LETTERS TO THE EDITOR

Familial hydrocephalus

Familial cases of congenital hydrocephalus have often been reported and may result from distinct monogenic disorders or may be multifactorially determined.[1] The commonest cause is X linked hydrocephalus associated with stenosis of the aqueduct of Sylvius and, in most families, the genetic basis of this condition is known.[2] By contrast, familial adult onset cases are unusual and the genetic basis is unknown.[3] We report a family in which the presumed mode of inheritance is autosomal dominant with variable penetrance.

The family pedigree is shown in figure 1. There was no consanguinity.

Patient II-1 was a 76 year old man who presented at the age of 62 years with a 3 year history of progressive gait ataxia, an 18 month history of urinary frequency and occasional urge incontinence, and a 12 month history of cognitive impairment. There was no other medical history of note and he was on no medication. Psychometry showed evidence of a severe and selective verbal memory deficit, impaired attention, and a reduced ability to work at speed, with relative preservation of visual memory, perceptual, and spatial skills. His gait was broad based. Examination of the cranial nerves was normal; there was no disc swelling. There was mild weakness of knee extension bilaterally; reflexes were brisk with flexor plantar responses; there was mild limb ataxia. The remainder of the neurological examination was normal. General examination was normal. Brain CT showed gross communicating hydrocephalus with marked distortion of the fourth ventricle (fig 2). A VP shunt was inserted without perioperative complications; postoperative CT showed some reduction in ventricular size. At review 6 months later his gait and urinary disturbance had largely resolved. Repeat psychometry showed some improvement in his verbal memory and significant improvement in word retrieval skills and ability to work at speed.

Patient III-2 was a 47 year woman with a 20 year history of progressive gait disturbance which had been severe for 2 years and an 18 month history of morning headache associated with nausea and vomiting. She reported no cognitive or urinary disturbance. There was no other medical history of note and she was on no medication. Bedside cognitive assessment was normal. Her gait was broad based and spastic. There were saccadic intrusions into pursuit eye movements; examination of the cranial nerves was otherwise normal; there was no disc swelling. Tone was increased in the legs with mild pyramidal pattern weakness, brisk reflexes, and bilateral extensor plantar responses. There was mild limb ataxia. The remainder of the neurological examination was normal. General examination was normal.

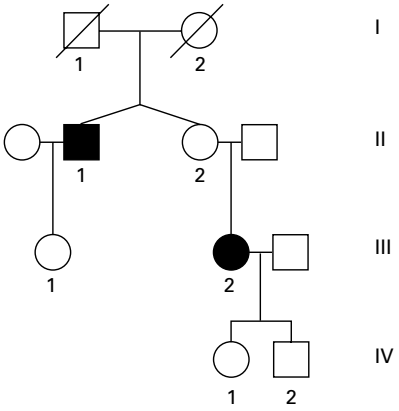

Figure 1 Family pedigree.

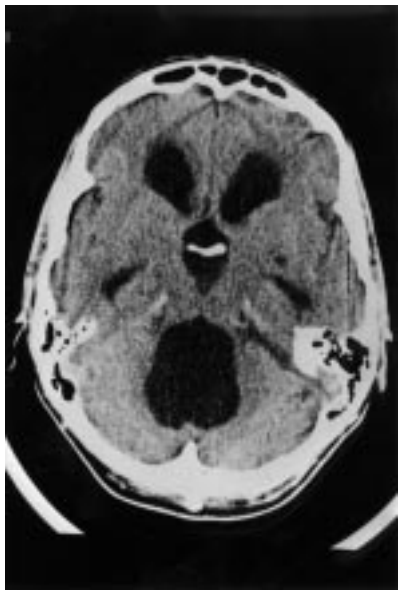

Figure 2 CT of patient II-1 showing communicating hydrocephalus.

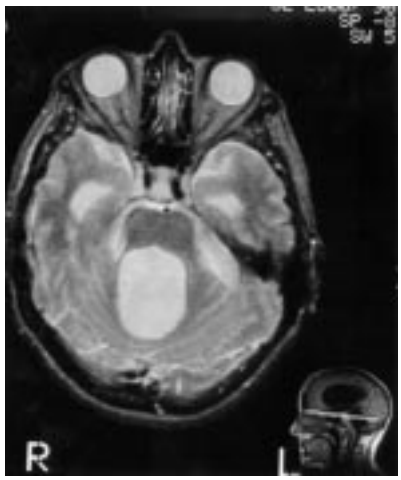

Figure 3 Brain MRI of patient III-2 showing communicating hydrocephalus.

Brain MRI showed gross communicating hydrocephalus with marked distortion of the fourth ventricle (fig 3); there was no evidence of a Chiari malformation or other abnormality. Intracranial pressure monitoring showed predominantly normal pressure but intermittent pressure waves. A VP shunt was inserted without perioperative complications. At review 2 months later her gait disturbance had markedly improved and her headache had resolved.

