LETTERS TO THE EDITOR

Recurrent confusion and ataxia triggered by pyrexia in a case of occult multiple sclerosis

It has long been known that an increase in body temperature may worsen reversibly the signs and symptoms of multiple sclerosis, probably by the production of conduction block in partially demyelinated nerve axons. We present the case of a man whom we believe has multiple sclerosis, who has a nine year history of brief episodes of profound neurological dysfunction, always in association with pyrexial illnesses. The unusual feature of this case is that, until recently, between these attacks our patient remained subjectively well, and that there was no history suggesting episodes of acute demyelination.

A 44 year old man was admitted in May 1992 with a 12 hour history of increasing confusion, blurring of vision, and ataxia, associated with a fever. On admission he was pyrexial at 39°C, but there were no signs of localised infection or any features of meningism. He was drowsy and mildly confused. The cranial nerves were normal apart from bilateral failure of adduction with ataxic nystagmus of the abducting eyes typical of an internuclear ophthalmoplegia, down-beat nystagmus on down-gaze, and up-beat nystagmus on up-gaze. There was a mild bilateral ptosis and a slight left upper motor neuron facial weakness. Bulbar function was intact. In the limbs power was normal, but tone was slightly increased generally and the reflexes were exaggerated, particularly on the left. The left plantar reflex was extensor, the right flexor. There was pronounced cerebellar ataxia in all four limbs, again more pronounced on the left, and he was unable to walk unassisted. Sensation was normal. The only abnormal investigations were a noticeable peripheral neutrophilia (granulocyte count $11.6 \times 10^9/l$), and a raised C reactive protein concentration of 77 mg/l (normal range 0-10). Cerebrospinal fluid contained 1 white blood cell/mm³, 0.21 g/l protein, and 4.7 mmol/l glucose.

The initial diagnosis was of a viral encephalitis, despite normal CSF and brain CT, and treatment was commenced with intravenous acyclovir and oral paracetamol for his fever. The next morning he was afebrile and greatly improved. By the time of his discharge three days later the only abnormal neurological signs were asymptomatic bilateral internuclear ophthalmoplegia, an upgoing left plantar, and mild left limb ataxia, which were present when he was re-examined six months later.

It transpired that on several occasions over the past nine years he had become confused and ataxic while experiencing an otherwise mild pyrexial illness. In 1983 he developed pyrexia of 39.8°C associated with confusion and ataxia and was admitted to hospital. A diagnosis of viral pneumonia was made and his condition improved dramatically when he was treated with paracetamol and ice packs. He left hospital

12 days later, fully recovered. In December 1988 he experienced a similar short lived episode of pyrexia, confusion, and ataxia, having developed a left lower lobe pneumonia, which responded to penicillin. In December 1991 he developed an *Escherichia coli* urinary tract infection causing urinary frequency, urgency, and dysuria. He developed a pyrexia and again became confused and ataxic until antipyretic and antibiotic drugs were instituted.

Further analysis of the CSF collected on his admission showed the presence of oligoclonal IgG bands that were absent from plasma, although the CSF IgG:albumin ratio was normal at 0.20 (normal range 0-0.25). An MRI of the brain two days after his discharge showed the presence of multiple areas of increased signal intensity in the periventricular regions, the corpus callosum, the base of the fourth ventricle, the left cerebellar peduncle, and the lower medulla. The appearances were typical of widespread demyelination caused by multiple sclerosis. Repeat MRI five months later appeared identical. Visual evoked responses recorded eight months after his admission were of grossly increased latency.

In 1889, Uhthoff¹ reported a transient reduction of visual acuity in patients with multiple sclerosis after exercise, and in 1937 Simons² noted a deterioration of muscle strength in 62% of patients with multiple sclerosis when exposed to heat. Whether the effect of exercise is caused entirely by a concurrent rise in body temperature remains controversial,³ but it is likely that this plays an important part. Experiments on artificially demyelinated nerve fibres have shown that conduction block may be produced by small temperature rises.⁴ This may explain the severe but transient neurological dysfunctions induced in our patient by a variety of pyrexial illnesses over a period of nine years.

The unusual feature of our patient's history is the absence of any previous illness suggesting an episode of acute demyelination. The only similar case that we have identified in the literature is of a woman who was unable to walk for two weeks during a febrile illness at the age of 17, and then remained asymptomatic until developing overt multiple sclerosis 19 years later.⁵ It is now well recognised that multiple sclerosis plaques are sometimes discovered at necropsy in patients with no untoward neurological history.⁵ We believe that occult multiple sclerosis should be considered as an underlying diagnosis when pyrexia is accompanied by otherwise unexplained neurological signs and symptoms.

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- 1 Uhthoff W. Untersuchungen über die bei der multiplen Herdsklerose vorkommenden Augenstörungen. *Arch Psychiat Nervenkr* 1889;21:303-420.
- 2 Simons DJ. A note on the effect of heat and of cold upon certain symptoms of multiple sclerosis. *Bulletin of the Neurological Institute of New York* 1937;6:385-6.
- 3 Saul RF, Selhorst JB, Waybright EA. Optic nerve conduction: opposing effects of exercise and hyperventilation. *Ann Neurol* 1981; 10:79-80.

