LETTERS

Remission of progressive multifocal leukoencephalopathy in SLE after treatment with cidofovir: a 4 year follow up

Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection caused by human polyomaviruses such as the JC virus. It usually occurs as a severe complication of immunosuppression in patients with primary disorders of the immune system or secondary impairment of immune function, for example, after iatrogenic states of immunosuppression. PML usually takes a rapidly progressive course and advances to death within 1 to 18 months. Today, PML is mainly seen in AIDS, while previously it was typically found in patients with granulomatous, neoplastic, or infectious diseases. In granulomatous diseases particularly, PML is thought to occur as a result of iatrogenic states of immunosuppression, but it is also seen in patients aggressively treated with immunosuppressive agents for systemic lupus erythematosus (SLE).\(^1\) PML progresses to death in most of these patients even after withdrawing immunosuppressive therapy.\(^1\) Therefore additional therapy, aimed at supporting a more rapid restoration of immune function has been warranted.

Case report

We report a 40 year old woman diagnosed with SLE at the age of 20 years, based on four American College of Rheumatology criteria (erythema, arthritis, elevated antinuclear antibodies, and anti-dsDNA antibodies). Owing to neuropsychiatric lupus (the patient had experienced several psychotic episodes) with suspected vasculitic changes on cerebral magnetic resonance imaging (MRI), the patient had undergone 12 cycles of cyclophosphamide pulse therapy in 1995/96 followed by immunosuppressive treatment with mycophenolate mofetil in 1998, and azathioprine in 1999. Follow up cerebral MRI scans at that time were normal.

In January 2001, she again developed psychiatric episodes and an initially mild ataxia. She had repeatedly been put on low doses of corticoids but on no other immunosuppressive therapy during the previous 2 years. MRI revealed a lesion in the left cerebellum, which was hyperintense on T\(_2\) and hypointense on T\(_1\) weighted images. No lesions were seen in the cerebral hemispheres. Central nervous system manifestation of SLE was suspected, although the patient revealed only moderate signs of SLE activity (elevated anti-dsDNA antibodies, slightly decreased complement levels C3c and C4, increased erythrocyte sedimentation rate, but normal C reactive protein). There were no signs of severe immunosuppression; laboratory data showed normal levels of immunoglobulins and only slightly decreased lymphocytes, especially CD8+ T lymphocytes. The patient received two pulses of cyclophosphamide and high doses of corticosteroids to reduce the presumed cerebral SLE activity. In addition, she received antipsychotic medication.

While the psychosis was readily controlled by this treatment, the patient deteriorated neurologically. She developed a severe, disabling, rapidly progressive, left sided ataxia and was unable to walk. A control MRI of the brain in February 2001 revealed a progression of the lesion in the left cerebellum and a new lesion in the middle cerebellar peduncle. The lesions again presented as hyperintense on T\(_2\) and hypointense on T\(_1\) weighted images (fig 1A). Owing to the neurological deterioration after initiation of immunosuppression and the presentation of the lesions on MRI, PML was considered as a differential diagnosis. PCR revealed JC virus DNA in the cerebrospinal fluid (CSF). As cerebral SLE and PML require an intense but divergent therapy, a brain biopsy was obtained from the cerebellar lesion. Histo-pathology confirmed the diagnosis of PML. HIV tests were negative, T cell counts were normal, and signs of malignancy were lacking. Immunosuppression was discontinued. Because PML is usually lethal in patients with SLE even after omission of immunosuppression,\(^2\)\(^,\)\(^3\) we considered options for an active antiviral therapy. There was evidence from several reports in AIDS patients that cidofovir, an inhibitor of viral DNA polymerase, may reduce the size of PML lesions and thus prolong survival.\(^2\)\(^,\)\(^3\) Lacking therapeutic alternatives we therefore administered intravenous cidofovir (5 mg/kg body weight) at initially bi-weekly intervals, after obtaining informed consent. After the third and fourth cycle, the patient improved dramatically. She was able to walk again and only showed a mild residual ataxia. MRI revealed reduction of the lesions in the cerebellum and middle cerebellar peduncle with no new sites of active disease (fig 1B). PCR for JC virus DNA in the CSF was now negative. The treatment with cidofovir was continued with longer intervals (8–12 weeks). The therapy was generally well tolerated. After the fifth cycle, mildly increased creatinine levels were found. After one cycle with 4 mg cidofovir/kg body weight, kidney function was quickly normalised and the following cycles could be administered at the initial dosage. Fourteen months after initiation of the treatment, the patient had completed the 10th cycle of therapy with no signs of disease activity. MRI scans of the brain showed further regression of the lesion with no signs of

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**Figure 1** T2 weighted MRIs showed (A) extended white matter lesions in the middle cerebellar peduncle and left cerebellum, February 2001; (B) regression of the lesions after four cycles of cidofovir, July 2001; and (C) further regression with residual gliotic lesions, July 2004.
active inflammation (not shown), and cidofovir treatment was discontinued. At present, (4 years follow up after the first treatment and 2.5 years after the last cycle of cidofovir), the patient still shows no signs of disease activity. CSF PCR for JC virus DNA remains negative, and a recent MRI scan of the brain was unchanged (fig 1C). As of March 2005, the patient lives at home, is able to walk, and is independent.

