellular shift of potassium secondary to the adrenergic effects of cocaine; a hyperadrenergic cause of periodic paralysis in patients suffering from thyrotoxicosis has also been postulated. In their report, as in this case, the patient responded quickly to potassium supplementation. An alternative mechanism may have been cocaine's potential effects on potassium channels.[2 3] The increased CK and serum glucose concentrations were felt to be the result of cocaine's effects.

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References

1 **Nalluri P**, Venkatesh S, Rao A. Cocaine-induced hypokalemic paralysis. *Muscle Nerve* 2000;**23**:1773.
2 **O'Leary ME**. Inhibition of human ether-a-go-go potassium channels by cocaine. *Mol Pharmacol* 2001;**59**:269–77.
3 **Zhang S**, Rajamani S, Chen Y, *et al*. Cocaine blocks the HERG, but not KvLQT1+mink, potassium channel. *Mol Pharmacol* 2001;**59**:1069–76.

Sulcal abnormalities on brain magnetic resonance imaging in the Guillain–Barré syndrome

The Guillain–Barré syndrome is an immunologically mediated condition affecting the peripheral nervous system. There is evidence that Guillain–Barré syndrome, Miller–Fisher syndrome, and Bickerstaff brain stem encephalitis form a closely related spectrum of disorders.[1] Magnetic resonance imaging (MRI) abnormalities in the spinal cord in these conditions have been well described,[2] but intracranial findings are infrequent. We report resolution of sulcal changes on serial MRI of the brain concomitant with clinical recovery in a typical case of Guillain–Barré syndrome.