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.9 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.9 By contrast, familial adult onset cases are unusual and the genetic basis is unknown.9 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; posteroventricular 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.

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.9 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),9 although some families with otherwise typical X linked aqueduct stenosis do not show linkage to this locus.9 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.9 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).9 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. 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.9 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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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.
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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 either 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 recovery in our patients suggest that the primary pathology was focal demyelination causing conduction block, although there was also EMG evidence of axonal dysfunction, 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. Both patients 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 a 23-year-old man who woke up fully aware on Monday and drank at least two litres of vodka (900 g alcohol) a week. He returned from a party where he had drank a large quantity of alcohol and fell next to his bed but did not lose consciousness. He was unable to get out his bed and slept 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 he had examined; 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 finger extension. 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 (300 µmol/l) due to dehydration, a macrocytosis (mean corpuscular volume 98.1 fl), compatible with chronic alcohol misuse. Nerve conduction studies showed normal right upper limb sensory and motor conduction and was compatible with the left side. The only abnormal motor conduction study was pro-longation of the distal latency (9.9 ms) and reduction of the CMAP (0.8 mV) of the right median nerve. 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. EMG of the right triceps, flexor carpi radialis, and first dorsal interosseous were normal as was sampling of the cervical paraspinous 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 made some improvement, with painless atrophy (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 neurophysiological 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, whereas the spinats and rhomboids suggests that the site of injury was distal in the plexus. Further studies by EMG in the second patient showed no voluntary activity and frequent fibrillations in both arms. EMG of the right triceps, flexor carpi radialis, and first dorsal interosseus was normal as was sampling of the cervical paraspinous 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 made some improvement, with painless atrophy (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 neurophysiological examination.

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traction to the right plexus. Seventy five per cent of postoperative plexopathies show involvement of the whole plexus whereas 18% are restricted to the upper trunk, usually in its entirety. Our cases were consistent with these findings.

The neurophysiological features and pattern of recovery suggest that compressive brachial plexopathy is primarily due to focal demyelination with some degree of axonotmesis depending on severity. Rapid recovery in our patients suggests that the primary pathology was focal demyelination, causing conduction block, although there was also clear EMG evidence for axonal degeneration, particularly in the right arm of the first patient, in whom recovery was consequently delayed. Ultimately, both patients made a good recovery as is typical in postoperative plexopathy, recovery time depending on the balance between demyelination and axonal degeneration. The occurrence of bilateral plexopathy, as in our first patient, is unusual after closed trauma but has been reported after bilateral shoulder dislocations and postpartum.1

The concurrent plexopathy and raised creatine kinase in our first patient is noteworthy. This may have been due to either prolonged immobilisation on a hard surface, disturbed circulatory myotonicity, or a combination of the two. Rhabdomyolysis was common in a series of elderly patients who remained on the floor for at least an hour after collapse, as evidenced by a raised serum myoglobin in 16 of 18 and creatine kinase in 14 of 18. Concurrent rhabdomyolysis and brachial plexus lesions have been described in the neuroleptic malignant syndrome and alcohol intoxication.

Alcohol related brachial plexopathy is part of the multitude of alcohol related neurological disorders. It is surprising that this entity is rarely reported, by comparison with plexopathy associated with other nervous system depressants; perhaps this is due to differences in the depth and duration of intoxication. It should be considered and looked for in patients with upper limb deficits related to intoxication.

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Positive response to therapy in a patient with seropositive paraneoplastic cerebellar degeneration and an endometrioid carcinoma of the vesicovaginal septum

Paraneoplastic cerebellar degeneration is a rare complication of human cancer. This disorder is characterised by subacute onset of pancerebellar symptoms, often associated with dysfunction of other areas of the CNS. The onset of the degeneration may occur months before or after the detection of the primary cancer.2,3 It is usually associated with antineuronal antibodies directed against antigens coexpressed by the cells that undergo degeneration and by the associated tumour. Anti-Yo antibodies can be found in the serum and CSF of patients with paraneoplastic cerebellar degeneration with breast or gynaecological tumours. These antibodies show a coarse granular staining pattern of the cytoplasm of Purkinje cells, while the nucleus remains unstained.4 Patients with paraneoplastic cerebellar degeneration without anti-Yo antibodies may have other tumours, most commonly bronchial carcinoma or Hodgkin's lymphoma, and may be positive for anti-Hu, anti-voltage gated calcium channel, or anti-Tr antibodies.5 Although the antibodies provide a diagnostic test for the associated tumours, it is generally thought that destruction of the Purkinje cells by autoactive T cells is the major pathogenic mechanism, and previous reports suggest a lack of response to conventional immunosuppressive treatment.5