- 4 Davis FA, Jacobson S. Altered thermal sensitivity in injured and demyelinated nerve. A possible model of temperature effects in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1971;34:551-61.
- 5 Mackay RP, Hirano A. Forms of benign multiple sclerosis. Report of two "clinically silent" cases discovered at autopsy. *Arch Neurol* 1967;17:588-600.

Hyperkalaemia mimicking acute Guillain-Barré syndrome

Severe electrolyte disturbances may mimic the Guillain-Barré syndrome. We report a patient with extreme hyperkalaemia who developed an acute flaccid tetraparesis showing the typical electrophysiological findings of acute Guillain-Barré syndrome. After normalisation of the potassium concentration by dialysis, all neurological symptoms gradually disappeared within two days.

The patient was a 36 year old woman who had malignant nephrosclerosis and chronic renal failure for three months. Within 24 hours she developed a severe symmetric tetraparesis and painful dysaesthesia. Two grand mal seizures were also noted the day before admission.

On admission the patient was drowsy with symmetric tetraparesis, more pronounced in the legs (MRC 2/5) than in the arms (MRC 3/5), and areflexia. She complained of painful dysaesthesia on light touch. Vibration sense at the ankle was diminished bilaterally. Examination of cranial nerves was normal. There was no dyspnoea and no weakness of the respiratory muscles.

The initial serum potassium concentration was very high (8.4 mmol/l (normal <4.5 mmol/l)), and the sodium concentration was slightly reduced (132 mmol/l). The calcium concentration was normal (2.2 mmol/l). Creatinine was 16.6 mg/dl (normal <1.3 mg/dl) and urea 187 mg/dl (normal <22 mg/dl). Blood pressure was increased (190/140 mm Hg). Cranial CAT and CSF were normal.

Initial nerve conduction studies showed markedly reduced and dispersed compound muscle action potential amplitudes, conduction block, reduced conduction velocities, and grossly prolonged distal motor latencies. Sural nerve action potentials were absent (table). Electromyography with concentric needle electrodes in weak muscles (hypotenar, quadriceps, tibial anterior muscles) showed normal insertional activity and did not show pathological spontaneous activity. On voluntary activation, only few and normal looking motor units with amplitudes between 400 and 1100 μ V could be activated. Motor units with amplitudes smaller than 400 μ V were missing. Motor unit discharge rates did not exceed 16 Hz. The EEG showed a slowing with theta waves (5-6/s) without epileptic paroxysms. In the absence of cardiac dysfunction the ECG was characterised by tall, "tent shaped" T waves, decreased amplitude of the P waves, and widening of the QRS complexes.

Haemodialysis was performed under intensive care monitoring. Within two days all neurological symptoms subsided completely. Electrophysiological testing after 10 days showed a complete remission of all

Nerve conduction studies before and after normalisation of hyperkalaemia

	Sural nerve		Tibial nerve (motor)			Median nerve (motor)		
	Amplitude (μV)	Velocity (m/s) (34° C)	Amplitude (mV) (proximal/distal)	Velocity (m/s) (34° C)	Latency (ms) (proximal/distal)	Amplitude (mV) (proximal/distal)	Velocity (m/s) (34° C)	Latency (ms) (proximal/distal)
Day 1: K ⁺ (8.4 mmol/l)	No response	No response	0.16/0.3	18.0	44.4/22.4	2.7/6.2	20.0	25.0/9.4
Day 10: K ⁺ (4.0 mmol/l)	23.0	37.0	16.9/19.6	38.0	16.8/6.2	13.2/13.1	41.0	11.0/4.6
Normal findings	>10.0	>40.6	>2.9 (distal)	>41	<15.1/6.0	>3.5 (distal)	>48.0	<8.8/4.6

abnormalities except slightly slowed conduction velocities (table). Needle EMG of hypothenar and quadriceps muscles showed normal recruitment, duration, and amplitude of motor unit action potentials. An EEG and ECG were in the normal range.

The clinical presentation of our patient with rapidly progressive tetraparesis, areflexia, and mild sensory symptoms would have been entirely consistent with the diagnosis of Guillain-Barré syndrome. This suggestion seemed confirmed by nerve conduction studies showing extremely delayed distal latencies, conduction block (median nerve), and delayed motor and sensory conduction velocities. Only the history of concurrent convulsions was suspicious, but this could have been explained by coincidental hypertensive encephalopathy due to chronic renal disease.

Although slowly rising serum potassium concentrations are usually well tolerated, an acute increase in serum potassium can cause life threatening cardiac complications. Only rarely are pronounced neuromuscular symptoms an initial feature of hyperkalaemia.¹ Neurological symptoms that usually develop at serum concentrations higher than 8 mmol/l² include dysaesthesia and weakness, sometimes presenting as Guillain-Barré syndrome.^{3,4} The respiratory musculature seems to be relatively well preserved³ as in our patient.