Discussion

We report a patient with SLE who survived PML after treatment with cidofovir and discontinuation of immunosuppression. First evidence for possible efficacy of cidofovir in the treatment of PML in a patient with SLE was presented in a case report. Discontinuation of immunosuppression and treatment with cidofovir resulted in reversal of JC virus positivity and stabilisation of MRI lesions. However, the patient died due to serious kidney failure.

It remains unclear whether the improvement in both patients was induced or supported by cidofovir or whether it could have been acquired by discontinuation of immunosuppression alone. However, patients with PML in SLE usually die after discontinuation of immunosuppression alone. Interestingly, our patient did not show signs of severe immunosuppression at the point of manifestation of PML. These observations may suggest a predisposition of patients with SLE to PML that may not be explained by their immunosuppression alone.

We conclude that cidofovir should be offered to SLE patients developing PML due to immunosuppression in addition to withdrawal of immunosuppressive therapy, as death is likely without antiviral therapy. Cidofovir may be effective against PML caused by non-AIDS related states of immunosuppression.

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References


Dramatic improvement in non-AIDS related progressive multifocal leucoencephalopathy

Progressive multifocal leucoencephalopathy (PML) is a rare disorder occurring when a strain of papovavirus (JC virus) infects the central nervous system. It results in a generally quick and fatal outcome. It is associated with cell mediated immune deficient diseases but some few cases were reported in immunocompetent hosts. Since 1981, it has been commonly associated with AIDS. In AIDS, the long term survival without real neurological improvement has been reported in patients treated with highly active antiretroviral therapy (HAART). Few cases of improvement with cidofovir or cytosine arabinoside have been described in AIDS related or non-AIDS related PML, but in larger trials in AIDS related PML, no clinical benefit was found. As a whole, the treatment of this progressive demyelinating disease remains controversial, in particular in the rare cases of non-AIDS related PML. We describe a patient with an underlying haematological disease, without clear cut immune cell deficiency, who developed rapidly progressive PML. The patient showed clinical, virological, and imaging improvement when treated with an association of intravenous and intrathecal cytosine arabinoside combined with intravenous cidofovir.

A 48 year old man presented with progressive multiple leuкоencephalopathies, hepatosplenomegaly, weight loss, and blood cell count abnormalities. Fine needle aspiration cytology of lymph nodes with previously diagnosed marginal zone B cell lymphoma. There was also bone marrow and blood proliferation. A few weeks after the diagnosis, the patient noticed rotatory vertigo and visual problems suggestive of a right homonymous hemianopia. Because of dissemination and the large tumour mass, chemotherapy (CHOP: cyclophosphamide, doxorubicin, vincristine and prednisone) was started one month after the onset of neurological symptoms. Following the first course of chemotherapy, his neurological symptoms worsened, and language disorders appeared. No real immunodeficiency was shown—the absolute CD4 count was 549/mm³ (normal 500–1000) and there was discrete hypogammaglobulinaemia (4.6 g/l; normal 5–12). The patient was HIV and HTLV1 seronegative. Cerebral magnetic resonance imaging showed a non-contrast-enhancing lesion in the left occipital white matter (fig 1A).

Cerebrospinal fluid (CSF) analysis was normal apart from a moderate increase in CSF protein (0.7 g/l). Suspicions of PML was confirmed by a positive polymerase chain reaction (PCR) for JC virus DNA. Chemotherapy was discontinued but neurological symptoms worsened rapidly and the patient developed a right hemiplegia, global aphasia, alexia and agraphia, apraxia, and cortical blindness concurrently with MRI deterioration (fig 1B).

Three months after his first symptoms, treatment was started with intravenous aracine 2 mg/kg/d for five days every three weeks, combined with intrathecal aracine (30 mg) weekly and intravenous cidofovir 5 mg/kg/d once every two weeks. The main adverse effect of this treatment was grade IV bone marrow toxicity, inducing spacing in the rhythm of treatment administration. One week after treatment onset, the patient stabilised and after one month began improving. After three months, he had recovered completely from his hemiplegia, and had significant improvement in his aphasia and cortical blindness. Right hemianopia and minor alexia without agraphia persisted. This dramatic improvement was confirmed by cerebral imaging, by the absence of JC virus DNA detection in CSF, and by a specific response of CD4+ T cells against JC virus. We decided to continue subcutaneous aracine 2 mg/kg/d for five days monthly and intravenous cidofovir twice weekly. Fifteen months after treatment onset, the patient was aphalamic and cerebral edema had almost disappeared, suggesting individual beneficial effects of these drugs. To our knowledge, these drugs have not been used in combination before. In comparison to previous reports, the present case suggests a more rapid and prolonged effect of this therapeutic combination than with either aracine or cidofovir treatment alone. This efficacy may be explained by a synergy between the drugs and by their different routes of administration. We thought that the improvement in our patient was related to the treatment because there was a temporal link with treatment onset and because of the radiological findings. However, cases of PML stabilising without specific treatment have usually been associated with an inflammatory response to the virus, indicated by contrast enhancement on imaging). The main limiting factor of this treatment was bone marrow toxicity. During the periods of immune deficiency, the patient’s neurological condition did not deteriorate, suggesting that PML occurrence in this patient was linked to a qualitative defect of his cells rather than to their absolute count. Immunological studies have shown that JCV specific CD4-T cell responses play a

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major role in the control of PML development; for example, in one study 9 specific T cell response was demonstrated in a series of 14 patients before treatment, whereas nine of 10 survivors recovered specific immunity. Our patient thus probably had no specific T cell response against JCV before treatment, but recovered a moderate but significant response while on treatment, possibly explaining PML regression. Such a restoration of T cell response can be achieved by HAART in AIDS. This observation suggests that the combination of aracantine and cidofovir could have had a similar action in restoring a specific T cell response against JCV in our patient. A direct effect of these nucleosidc analogues against JC virus DNA may also explain the rapid clinical and radiological improvement in our patient.