A 47 year old woman had no history of neurological disease until March 1996. There was a history of surgical correction of a urethral diverticulum at the age of 34, and at 44 years she had been treated for a "vaginal cyst" (likely a Naboth cyst) by aspiration. In March 1996 she complained of blurred vision, diplopia, dysphagia, and gait ataxia with balance disturbance. Brain MRI and an ultrasound of the pelvis were reported normal, but serum anti-Yo antibody was negative, but serum anti-Yo antibody was positive by immunohistochemistry, confirmed by immunoblotting with purified antigen (DPC Biemann).2 By 29 October 1996 there was marked gait ataxia, myasthenia, diplopia, dysphagia, cerebellar dysartria, pyramidal signs, and arm and leg dysmetria with tremor. At this time MRI demonstrated cerebellar atrophy (figure A) and CT and MRI of the pelvis (figure C, D) both revealed a 3.5 cm diameter lesion located in the vesicovaginal septum, infiltrating the bladder and vaginal wall. A transvaginal biopsy was performed and the histological examination showed the presence of malig

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MRI. If no malignancy is found, surgical exploration should be considered, particularly in postmenopausal women. In addition, although many cases may not respond to plasma exchange, intravenous immunoglobulin or immunosuppressive drugs, perhaps because the neuronal damage is irreversible, the successful results in the present case indicate that continuous immunosuppressive therapy should be carefully considered.

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Isolated infarction in the territory of lateral posterior choroidal arteries

Lateral posterior choroid arteries (LPCAs) originate from the distal PCA trunk in the proximity of the origin of thalamogeniculate arteries or the cortical branches. Infarction of LPCAs, therefore, often accompany lesions of other PCA cortical branches or perforating branches. Their clinical features have often been masked by the associated and combined cortical and subcortical lesions. Accordingly the clinical features of a discrete infarction of the LPCA have been reported.

Figure 1 (A, B) sagittal spin echo (SE) T1 weighted images of the brain obtained in November 1996 and 1 year later: This shows cerebellar atrophy, which clearly increased after 1 year. (C, D) Unenhanced coronal and sagittal FSE T2 weighted MR images of the pelvis: the vesicovaginal septum is occupied by an infiltrating neoplastic mass (arrowheads).
only a few times.\textsuperscript{1,2} This paper reports on two such patients and pertinent articles are reviewed.

The first patient, a 62 year old woman with a history of untreated supraventricular arrhythmia for 10 years had sudden onset of non-pulsatile headache on the vertex. At the same time she noted blurred vision in the left visual field for a few days. The headache continued for 5 days and she visited a nearby hospital. No visual field defect was noted on confrontation. Brain CT showed a low density lesion in the posterior thalamus. As the location of the lesion was unusual, the patient was referred to our institution 3 weeks later. On admission she was free of neurological deficits including higher cortical function. The visual acuity was 12/20 on the right and 10/20 on the left. Goldman's perimetry did not disclose any visual field defect, either. The repeated CT showed a localised low density lesion at the posterolateral thalamus extending to the area of the lateral geniculate body inferolaterally and the posterior caudate nucleus superiorly (figure A, B, and C). No other remarkable lesions were noted. Laboratory study was normal but the ECG showed atrial fibrillation.

Vertebral angiography showed no obstructive or stenotic change in the posterior cerebral arteries. LPCAs were demonstrated on both sides. Brain MRI demonstrated a lesion of abnormal intensity at the posterolateral thalamus, the posterior part of caudate nucleus, and the lateral geniculate body (figure D). She was medicated with 200 mg/day ticlopidine and remained free of stroke for the next 4 years.

