Familial hydrocephalus

Familial cases of congenital hydrocephalus have often been reported and may result from distinct monogenic disorders or may be multifactorially determined. 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. By contrast, familial adult onset cases are unusual and the genetic basis is unknown. 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 his word retrieval skills and ability to work at speed.

Patient III-2 was a 47 year old woman with an 18 month 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 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. 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), although some families with otherwise typical X linked aqueduct stenosis do not show linkage to this locus. 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. 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). 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%.

We are aware of only one other report of familial adult onset, non-syndromal hydrocephalus. 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 bases 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 either alcohol myotoxicity or prolonged immobilisation. In the second patient damage was on the right, involving predominantly the upper trunk. Neuropsychological studies and the rapid complete recovery in our patients suggest that the primary pathology was focal demyelination causing conduction block, although there was also EMG evidence of denervation changes in the right C5-T1 dermatomes bilaterally with absent vibration and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers.

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 98.1 fl), compatible with chronic alcohol misuse.

Nerve conduction studies showed normal right upper limb sensory action potentials, which were only slightly reduced on the left. Upper limb motor conduction velocities 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 latency (7.9 ms) compared 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 and ulnar nerves, which showed no voluntary activity and frequent fibrillations and positive sharp waves in the right median and ulnar nerves.

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 no power (MRC grade 0) and no sensation (MRC grade 4) in the left C5-T1 dermatomes (C5-T1 myotomes) whereas the left involved mainly the upper part (C5–6 myotomes). This pattern of involvement, with sparing of the right arm, suggests that the site of injury was distal in the plexus and 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.

Electrophysiological studies in the right arm in the first patient showed reduced sensory amplitudes of the right radial (5 mV), median (3 µV), and ulnar (1.5 µV) nerves. Median and ulnar motor conduction velocities 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 the right but none on the left. 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, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and proprioception in his fingers.

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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. 1 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. 2 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 considerably 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. 3 The occurrence of bilateral plexopathy, as in our first patient, is unusual after closed trauma but has been reported after bilateral shoulder dislocations and postoperatively. 4

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, direct alcohol myotoxicity, 5 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. 6 Concurrent rhabdomyolysis and brachial plexus lesions have been described in the neurotoxic malignant syndrome 7 and alcohol intoxication. 8

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.

We thank Professor RAC Hughes and Dr MK Silver for valuable comments. ES is supported by the Special Trustees of St Thomas’ Hospital.

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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 and there is no evidence of its recurrence. 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 detected in 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. 1 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 channels, or anti-Tr antibodies. 2 Although the antibodies provide a diagnostic test for the associated tumours, it is generally thought that destruction of the Purkinje cells by autoreactive T cells is the major pathogenic mechanism, and previous reports suggest a lack of response to conventional immunosuppressive treatments. 3

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 as being normal, but serum anti-Yo antibody was positive by immunohistochemistry, confirmed by immunoblotting with purified antigen (DPC Biermann). 4 By 29 October 1996 there was marked gait ataxia, nystagmus, diplopia, dysphagia, cerebellar dysarthria, 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-

nent cells. The staging markers excluded further distant tumour localisation and the patient underwent an anterior pelvic exenteration with ileal conduit. Pathological examination disclosed a very rare endometrioid carcinoma, and confirmed extensive bladder involvement. The tumour seemed to arise from islands of endometriosis. Four cycles of adjuvant chemotherapy with carboplatinum and cyclophosphamide (respectively 300 mg/m² and 500 mg/m², day 1, every 3 weeks) were administered between April and September 1997. From then until the present time she has been treated monthly with cyclophosphamide at a dose of 1 g, day 1, every 4 weeks.

Four months after surgery a small vaginal tumour recurrence was diagnosed during a follow up gynaecological examination. Brain MRI demonstrated a slight progression of the cerebellar atrophy (figure B). The patient was subsequently admitted to our hospital for intracavitary boosts. At the last follow up examination (September 1998, 21 months from primary surgery) the patient had no evidence of disease, was able to read, to eat precut meals, to sit independently, and to walk short distances by using a wheeled walking support.

It is well recognised that microscopic ovarian cancer, only detected at laparotomy, can be associated with paraneoplastic cerebellar degeneration. 5 Malignant transformation of benign endometriosis is a well documented phenomenon, but it occurs most commonly in the ovaries, and cancer arising at extragonadal sites is a rare event. 6 In our patient we found an endometrioid adenocarcinoma located in the vesicovaginal septum, probably arising from islands of asymptomatic endometriosis and the delay in diagnosis was due not only to the small size but also to the unusual position of the tumour. We are not aware of any previous reports of paraneoplastic cerebellar degeneration associated with malignant transformation of benign endometriosis arising neither from the adnexa nor from the uterus.

A striking feature of this case was the improvement in neurological symptoms on the treatment of the tumour and subsequent immunosuppression. In most previous cases of paraneoplastic cerebellar degeneration, the early detection and removal of the tumour has not affected the neurological symptoms, 7 nor has there been improvement or slowed progression of the disease after immunosuppressive treatment. 8 There are only rare reports of successful immunosuppressive treatment with intravenous immunoglobulin therapy 9 or courses of cyclophosphamide. 10 In the second case, a very good response to cyclophosphamide was described but the sudden interruption of drug treatment led to a progressive worsening of symptoms, indicating that the clinical response was related to immunosuppression rather than a long term effect of tumour therapy.