Despite its substantial bone marrow toxicity, this observation suggests that the new association of intrathecal and intravenous aracantine with intravenous cidofovir could be useful in patients with PML, particularly those with an underlying haematological disease. It is worth noting that bone marrow toxicity did not lead to deterioration of the neurological status of the patient, supporting the view that a specific defect in CD4 function is more important than the absolute CD4 count. The dramatic improvement observed in our patient warrants further prospective studies testing this drug combination.

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References


Diaphragmatic paralysis and respiratory failure as a complication of Lyme disease

There have been five recorded cases of diaphragmatic paralysis as a complication of neuroborreliosis. Here we report another case of Lyme meningoradiculitis, caused by an identified tick, leading to bilateral diaphragmatic paralysis with an abbreviated course on treatment.

Case report

A 59 year old female presented with a recent history of abdominal pain and falls because of a weakness in her right leg. She had been complaining of flu-like symptoms with twitches in her back and pain in her right side for a month. She gave a history of recently having been bitten by ticks whilst gardening. There was no history of any recent rash. On the day of presentation, she complained of a mild cough, reduced appetite, abdominal distension, constipation, and dysuria. She was a lifelong smoker but was generally healthy.

On presentation her blood pressure was 206/107 mm Hg. There was some epigastric tenderness. She had bruising on her right leg that she associated with the falls. The chest radiograph on admission was unremarkable. Abdominal x ray showed dilated loops of small bowel and a loaded colon. Her only blood abnormality was hyponatraemia at 121 mmol/l. She was admitted for further investigations.

On day 3 of admission she became increasingly short of breath and on examination had decreased bibasal air entry. On day 4 her respiratory rate was 25/min and arterial blood gases (ABG) demonstrated hypoxaemia but adequate ventilation with P 7.51, P02 6.7 kPa, and Pco2 4.7 kPa. Her chest radiograph showed left basal changes. On day 5 her P02 had risen to 6.8; she was admitted to the intensive care unit and non-invasive ventilatory support was commenced. She had a decreased inspiratory pressure and a decreased vital capacity. She was noted to have absent gag reflex and poor swallowing and on day 6 was intubated to protect against aspiration pneumonia. The patient remained fully conscious and co-operative, easily triggering the ventilator but requiring significant inspiratory pressure support of 20 cm H2O.

Neurological examination demonstrated right hip and knee extensor weakness (2/5), absent right knee jerk, and a loss of sensation on her left lateral thigh. Because she lived in a known endemic area we thought about Lyme disease, but we also considered differential diagnoses such as Guillain-Barre syndrome, listeriosis, and acute polyomylitis. We commenced treatment with doxycycline whilst awaiting the results of further investigations. Around this time the patient indicated a small black lesion on her upper abdomen that was removed and on closer examination was identified as tick mouth-parts (fig 1).
In all previous cases of diaphragmatic palsy as a complication of Lyme disease, either the patient reported dyspnoea or hypoxia was noted on ABG. The diagnosis of phrenic nerve palsy was made by the following methods: hemidiaphragm elevation, fluoroscopic screening of diaphragmatic movements, or electrical stimulation of phrenic nerves. Our patient had a lymphocytic meningitis with sensory and motor neuropathies including bilateral phrenic nerve palsies. Diaphragmatic paralysis due to Lyme disease was diagnosed on the basis of clinical features, chest ultrasonography, the presence of the tick head, and serology indicating a recent infection with *B. burgdorferi* as well as a rapid response to antibiotic therapy.

The clinical diagnosis of Lyme disease may be supported by serologic testing. *B. burgdorferi* antibody tests may be negative in early infection, but patients are usually seropositive at or shortly after presenting with neurological symptoms. In some patients, antibodies against *B. burgdorferi* may be detectable in CSF slightly earlier than serum. Culture and *B. burgdorferi* deoxyribonucleic acid detection using polymerase chain reaction may also be used but were not in our case.

The three patients reported in the literature with respiratory failure caused by neuroborreliosis were ventilated for 3 months, 1 month, and 13 months, respectively, whilst our patient required ventilation for only 22 days. We speculate that early recognition of the possibility of Lyme disease and appropriate treatment shortened our patient’s acute illness.

In conclusion, it is important to consider Lyme disease in the differential diagnosis of acute respiratory failure – with or without erythema migrans.

References


Benign paroxysmal positional vertigo (BPPV) predominantly affects the right labyrinth

We read with great interest the article “Benign paroxysmal positional vertigo predominantly affects the right labyrinth”, by M von Brevern et al., which prompted us to review our data of the last 10 years (1995–2004). A total of 661 patients, referred to the ear, nose, and throat department or to the neurology department, were diagnosed as having benign paroxysmal positional vertigo (BPPV) in its various forms. The pathology was located in the posterior canal in 477 patients, in the horizontal canal in 142, and in the anterior canal in 22. Multiple canals were affected in 20 patients (table 1).