No other family member had any neurological complaints. Patient II-2 (the twin sister of patient II-1 and mother of patient III-2) was reviewed at the age of 75 years. She was asymptomatic and neurological examination was normal. Brain CT showed no evidence of hydrocephalus.

We report on a family containing two members who presented in adult life with gait disturbance and, in one case, urinary symptoms and cognitive decline. Neuroimaging in both cases showed communicating hydrocephalus with marked distortion of the fourth ventricle and each patient gained significant symptomatic benefit from a VP shunt. Although it is possible that this represents a chance association, it seems likely that this family carries a genetic predisposition to the development of communicating hydrocephalus. The presumed mode of inheritance is autosomal dominant with variable penetrance, although X linked inheritance cannot be excluded.

Familial cases of congenital hydrocephalus, both syndromal and non-syndromal, are well described.[1] Most cases of X linked hydrocephalus with associated stenosis of the aqueduct of Sylvius are caused by mutations in the gene for neural cell adhesion molecule L1 (L1CAM),[2] although some families with otherwise typical X linked aqueduct stenosis do not show linkage to this locus.[4] It has been suggested that the aqueduct stenosis seen in this condition may be a secondary phenomenon and that the hydrocephalus begins as a communicating form.[5] Mutations of L1CAM are also seen in families with the MASA syndrome (mental retardation, aphasia, spastic paraplegia, adducted thumbs) and spastic paraplegia type 1 (SPG1).[6 7] In some other cases of non-syndromal hydrocephalus, autosomal recessive inheritance is suggested by the occurrence of hydrocephalus in siblings of both sexes born to normal but often consanguineous parents.[8] One study of 261 pregnancies suggested that, apart from X linked cases, most cases of congenital hydrocephalus were multifactorially determined with a recurrence risk of about 4%.[9]

We are aware of only one other report of familial adult onset, non-syndromal hydrocephalus.[3] This describes two siblings with late onset gait disturbance, urinary frequency, and cognitive impairment. Neuroimaging demonstrated hydrocephalus; intracranial pressure monitoring was not performed. Both cases improved markedly after shunt procedures. Details of the family history of these cases was not provided but it has been assumed that they represent autosomal recessive inheritance. The phenotype of these cases is strikingly similar to the cases we describe and this may support the suggestion that an autosomal locus contributes to the development of apparent "normal pressure" hydrocephalus.

In conclusion, we report the second case of familial adult onset, non-syndromal hydrocephalus. The presumed mode of inheritance is autosomal dominant but further studies will be required before the genetic basis of such cases can be elucidated.

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Brachial plexopathy related to alcohol intoxication

Brachial plexopathy associated with alcohol intoxication is rarely reported. We describe two patients with injuries to the brachial plexus thought to be the result of either stretch or compression of the plexus while intoxicated. In the first patient, damage was bilateral affecting the entire plexus on the right and the upper plexus on the left. This patient had associated rhabdomyolysis due to direct alcohol myotoxicity or prolonged immobilisation. In the second patient damage was on the right, involving predominantly the upper trunk. Neurophysiological studies and the rapid and complete recovery in our patients suggest that the primary pathology was focal demyelination causing conduction block, although there was also EMG evidence of axonal degeneration, particularly in the right arm of the first patient, in whom recovery was consequently delayed. Injury to the brachial plexus should be considered in patients with upper limb deficits related to intoxication.

The association between brachial plexopathy and both anaesthesia and intoxication is well recognised but this condition has been rarely described resulting from alcohol. We describe two patients with injuries to the brachial plexus who underwent neurophysiological studies, one with unilateral and the other with bilateral damage arising from prolonged immobilisation associated with alcohol intoxication. One patient had associated rhabdomyolysis due to either direct alcohol myotoxicity, prolonged immobilisation on a hard surface, or a combination of the two.

The first patient was an obese 69 year old man who lived on his own and drank at least two litres of vodka (900 g alcohol) a week. He returned from a party where he had drunk a large quantity of alcohol and fell next to his bed but did not lose consciousness. He was unable to get onto his bed and slept on the floor. The next morning he woke with profound weakness and sensory loss in both arms but no facial or lower limb weakness and no neck or limb pain. He was admitted to hospital and because of difficulty initiating micturition, a urethral catheter was inserted. He was fully conscious and orientated; examination of his cranial nerves was normal. He had severe right upper limb weakness; shoulder abduction was MRC grade 2 using mainly supraspinatus and there was only a flicker of movement at the wrist and fingers. Left shoulder abduction and elbow flexion power were MRC grade 1, elbow extension grade 4, wrist dorsi and palmar flexion and finger flexion and extension grade 3. Strength in the lower limbs was normal. The deep tendon reflexes were absent in the upper limbs except for the left triceps, normal at the knees, absent at the ankles, and plantar reflexes were flexor. Pain and light touch sensation was diminished in the C5 to T1 dermatomes bilaterally with absent vibration and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, an abdominal and pelvic ultrasound was normal and he was able to pass urine normally when the catheter was removed.