To our knowledge there are so far no reports on follow up nerve conduction studies of patients with hyperkalaemic paresis presenting with findings otherwise typical of Guillain-Barré syndrome. Our electrophysiological data reflect the progressive inexcitability of nerve fibres due to extracellular hyperkalaemia leading to multiple functional conduction delays and blocks and thus mimicking acute Guillain-Barré syndrome.

The fact that the sensory nerve action potential (sural nerve) was initially absent whereas the EMG showed normal electrical insertional activity of muscles suggests that muscle fibres were much less influenced by hyperkalaemia than were nerve fibres. The predominance of medium size and larger motor units on EMG argues against a selective affection by hyperkalaemia of the largest and fastest conducting nerve fibres. Thus a homogeneous slowing of conduction in fibres of all sizes is the most likely cause of the slowed conduction velocities seen here. Also, conduction failure was present in a substantial proportion of fibres on initial examination. Distal segments of the nerves seemed only marginally more affected than proximal sites. This suggests that conduction defects were diffuse rather than focal.

Recently, a case with hypokalaemia mimicking Guillain-Barré syndrome was reported.⁵ Electrophysiology in this case showed a

predominant decrease of compound muscle action potentials whereas sensory nerve action potentials were preserved. Thus by contrast with the situation in hyperkalaemia, muscle membranes in hypokalaemia seemed to be more severely affected than nerve fibres.

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- 1 Pollok M, Baldamus CA. Störungen des Kaliumhaushaltes. In: Classen M, Diehl V, Kochsiek K, eds. *Innere Medizin*. München: Urban und Schwarzenberg, 1991:1271-4.
- 2 Sterns RH, Narins RG. Disorders of potassium balance. In: Stein JH, eds. *Internal medicine*. Boston: Little, Brown and Co, 1990:853-6.
- 3 Radó JP. Successful treatment of hyperkalaemic quadriplegia associated with spiro-lactone. *Int J Clin Pharmacol Ther Toxicol* 1988;26:339-45.
- 4 Knochel JP. Neuromuscular manifestations of electrolyte disorders. *Am J Med* 1982;72:521-35.
- 5 Warner TT, Mossman S, Murray NMF. Hypokalaemia mimicking Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry* 1993;56:1134-5.

Botulinum toxin and sweating

Botulinum toxin A is widely used in the treatment of dystonic disorders. It acts by inhibiting the release of acetylcholine at the presynaptic level.¹ The neuromuscular blockade it produces is irreversible and recovery occurs over about three months by resprouting of the axons and formation of new acetylcholine receptors.¹ Both motor nerves to skeletal muscles and autonomic cholinergic fibres seem to be similarly blocked by the toxin.² In addition to skeletal muscle paralysis, autonomic dysfunction is the rule in botulism, and objective autonomic function tests are abnormal, indicating both sympathetic and parasympathetic dysautonomia.³ Similar but minor abnormalities in autonomic tests have been reported after local injections of the toxin.⁴

Botulinum toxin has long been known to block postganglionic sympathetic cholinergic fibres to sweat glands in animals.² Although it might be expected that the toxin would have a similar effect on sudomotor fibres in humans, objective tests of sweating seem not to have been previously reported in patients with botulism or in those receiving local injections. We studied facial sweat-

ing in patients treated with botulinum toxin A injections for hemifacial spasm.

Three patients (one woman and two men aged 69, 76, and 78 respectively) attending the botulinum toxin clinic for one, 1.5, and seven years respectively for treatment of hemifacial spasm agreed to participate in the study. All were receiving intermittent treatment with botulinum toxin A injections (60-120 mouse units; Dysport-Porton Products) around the orbit on the side of hemispasm. None of the patients was receiving anticholinergic drugs. In two of the patients, facial sweating was tested one week after the last injection session. In one patient the sweat test was performed three months after the previous injections and repeated one week after the last session of injections. Sweating was tested with Ponceau red dye and starch mixture. This is a pink powder that changes colour to bright red when wet.

The powder was dusted on to the face with cotton wool. Thermoregulatory sweating was induced by keeping the subjects with the trunk and limbs enveloped in polythene sheeting in a warm humid room. The room temperature was maintained at 32-35°C with an electric fan heater and humidity was maintained by boiling an elec-

tric kettle. Heating continued until facial sweating, as detected by the change of colour of the dye, was evident. This took 30 to 50 minutes. The distribution of sweating on the face was charted and photographed.

Facial sensation, pupil size, and reaction were normal in all three patients. Two of the patients had developed a mild ptosis as a side effect of previous injections. In all three patients there was an area of anhidrosis around the orbit including the upper part of the cheek and the side of the nose, the temple, the eyebrow, and the lower part of the forehead, on the side of the injections. The shape and size of the anhidrotic area was similar in all three patients (figure). In the one patient, the result of the sweat test was similar three months after previous treatment.

This brief study seems to provide strong evidence that sudomotor efferents are affected by botulinum toxin A. As in cholinergic neuromuscular transmission, diffusion of the toxin and inhibition of acetylcholine release from the presynaptic terminals of the sudomotor nerves seems to be the underlying mechanism producing anhidrosis after botulinum toxin A injections. A similar anhidrotic effect of the injected toxin was shown by Ambache in