The right ear was 1.50 times more frequently involved than the left. The predominance of the right ear was seen in all types of BPPV (table 1).

Hence, our data confirm the preponderance of right sided BPPV. The predilection of right sided BPPV was seen in all variants. Horizontal canal BPPV was observed in 22%, confirming our previous data. The apogeotropic form should not be considered as a rarity as it contributes to 23% of horizontal canal BPPV in our series and 38% in the series of Casani et al.

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**Table 1** Laterality of the affected ear in different forms of BPPV

<table>
<thead>
<tr>
<th>Horizontal canal</th>
<th>No. of patients</th>
<th>Posterior canal</th>
<th>Geotropic</th>
<th>Apogeotropic</th>
<th>Anterior canal</th>
<th>Multiple canals</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right n = 379</td>
<td>266</td>
<td>61</td>
<td>23</td>
<td>15</td>
<td>14</td>
<td>57%</td>
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<tr>
<td>Left n = 253</td>
<td>185</td>
<td>48</td>
<td>10</td>
<td>7</td>
<td>3</td>
<td>38%</td>
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<tr>
<td>Bilateral n = 29</td>
<td>26</td>
<td>72%</td>
<td>77%</td>
<td>22%</td>
<td>3%</td>
<td>100%</td>
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<td></td>
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<td>23%</td>
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<td>Total n = 661</td>
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Aciclovir induced posterior leucoencephalopathy

Aciclovir is an extremely effective agent for the treatment of herpes simplex encephalitis and varicella–zoster infections in immunocompromised individuals. Encephalopathy induced by aciclovir is an infrequent but well recognised adverse effect of aciclovir. The predisposing factors to aciclovir induced encephalopathy (AIE) include age, acute or chronic renal failure, and other neurotoxic drugs. Tremors (40–58%), disorientation (40–90%), agitation (22–38%), hallucinations (25%), and delirium (25%) are common presentations of AIE, whereas seizures (10%), cerebellar ataxia (11%), sensory symptoms (9%), speech disorders (9%), fever (10%), and cranial nerve palsies (0%) are much less frequent. The supportive diagnostic criteria for AIE include a temporal association between the symptoms and aciclovir use, as well as acellular cerebrospinal fluid (CSF) in cases without herpes simplex or varicella–zoster encephalitis. In the majority of cases symptoms develop within 72 hours of starting aciclovir treatment, although up to 120 days has been reported. The clinical recovery may take several days (five days in 57% of cases) following discontinuation of aciclovir. The EEG typically shows diffuse slow wave activity rather than focal abnormalities.

The radiological features are not well described in AIE. Case reports have identified multifocal white matter signal abnormalities involving the cerebellum, pons, and periventricular region as well as evidence of vascular encephalopathy on MRI. We report a case of AIE with MRI features consistent with posterior leucoencephalopathy with clinical and radiological improvement following the discontinuation of aciclovir, along with raised serum and CSF concentrations of aciclovir and 9-carboxymethoxymethylguanine (CMMG), the main metabolite of aciclovir.

Case report

A 47 year old women with a 15 month history of cANCA+ glomerulonephritis and chronic end stage renal failure (serum creatinine 957 μmol/l), managed on continuous ambulatory peritoneal dialysis, azathioprine (100 mg/day), and prednisolone (10 mg/day), developed a mid-thoracic varicella–zoster rash. She was given a reduced dose of intravenous aciclovir (250 mg three times daily). Within 48 hours she became agitated, developed visual hallucinations and drowsiness (Glasgow coma scale (GCS): overall 6; eye 1, motor 4, verbal 1). On admission to the intensive care unit she was apyrexial, the highest blood pressure recorded was 180/104, while agitated, and fundoscopy was unremarkable. The tendon reflexes were exaggerated, with extensor planter responses. Oculolepalic and corneal reflexes as well as spontaneous respiration were present.

Laboratory investigations showed a haemoglobin of 9.7 g/l, white cell count 5.8 x 10⁹/l, urea 22 mmol/l, ESR 90 mm/h, C reactive protein 27 mg/l, albumin 22 g/l, ammonia 10 mmol/l, and cANCA negative. Computed tomography of the head, done immediately after she became obtunded, showed posterior white matter hypodensities. The lumbar CSF contained no white cells and four red blood cells per mm³, with a protein of 0.63 g/l and a CSF/serum glucose ratio of 3.96.4. The opening pressure was 41 cm. CSF cultures, including culture for acid fast bacilli, were negative. CSF testing by polymerase chain reaction was negative for herpes simplex virus I and II, varicella–zoster virus, cryptococcal antigen, and JC virus. An EEG showed excessive slow wave activity. Magnetic resonance imaging (MRI) of the brain and an MR venogram (done after five days on aciclovir) showed symmetrical posterior white matter changes predominantly in the occipital and parietal lobes (fig 1A and 1B) without evidence of venous sinus thrombosis, gadolinium enhancement, or matched defects in diffusion weighted images.