Magnetic resonance imaging of his cervical spine was normal and CT of the brain demonstrated diffuse cerebral and cerebellar atrophy. He had a raised blood urea (10.2 mmol/l) and creatinine (203 μmol/l) due to dehydration, a macrocytosis (mean corpuscular volume 100.4 fl), and a low albumin (26 g/l). Other blood tests, including B_{12}, folate, thyroid and liver functions, protein electrophoresis, and antinuclear antigen serology were normal. His creatine kinase on admission was 15 000 U/l, which was not associated with myoglobinuria. This did not require any further treatment and had returned to normal concentrations (35 U/l) within a week.

Electrophysiological studies in the right arm in the first week showed reduced sensory amplitudes of the right radial (5 μV), median (3 μV), and ulnar (1.5 μV) nerves. Median and ulnar motor conductions were normal apart from reduced F wave persistence. The compound muscle action potential (CMAP) of the deltoid to Erb's point stimulation was of low amplitude (1.1 mV) and there was a little fibrillation on right deltoid EMG. Left arm conduction studies, including F responses and proximal stimulation and EMG were essentially normal. Repeat testing 2 weeks later showed low amplitude CMAPs from right median and ulnar nerves (both 2.8 mV) with absent F waves. The deltoid CMAP to Erb's point stimulation was absent on the right and markedly reduced (0.6 mV) on the left. There were moderate but extensive active denervation changes in the right C5-T1 myotomes but denervation was restricted to the deltoid and biceps muscles on the left. The spinati, rhomboids, and paraspinal muscles were normal bilaterally, suggesting that the lesions were at the cord rather than trunk level in the plexus.

A diagnosis of bilateral brachial plexopathy due to prolonged immobilisation with associated rhabdomyolysis was made. The patient underwent active rehabilitation and at discharge from hospital 2 months later, his left arm was almost fully functional. His recovery continued and at follow up, about 4 months after the episode, strength was normal in his upper limbs, sensation was reduced on the left in the C5/6 dermatome but he had developed severe truncal and gait ataxia due to the continued consumption of alcohol.

Patient 2, a 67 year old woman, known to be alcoholic, had gone to bed at midday. She denied having been drinking but this was considered very likely. On waking at 4 00 pm she was unable to move her right arm. There was no pain and the only sensory symptom was occasional tingling in the inside of her forearm. Her condition had improved marginally when she first presented after 2 weeks. Examination of her cranial nerves and left upper limb was normal and she had mild gait ataxia. There was no power (MRC grade 0) in the right deltoid, biceps, and brachioradialis and severe weakness (MRC grade 2) in the supraspinatus and infraspinatus. All reflexes were brisk and symmetric apart from an absent right biceps reflex. Sensation was normal.

Magnetic resonance imaging of her cervical spine showed minor disc osteophyte bars at the C5/6 and C6/7 levels, the canal dimensions were generous, and there was no evidence of either cord compression or signal change in the cord. She had a raised γ-glucuronyl transferase (γ-GT) (140 IU/l) and alanine aminotransferase (82 IU/l) and a macrocytosis (mean corpuscular volume 98.1 fl), compatible with chronic alcohol misuse. Nerve conduction studies showed normal right upper limb sensory action potentials, comparable with the left side. The only abnormal motor conduction study was prolongation of the distal latency (9.9 ms) and reduction of the CMAP (0.8 mV) of the right musculocutaneous nerve. Studies by EMG showed no voluntary activity and frequent fibrillations and positive sharp waves in the right supraspinatus, infraspinatus, biceps, brachioradialis and pronator teres, and occasional fibrillations in the deltoid, all mainly C5/6 innervated muscles via the upper trunk. An EMG of the right triceps, flexor carpi radialis, and first dorsal interosseous were normal as was sampling of the cervical paraspinal muscles.

These findings were thought to be most compatible with a partial brachial plexopathy involving the upper trunk due to compression or traction. Three weeks later the patient had markedly improved, with only minimal weakness (MRC grade 4) in the previously severely affected muscles. The right biceps reflex was still absent. Three months later, she was asymptomatic with a normal neurological examination.

These patients represent a range of alcohol related brachial plexus injury. In our first patient, the right side showed extensive damage involving the entire brachial plexus (C5-T1 myotomes) whereas the left involved mainly the upper part (C5–6 myotomes). This pattern of involvement, with sparing of the spinati and rhomboids suggests that the site of injury was distal in the plexus at the level of the cords. The findings in the second patient are most compatible with a partial brachial plexopathy involving the upper trunk. The findings in both patients are most likely due to compression or stretching of the brachial plexus. Both patients had normal paraspinal EMG and cervical MRI studies, making more proximal lesions unlikely.

Cadaver studies have shown that shoulder abduction to 90°, particularly if bilateral, combined with contralateral rotation of the head and arm extension increases tension on the plexus.[1] We postulate that our patients slept with the affected arms extended and the head rotated to the left, giving maximum