The second patient, a 72 year old woman with an 8 year history of hypertension noted right sided homonymous type hemianopia for a few minutes on waking up in the morning. At the same time she felt transient bilateral hand dysaesthesia. She had no headache or dizzy sensation. When she arrived at the hospital 2 hours later, she was free of neurological deficits including visual field on confrontation. Three hours later CT showed no abnormality. Results from Goldman's perimetry were normal. Three days later repeated CT showed a newly appearing low density lesion at the left posterior thalamus, the lateral geniculate body, and the tail of the caudate nucleus (figure E, F). The superconductive MRI with T1 and T2 weighted images a month later and the CT scan 2 months later showed no abnormality. Cerebral angiography was not carried out. She was medicated with 200 mg/day ticlopidine and 300 mg/day pentixyline and has been well for the past 2 years.

We reported two cases of infarction at the posterolateral thalamus, the lateral geniculate body, and the posterior part of the caudate nucleus.\textsuperscript{1–3} Reports on patients with discrete LPCA infarction are few.\textsuperscript{2–5} The main symptom has been related to visual field defect. It is commonly quadrantanopia or hemianopia. Characteristic visual field defects of LPCA occlusion have been described as homonymous horizontal sectoranopia or wedge shaped homonymous hemianopia.\textsuperscript{4,5} These authors stated that, with and without evidence of CT, these unusual visual field defects were due to ischaemia at the lateral geniculate body, and dual blood supply from the LPCA of PCA and anterior choroid artery of the ICA may explain this unusual visual field defect. Neau and Bougousslavisky have also stated that, although it occurs infrequently, its is specific to the lesion at the lateral geniculate body.\textsuperscript{5} The other signs were hemisensory disturbance, to a lesser extent neuropsychological
In our patients the symptoms were mild and transient. The first patient had blurred vision on the left side for 5 days and in the second patient, the visual field defect lasted for 4 days. Few patients could disclose the corresponding lesions of the LPCA occlusion.

The LPCAs mainly originate from the ambient segment of the PCA trunk or its cortical branches. The number of twigs averaged 4.0 (range 1–9). When two or more branches are present, anterior branches penetrate the choroid fissure to supply the choroid plexus of the inferior horn of the lateral ventricle. Posterior branches supply the choroid plexus in the trigone of the lateral ventricle and anteriorly in the third ventricle. They also supply the pulvinar, medial, and lateral geniculate bodies, fornix, and midbrain tegmentum. Many anastomoses between the branches of the LPCA and anterior choroidal artery are present at the anterior third of the temporal horn as are many connections between the LPCA and medial posterior choroidal arteries at the level of the fornmen of Monro.

In frequent occurrence of occlusion of the LCA is speculated to be due to such multiple branches and rich anastomosis. The number of arteries and development of anastomosis vary. Such ample anatomical variation in the supplying territory of these arteries may explain the wide range of severity and duration of symptoms of both our patients and others reported. Our patients represent the milder form of the clinical features of infarction of the LPCA, which has not been highlighted. The LPCA occlusion may present only with such minor complaints. Because LPCA occlusion may be prodomal signs of more serious brain ischaemia, we need to know a wide range of the clinical symptoms related to occlusion of the LPCA.

Neurostimulation of the ventral intermediate thalamic nucleus alleviates hereditary essential myoclonus

Therapy in hereditary essential myoclonus (HEM), a disabling movement disorder, is difficult in most cases, especially in regard to the myoclonic syndrome. This is the first report on the amelioration (around 65%) of HEM by high frequency deep brain stimulation of the ventral intermediate thalamic nucleus (VIM) of a 61-year-old male patient with medically intractable HEM.

The jerky movement disorder began in his neck and shoulders around the age of 6 and gradually progressed, especially in the proximal right arm, leading to a severe reduction of dexterity and inability to write. He was unable to continue working as a janitor when he was 55.

On examination he presented mainly oscillating, “lightning”, irregular, jerky, asynchronous movements of his forehead, neck, proximal right arm, less severe of the left arm, and discretely of the upper trunk, which was exacerbated by walking, writing or drinking and could be elicited by loud acoustic stimuli. The disorder improved at rest and disappeared in sleep. Additionally, he had a slight torticollis to the left, superimposed by inconstant no-no-no myoclonus and a discrete action tremor of both hands, all of which complies with the HEM criteria as outlined by Quinn. The remaining neurological status was unremarkable.