On admission, azathioprine was stopped and intravenous methylprednisolone (300 mg/day for three days) was started for presumed CNS vasculitis. There was no improvement 72 hours after this treatment and after eight days of aciclovir. Aciclovir was discontinued when AIE was suspected, and peritoneal dialysis was maintained. Within 48 hours of discontinuation of aciclovir, the GCS improved (eye score 3, motor score 6, verbal score 3) and neurological examination showed bilateral upper limb postural tremor, which resolved over 24 hours. The Adenbrook’s score was 77/100. Repeat MRI (fig 1C, 1D) showed a significant improvement. Analysis of aciclovir and CMMG levels in the serum and CSF showed high values, at levels generally associated with neurotoxicity. The serum aciclovir and CMMG concentrations were, respectively, as follows:

- 5 days post-aciclovir initiation: 34.9 μmol/l and 91.7 μmol/l;
- 6 days post-aciclovir: 35.4 μmol/l and 148.3 μmol/l;
- 7 days post-aciclovir: 17.2 μmol/l and 141 μmol/l.

The CSF aciclovir and CMMG concentrations four days post-aciclovir initiation were, respectively, 5.99 μmol/l and 2.25 μmol/l (CMMG levels are not generally associated with neurotoxicity unless there is neurotoxicity (Hedlund A (submitted for publication)), supporting a diagnosis of AIE.

Comment

The clinical presentation of our patient, her rapid recovery, and the CSF and EEG findings are characteristic of AIE. The CSF findings are not typically associated with herpes simplex or varicella–zoster encephalitis. The lack of significantly raised blood pressure or papilloedema excludes hypertensive posterior leucoencephalopathy. ANCA+ vasculitis causing posterior leucoencephalopathy has been reported but only in the presence of severe hypertension. AIE, an infrequent but well recognised adverse effect of aciclovir, has until now been diagnosed.
mainly on clinical features. Factors predisposing to AIE include age, acute or chronic renal failure, and other neurotoxic drugs. The diagnosis is facilitated by analysis of aciclovir and CMMG in serum and CSF. In cases with renal failure, the half life of aciclovir extends from 3 to 20 hours and as a result aciclovir is metabolised to CMMG by alcohol and acetaldehyde dehydrogenases. At present, reliable dose recommendations are not available for patients with renal failure.

In a case study of 93 patients, mainly with renal failure, we found mean (SD) serum aciclovir concentrations of 21.0 (30.7) μmol/l (in 49 patients with neurotoxicity) and 7.2 (6.7) μmol/l (in 44 asymptomatic patients receiving aciclovir), while CMMG concentrations were 34.1 (39.4) μmol/l in patients with neurotoxicity and 4.7 (4.7) μmol/l in asymptomatic patients. CMMG levels of >10 μmol/l seemed to be associated with neurotoxicity. A high CMMG level is a strong predictor of AIE and the value of measuring CMMG are being undertaken at Karolinska Institutet, Stockholm, Sweden.

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References

Normal memory and no confabulation after extensive damage to the orbitofrontal cortex

Subarachnoid haemorrhage caused by the rupture of an anterior communicating artery (ACoA) aneurysm is often followed by amnesia, confabulation, and personality change including social decision making.2-4 However, the regions responsible for each symptom have not been determined conclusively. We describe a patient who showed personality change, but neither memory impairment nor confabulation, after extensive damage to the bilateral orbitofrontal cortex. Our present study provides conclusive evidence as to whether or not damage to the orbitofrontal cortex alone cannot cause amnesia and confabulation.

Case report

The patient was a 45 year old, right handed man with a 16th grade education. He was not an aplanetic person and worked hard as a manager before the onset. His past medical history was unremarkable and he had no medication. He had sudden onset of headache, became unconscious, and was admitted to an emergency hospital. Brain computed tomography showed a subarachnoid haemorrhage in the cisterns around the brainstem, longitudinal cerebral fissure, and bilateral Sylvian fissure caused by a ruptured aneurysm of the ACoA. On the same day, he underwent an operation to repair the ruptured aneurysm. There were slight brain oedema and vasospasm (four to 10 days). He did not become delirious, agitated, or suspicious. He had had no psychiatric disorders. He took meningin each day to prevent secondary seizures. His family noted that he showed mild anterograde amnesia, which improved over two months, but no retrograde amnesia.

The patient was discharged home after three months. He began working again as a manager at his company, but could not do his job as well as before the onset. Twenty months after the onset, he was admitted to our hospital because of his problems.

On admission, the patient was fully alert and oriented. General physical and neurological examinations were unremarkable. During his stay in hospital, he had no problems communicating with others, kept his appointments and could find his way around the hospital. His family and his superior at his company reported that his personality had changed since the onset of his illness (in terms of lack of concern for others including his family, his appearance, and his future; the loss of spontaneity, initiative, and self motivation; disinhibition; and rigidity of thought) generally agreed in the literature to be the result of dysfunction of the frontal lobe, particularly the orbitofrontal cortex.

Importantly, the patient showed no memory deficit. Damage to the basal forebrain without damage to the frontal lobe causes amnesia.2-4 With regard to the orbitofrontal cortex, it has been argued that destruction of this region is not necessary for the development of amnesia or basic cognitive function.2,4 However, there has so far been no conclusive evidence as to whether or not damage to the orbitofrontal cortex alone (especially the medial caudal part of it) gives rise to amnesia.3 Our present study provides evidence that damage to the orbitofrontal cortex alone does not result in amnesia and therefore strengthens the notion that the basal forebrain is one of the crucial sites for human memory.