In agreement with other authors 10 we think that the presence of anti-Yo antibody in patients with cerebellar symptoms warrants an aggressive diagnostic approach that must begin with careful clinical examination, then proceed with mammography, pelvic CT, and...
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) T2 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).
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 dysesthesia. 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. The territory supplied by the LPCA was defined after microanatomical studies on the vascularisation of the thalamus and previously reported CT or MRI templates.1–3 This territory comprises the choroid plexus of the lateral ventricle, the pulvinar, the posterior part of the dorsolateral nucleus, the lateral geniculate body, and the posterior part of the caudate nucleus. In some studies the hippocampus and the mesial temporal lobe were included as well.4–6 Based on those microsurgical and microangiographical studies, we determined that our patients had an isolated infarction in the territory of the LPCA.

Reports on patients with discrete LPCA infarction are few.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.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 Bogoaslausky have also stated that, although it occurs infrequently, its is specific to the lesion at the lateral geniculate body.5 The other signs were hemisensory disturbance, to a lesser extent neuropsychological...
dysfunctions such as aphasia, hemineglect, and memory disturbance, and more rarely hemiparesis.1,2

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 weeks. Although CT disclosed 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 in our patients. 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.3,4 Many anastomoses between the branches of the LPCA and anterior choroidal arteries 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 foramen of Monro.5

Infrequent occurrence of occlusion of the LPCA is presumed 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 prodromal signs of more serious brain complaints. 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.6 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) in 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 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, asymmetrical movements of his forehead, neck, proximal right arm, less severe of the left arm, and discreetly of the upper trunk, which was exaggerated 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 myoclonus and a discrete action tremor of both hands, all of which complies with the HEM criteria as outlined by Quinn.7 The remaining neurological status was unremarkable.

Four of the six children of the patient had possible myoclonus in a 61-year-old male patient with medically intractable HEM. 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 syndrome with regard to the rejected medical and social perspectives complicated the situation.

Extensive drug treatment trials (including monotherapy or combination therapy with the following agents: apomorphine, both oral and intrathecal baclofen, cefaloponic application of butulomazon toxin, carbamazepine, carbipidopa, clonazepam, clonidine, clozapine, fluphenazine, haloperidol, levothyroxin, levodopa, lithium, paroxetine, picaramet, pimodone, propranolol, tiapride, trihexyphenidyl, and valproate) had no effect on the myoclonic syndrome except for a mild improvement under diazepam.

Electroencephalography, including back averaging of the EEG activity preceding spontaneous jerks, polymyography, and somatosensory evoked potentials of the median nerve, cerebelar cortex and cutaneous liparum punc- ture did not show any abnormalities.

In this therapeutically hopeless situation, which was complicated by a latent suicidal syndrome secondary to the lacking therapeutic options, unilateral deep brain stimulation of the left VIM (essentially as outlined in Benabid et al) was performed after informed consent of the patient, for three reasons: Firstly, VIM stimulation is considered to be a “low risk” and effective therapy in patients with drug refractory essential tremor, which is also characterised by alcohol attenuation.8 Secondly, there are anecdotal reports on the improvement of myoclonic disorders by thalamotomy.9 Thirdly, in the absence of a therapeutic effect the electrode could have been removed or switched off.

Intraoperatively and in the subsequent 12 months deep brain stimulation (2.8 V, 130 Hz, 90 µs) produced a pronounced and persistent reduction of the jerks and the action tremor of the right arm and neck. However, exertion of the jerks of the neck and the trunk. The improvement could be postoperatively quantified by a roughly 65% decrease in myoclonus score (table).10 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.11 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.12 It is interesting to note that both diseases (HEM and essential tremor) may be improved by alcohol intake, which could hint at overlapping pathophysi- ological 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 myocloni.13 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, this 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 myoclonic sensitive site.14

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Myoclonus rating scores

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<th>Myoclonus at rest</th>
<th>Dis-ability score</th>
<th>Global assessment</th>
<th>Sum total</th>
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Myoclonus rating scores preoperatively, on and off deep brain stimulation (DBS) 10 months postoperatively, modified according to Truong and Fahn.10 Postoperative ratings were obtained by an observer (TT), who had been blinded to the stimulation status (”on” or ”off”).
Invasive intracranial aspergillosis secondary to intranasal corticosteroids

Intranasal corticosteroids are widely available; we describe a serious and previously unreported complication of their use. A 41 year old Asian woman was admitted acutely, 6 months after two generalised seizures. She described a 2 year history of anosmia, nasal stuffiness, and rhinorrhoea 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 cytoplasmic pattern (c-) antineutrophilic antibodies (ANCA) and perinuclear (p-) ANCA; an ECG; and chest radiography were all normal.

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 parasanal 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 parasanal 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 amphoterecin 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 mcg/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 sinusitis 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.

Amphoterecin 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 recently, stereotactic surgery, tried, from formal craniotomy to, more zole and amphotericin B.
dence suggests antagonism between itraconazole and amphotericin B. 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 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 chemotherapy 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.

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 amphotericin 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.
Neurostimulation of the ventral intermediate thalamic nucleus alleviates hereditary essential myoclonus

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doi: 10.1136/jnnp.67.3.415

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