Four of the six children of the patient had possible myoclonus in a 61-year-old male patient. Additionally, two of four siblings of our index patient were definitely affected by the movement disorder, whereas the parents seemed to be unaffected (a full account of the family history will be provided elsewhere, manuscript in preparation).

Alcohol consumption markedly attenuated the movement disorder with a clear rebound phenomena after alcohol withdrawal, leading to chronic alcohol misuse. A latent suicidal risk was regarded in the patient. Myoclonus and a discrete action tremor of both hands, all of which complies with the HEM criteria as outlined by Quinn. The remaining neurological status was unremarkable.

Intraoperatively and in the subsequent 12 months deep brain stimulation (2.8 V, 130 μs) produced a pronounced and persistent reduction of the jerks and the action tremor of the right arm and a partial reduction of the jerks of the neck and the trunk. The improvement could be postoperatively quantified by a roughly 65% decrease in myoclonus score (table). In practical terms, this was reflected by the use of the right hand for handwriting for the first time after 15 years of incapacity. Interestingly, the optimal stimulation parameters corresponded to those used in deep brain stimulation for essential tremor. The mild dystonic symptoms (slight cervical dystonia) were not affected by DBS with different stimulation parameters. Preoperative medication comprised 60 mg diazepam a day and could be reduced to 10 mg diazepam a day at 12 months postoperatively.

Stimulation of the VIM is an established neurosurgical method for the treatment of pharmacologically intractable essential tremor, although its mechanisms of action remain to be elucidated. It is interesting to note that both diseases (HEM and essential tremor) may be improved by alcohol intake, which could hint at overlapping pathophysiological mechanisms. Importantly, it has been reported that low frequency stimulation (2 Hz-5 Hz) of the VIM in patients with Parkinson’s disease may even trigger myoclonus. However, we have been unable to aggravate the myoclonic syndrome in our patient by low frequency stimulation (2 Hz-5 Hz), which may point to different mechanisms of actions of stimulus induced myoclonus in Parkinson’s disease versus HEM.

In conclusion, the case report suggests that neurostimulation of the VIM may be an effective therapeutic alternative for medically intractable HEM and suggests that the thalamus may be a myoclonus sensitive site.

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Myoclonus rating scores

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Myoclonus rating scores preoperatively, on and off deep brain stimulation (DBS) 10 months postoperatively, modified according to Truong and Fahn. Postoperative ratings were observed by an observer (TT), who had been blinded to the stimulation status (‘on’ or ‘off’).
a 2 year history of anosmia, nasal stuffiness, and rhinorrhea which was diagnosed 12 months previously, by both her general practitioner and an ear, nose, and throat surgeon, as allergic rhinitis, with patch testing confirming allergy to house dust mite II, although no imaging was performed at this time.

This was treated with the topical nasal steroid spray Fluticasone (Fluticasone propionate 50 mcg/spray). The remainder of the history was unremarkable and she had not been back to Asia for 6 years.

General examination was normal and there were no focal neurological signs, although she was rather confused and disinhibited.

Full blood count; urea and electrolytes; liver function tests; serum calcium; random blood glucose; thyroid function tests; serum trophilic antibodies (ANCA) and perinuclear (p-) ANCA; an ECG; and chest radiography were negative.

An EEG showed only diffuse slowing, consistent with a postictal state. Brain CT showed an ill defined area of reduced attenuation in the right frontal lobe, with no contrast enhancement, and a soft tissue mass in the paranasal and sphenoid sinuses, which was eroding through the base of the skull.

Brain MRI (fig 1) showed swelling of the right frontal pole with oedema and a small, intensely enhancing, soft tissue mass in the floor of the anterior fossa, which was probably in communication with the soft tissue mass in the paranasal sinuses.

A biopsy of the posterior ethmoid region showed granulomatous change with fungal hyphae seen and Aspergillus fumigatus was grown on culture. Cultures for tuberculosis were negative and HIV type 1 and 2 serology was negative.

Anticonvulsant therapy with modified release carbamazepine (carbamazepine MR) was started and the nasal spray was stopped. She was commenced on intravenous amphotericin B (250 mcg/kg/24 hours), which within 2 days led to renal impairment and had to be discontinued.