It should be noted that the assessment of memory in our present study is based on standardised tests. This means that is not measurable using these standardised tests (for example, temporal context memory) may be related to the function of the orbitofrontal cortex. We cannot draw a strong conclusion regarding frontal lobe function, because we did not use tests sensitive to damage to the ventromedial prefrontal cortex (for example, the Iowa Gambling Task).2-4

The patient showed no confabulation. Damage to the orbitofrontal lobe alone might not be sufficient for confabulation to be
Frontal lobe damage has been reported. Patient with confabulation and amnesia after development of confabulation. In contrast, lesions and amnesia are necessary for the manifestation of confabulation. Brain involvement or basal forebrain imaging examination are needed to determine neuroanatomical and neuropsychological sequelae. Further studies involving comprehensive neuropsychological and magnetic resonance imaging examination are needed to determine whether both frontal and basal forebrain involvement or basal forebrain involvement alone is required for the manifestation of confabulation.

**Figure 1** (A) Sagittal and (B) coronal T2 weighted magnetic resonance images showing extensive lesions in the bilateral orbitofrontal cortex. The core structures of the basal forebrain (medial septal nucleus, vertical and horizontal limb nuclei of Broca’s diagonal band, and nucleus basalis of Meynert) were not damaged. In the sagittal sections, the images in the upper row show the right hemisphere and those in the lower row show the left hemisphere. In each row, the first, second, and third images are 15 mm, 10 mm, and 5 mm away from the longitudinal cerebral fissure, respectively. In the coronal sections, the left side of the image corresponds to the right side of the brain. In the upper row, the first, second, and third images are 0 mm, 5 mm, and 10 mm rostral from the anterior commissure. In the lower row, the first, second, and third images are 20 mm, 30 mm, and 50 mm rostral from the anterior commissure.

**References**


**Adult onset SSPE: experiences in West Yorkshire over a 12 month period**

Subacute sclerosing panencephalitis (SSPE) is a rare delayed complication of measles virus infection in infancy. It is characterised by behavioural changes, myoclonus, cognitive impairment, visual disturbance, pyramidal and extrapyramidal signs, and ultimately coma leading to death. Typically, SSPE presents in childhood or early adolescence, but adult onset cases are recognised. Widespread measles immunisation in the UK has led to a dramatic fall in the incidence of SSPE in children, leading to the disease almost becoming extinct. However, a latent disease pool remains and cases may still come to the attention of adult neurologists, as borne out by our recent experience in West Yorkshire.

**Case histories**

An 18 year old man gave a three week history of blinking episodes lasting approximately one second, associated with a brief head jerk. These were not present in sleep. Examination revealed myoclonic jerks involving the neck associated with blinking. Initial electroencephalograms (EEGs), blood tests, and a magnetic resonance imaging scan were normal. Several anticonvulsant medications failed to suppress the jerks, which by four weeks had spread to the legs, causing unsteadiness. The mini mental test examination score at this stage was 26 of 30. He began to deteriorate rapidly, with disorientation, blunted affect, dystonic posturing of the left arm, bradykinesia, and rigidity. Cerebrospinal fluid (CSF) was sent for analysis of 14-3-3 and S-100 proteins, which were negative. A further EEG, nine weeks after onset, demonstrated high voltage periodic complexes occurring every 10 seconds, consistent with SSPE. CSF and serum measles titres were raised at 35110 mIU/ml and 152930 mIU/ml, respectively. The CSF to serum albumen ratio was 1:300, consistent with intrathecal antibody synthesis. There was no past history of measles, although he had received MMR (measles mumps rubella) immunisation at age 9. Oral inosiplex (isoprinosine) and subcutaneous interferon 2b were started and an Ommaya reservoir was inserted to administer intraventricular interferon 2b. By this stage, the myoclonus had subsided but he had gaze paresis, mutism, widespread spasticity, and required gastrostomy feeding. He received intraventricular treatment for six weeks before reservoir infection necessitated its removal. His condition plateaued and he was maintained on inosiplex alone. Eventually, he was discharged home in a dependent state.
A 25 year old woman presented to her general practitioner complaining of impaired concentration, mood swings, disturbed sleep, and myoclonic jerks. One month later, she had noticed a fine tremor in both hands and occasional spasms affecting her right foot. Her concentration was worse and she mentioned word finding difficulties. She also had a trend to stagger and fall. She was seen by a psychiatrist and somatisation was initially suspected. Later, she was referred to a neurologist. He noted that she had been acting oddly—for example, being found by her mother in a bath of cold water. Neurological examination was normal except for a mini mental test examination score of 20 of 30 with a child-like effect and slurred speech. A magnetic resonance imaging scan was unremarkable. She continued to deteriorate, developing right sided myoclonus. By this stage, she was unable to perform simple tasks, such as washing, and was aware of crawling sensations all over her body. Six months after her first presentation she had an EEG. This revealed repetitive complexes occurring every four to six seconds, often associated with a myoclonic jerk and consistent with SSPE. CSF analysis confirmed oligoclonal bands present in the serum, which were positive for measles antibody antigen by immunoblotting. She had contracted measles at age 11 months. She was started on oral piracetam and inosiplex, along with intermittent intravenous infusions of midazolam and diamorphine for symptom control, and nasogastric feeding was started. Her condition subsequently stabilised and she was discharged to a children’s hospice.

Discussion

The estimated incidence of SSPE in recent developed nations is 1/10 million of the population under the age of 20. The occurrence of two adult cases in the small region of West Yorkshire (population two million) within a few months of one another is remarkable. Although probably a chance finding, our experience emphasises the need for continued surveillance in populations where measles is no longer endemic. In theory more adult onset SSPE cases could present to neurologists in the future. This is because slow central nervous system spread of the virus over many years leaves open the possibility of SSPE to present in later life, decades after population eradication of measles. In addition, routine immunisation has led to a shift in the incidence of measles towards unvaccinated children age <1, who are at a higher relative risk of developing SSPE in later life after a longer incubation period.1,2 Recently, there has been an increase in the number of measles outbreaks after a decline in the uptake of the combined MMR immunisation because of safety fears.3

In our patients, SSPE was not initially suspected by the general practitioners and she was only subsequently diagnosed by a consultant neurologist. It is possible that this case and other presentations of SSPE in adults are an important reminder to general practitioners that measles may occur in adults and that such cases should be considered before other more common diagnoses are made. Furthermore, as SSPE is a rare but serious condition, it is important that clinicians should consider SSPE in adults presenting with neurological manifestations of unknown cause. However, we do not think that SSPE should be widely considered a diagnostic consideration in cases of adult encephalopathy because the risk to the general population is very low, even in the developed world where mass immunisation is common. In our hands, intravenous interferon x2b treatment for six months (35% v 34%).

There is no curative treatment for SSPE. Trials have been complicated by variable natural history and spontaneous long remissions of the disease, although it is eventually fatal (median survival, three years). One study demonstrated similar response rates among patients randomised to inosiplex, with or without intravitreous interferon x2b treatment for six months (35% v 34%).3 However, these figures were substantially higher than historical remission rates of between 5% and 10%. In our hands, intravitreous interferon was associated with initial worsening of encephalopathy and pronounced hyperpyrexia, possibly the result of chemically induced meningitis, and reservoir infection was a further complication. In both patients, disease appeared eventually to stabilise after antiviral treatment, particularly in patient 1, in whom rapid progression at onset was suggestive of fulminant SSPE, usually fatal within three months.

Prevention seems to be the best approach, with mass immunisation leading to a drastic reduction in reported cases of measles and associated complications. However, our experience suggests that SSPE in adults should not be forgotten. Clinicians should remain vigilant for this devastating disease.

References


LATERALITY OF SYMPTOMS IN PATIENTS ADMITTED TO A STROKE UNIT WHO HAD A DISCHARGE DIAGNOSIS OF A PSYCHIATRIC CONDITION

Some psychiatric conditions produce symptoms that can mimic an acute neurological disease, including stroke.5 In a study of stroke patients in the Western Cape region of South Africa, Stone et al concluded that it is not certain that the functional symptoms are more common on the left side than on the right side of the body. They found a preponderance of the left hemisphere in 39% of patients with psychiatric diseases compared with 15% in patients with stroke. In that meta-analysis, they did not find a significant difference in lateralisation between patients with and without psychiatric disease.

DISCUSSION

In this study, 1.5% of the patients admitted to a stroke unit presented symptoms unexplained by stroke or other neurological disease and fulfilling the criteria for psychiatric diagnosis. Contrary to our previous studies, our results did not show a preponderance of left sided symptoms. In a meta-analysis of all studies describing patients with medically unexplained symptoms, Stone et al concluded that it is not certain that the functional symptoms are more common on the left side than on the right side of the body. They found a preponderance of the left hemisphere in 39% of patients with psychiatric diseases compared with 15% in patients with stroke. In that meta-analysis, they did not find a significant difference in lateralisation between patients with and without psychiatric disease. The younger median age and female preponderance of patients with psychiatric conditions mimicking a stroke reflects the demographic characteristics of somatoformal...
and anxiety disorders. One interesting finding was the high frequency of vascular risk factors, which increases diagnostic uncertainty and could explain the admission to the stroke unit. A major limitation of our study is the lack of use diffusion magnetic resonance imaging to exclude definitively the unlikely possibility of a concomitant ischaemic lesion.

We conclude that left sided laterality of symptoms cannot be used as a tool to establish a psychiatric diagnosis in patients with chronic inflammatory demyelinating polyneuropathy and Charcot-Marie-Tooth disease, despite one image being rotated by 90 degrees; the illustration of text relating to genetically defined young onset spinal muscular atrophy with an elderly man who appears to have progressive muscular atrophy; and the spelling of fascioscapulohumeral (sic) dystrophy.

The authors point out that “no other book provides a complete overview in a structured and easily comprehensive pattern supported by figures and pictures”. There are, however, a number of excellent books related to diseases of muscle and nerve, some providing a wider range of clinical and pathological illustrations and a more critical review of clinical presentation, diagnosis, and treatment. At the present time the role claimed by this book remains unfilled.