Itraconazole syrup (200 mg twice daily) was substituted and adjusted according to serum concentrations, and the therapeutic range (4 hours postdose 5–15 mg/l) was achieved with a dose of 300 mg twice daily.

Over subsequent weeks she improved and became less confused and disinhibited, although the anosmia remained. On review 8 months later she remained well and a repeat MRI (fig 2), although still showing residual disease, showed a marked reduction in its extent and in particular a dramatic decrease in the size of the subfrontal lesion.

The fungal genus Aspergillus causes a range of diseases including allergic; non-invasive; invasive and fulminant aspergillosis. The two commonest strains are A flavus and A fumigatus. Invasive aspergillosis is characterised by tissue invasion with Aspergillus hyphae and is most commonly seen in immunocompromised people, but there are a few case reports in apparently immunocompetent people. It differs from allergic aspergillus sinus and allergic bronchopulmonary aspergillosis, which are immune mediated reactions to Aspergillus infection.

There are three possible routes of invasion into the CNS: haematogenous, usually from the lung; direct spread from an area adjacent to the CNS, and iatrogenic introduction, usually after neurosurgical procedures.

The commonest route of spread is haematogenous and the most frequent CNS manifestation is an intracerebral abscess, but it can also cause meningitis or meningoencephalitis; granulomas; cerebrovascular disease; vasculitis, or cranial nerve palsies.

Intracranial extension from an adjacent area is only seen in advanced cases, and extension through the skull base is rare.

The prognosis in this disease is very poor and invasive CNS aspergillosis is often a fatal disease regardless of the mode of therapy, with mortality upwards of 80%, and very few long term survivors of cranial and intracranial aspergillosis have been reported in the literature.

Amphotericin B is effective against Aspergillus but its toxicity and mode of administration limit its usefulness. Itraconazole is well absorbed orally, is comparatively non-toxic, and is effective against Aspergillus; however, serum concentrations need monitoring.
Local antifungal chemotherapy delivered to recently, stereotactic surgery, tried, from formal craniotomy to, more zole and amphoterecin B.

dence suggests antagonism between itracona-
therapy over monotherapy, and some evi-
dation of this preparation for our patient.

Some reports suggest that the syrup form is more reliably absorbed and hence the choice of this preparation for our patient. Other antifungal agents do not have sufficient activity against Aspergillus to be of any value, with the possible exception of the newer agent voriconazole.

There is little advantage of combined therapy over monotherapy, and some evidence suggests antagonism between itraconazole and amphoter cin B.

Various surgical approaches have also been tried, from formal craniotomy to, more recently, stereotactic surgery, all with varying, although usually poor, rates of success.

Local antifungal chemotherapy delivered to the lesion via a closed reservoir system has been tried and may prove a useful adjunct to treatment.

The correct method for treating this condition is unknown and its rarity makes large randomised trials of surgical or combined approaches untenable. Most studies to date advocate early aggressive surgical intervention, but the evidence to support this approach is not strong. It is probable that the most effective treatment will be a combination of different modalities, which is likely to vary depending on the extent of the disease.

In our patient there was no evidence of immunodeficiency and the biopsy confirmed invasive aspergillosis with the imaging showing continuity between the sinus and frontal lobe lesions. We think that there can be little doubt about the important part played by the intranasal steroids in our patient. Even if intranasal steroids did not lead to the introduction of Aspergillus, they certainly allowed the Aspergillus to flourish, possibly by impairing local cell mediated immunity. A similar situation to that which occurs when topical steroids are applied to fungal skin infections that are mistaken for eczema.

In view of the lack of consensus on management we decided to continue with antifungal chemotherapy alone, particularly given the likely importance of the intranasal steroids in our patient.

Antifungal chemotheraphy alone was previously thought to be largely ineffective due to its inability to cross the blood-brain barrier and reach fungal hyphae buried deep in fibrous tissue, and previous case reports have not shown any reduction in the disease bulk with chemotherapy alone. This was clearly not the case with our patient; however, how long we will need to continue treatment and whether she will ultimately still need surgery, remain unanswered questions.

Although a rare condition, in view of the high mortality, we think that this report emphasises that the continuing need for intranasal steroids should be assessed on a regular basis. Clinicians should also be alert to the possibility of an underlying condition, other than allergic rhinitis, in these patients.

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