R W Orrell

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### Table 1 Differences between patients with a psychiatric diagnosis and with left and right sided symptoms

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
<th>Left group</th>
<th>Right group</th>
<th>p value</th>
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<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age (median)</td>
<td>41.0</td>
<td>41.0</td>
<td>38.0</td>
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<tr>
<td>Sex (F/M)</td>
<td>28(80.0)/7(20.0)</td>
<td>9 (81.8)/2 (18.2)</td>
<td>4 (29.4)/4 (70.6)</td>
<td>0.66†</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Somatiform disorders</td>
<td>25 (71.4)</td>
<td>9 (81.8)</td>
<td>10 (90.9)</td>
<td>-</td>
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<td>Somatisation disorder</td>
<td>14 (40.0)</td>
<td>4 (36.4)</td>
<td>7 (63.6)</td>
<td>1.00†</td>
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<tr>
<td>Conversion disorder</td>
<td>11 (31.4)</td>
<td>5 (45.5)</td>
<td>3 (27.3)</td>
<td>-</td>
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<tr>
<td>Anxiety disorders</td>
<td>7 (20.0)</td>
<td>2 (18.2)</td>
<td>1.9 (91)</td>
<td>-</td>
</tr>
<tr>
<td>GAD</td>
<td>4 (11.4)</td>
<td>1 (9.1)</td>
<td>1 (9.1)</td>
<td>-</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>3 (8.6)</td>
<td>1 (9.1)</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Other</td>
<td>3 (8.6)</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Paresis</td>
<td>26 (74.3)</td>
<td>9 (81.9)</td>
<td>12 (85.7)</td>
<td>1.00†</td>
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<tr>
<td>Total</td>
<td>10 (30.6)</td>
<td>-</td>
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<tr>
<td>Right</td>
<td>12 (35.6)</td>
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<td>-</td>
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</tr>
<tr>
<td>Bilateral</td>
<td>4 (11.4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Involuntary movements</td>
<td>1 (2.9)</td>
<td>0</td>
<td>1 (7.1)</td>
<td>1.00†</td>
</tr>
<tr>
<td>Total</td>
<td>10 (28.6)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Right</td>
<td>12 (35.6)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bilateral</td>
<td>4 (11.4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Sensory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17 (48.6)</td>
<td>4 (36.4)</td>
<td>7 (50.0)</td>
<td>0.69†</td>
</tr>
<tr>
<td>Left</td>
<td>4 (11.4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Right</td>
<td>7 (41.2)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bilateral</td>
<td>6 (35.3)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Visual</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>14 (38.5)</td>
<td>1 (9.1)</td>
<td>2 (14.3)</td>
<td>1.00†</td>
</tr>
<tr>
<td>Right</td>
<td>14 (46.2)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bilateral</td>
<td>3 (8.6)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>19 (54.3)</td>
<td>3 (27.3)</td>
<td>9 (64.3)</td>
<td>0.15†</td>
</tr>
<tr>
<td>Left</td>
<td>11 (31.4)</td>
<td>11</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Right</td>
<td>14 (40.0)</td>
<td>-</td>
<td>2 (14.3)</td>
<td>-</td>
</tr>
<tr>
<td>Bilateral</td>
<td>10 (28.6)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* p value for Mann-Whitney U test (left group/right group); † p value for x² test (left group/right group).

GAD, generalised anxiety disorder.

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### REFERENCES


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**BOOK REVIEW**

**Atlas of neuromuscular diseases**


This book it titled an “atlas” and subtitled “a practical guideline”. I had the expectation of a heavily illustrated book of neuromuscular conditions with annotations. The book has been designed as a comprehensive coverage of disorders of peripheral nerve (including cranial nerves), muscle, neuromuscular junction, and motor neuron. Each condition is outlined in note form, with particular emphasis on causation—which can be lengthy and repetitive. The style of the text is abbreviated and can be difficult to read. The précis can be misleading or inaccurate at times. A useful list of references is given.

It is not clear to me to whom this book would appeal. The text is probably too comprehensive and potentially misleading or confusing for students, and does not add much to those already informed. The number and quality of the illustrations is disappointing. I had expected more clinical illustrations of the conditions described. As a practical guideline it is not helpful and in particular the therapeutic suggestions are too abbreviated, incomplete, and uncritical for clinical application. Problems to be addressed in the next edition include the use of the same nerve biopsy illustration for patients with chronic inflammatory demyelinating polyneuropathy and Charcot-Marie-Tooth disease, despite one image being rotated by 90 degrees; the illustration of text relating to genetically defined young onset spinal muscular atrophy with an elderly man who appears to have progressive muscular atrophy; and the spelling of fascioscapulohumeral (sic) dystrophy.

The authors point out that “no other book provides a complete overview in a structured and easily comprehensive pattern supported by figures and pictures”. There are, however, a number of excellent books related to diseases of muscle and nerve, some providing a wider range of clinical and pathological illustrations and a more critical review of clinical presentation, diagnosis, and treatment. At the present time the role claimed by this book remains unfilled.

R W Orrell

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CORRECTION

Bone conducted stimuli should be measured in units of dB FL (force level) as a ratio to a reference force of 1 \( \mu \)N. These levels are 10–20 dB higher, depending upon frequency, than the values given as “SPL”. The standard parameter 500 Hz 7 ms “112 dB SPL” tone burst stimulus, obtained with a 10 V peak to peak input, corresponds to an intensity of 127 dB FL (RMS).

M S Welgampola, S M Bosgren, G M Halmagyi, et al. Vestibular activation by bone conducted sound (J Neurol Neurosurg Psychiatry 2003;74:771-8). This relates to calibration of the output of the bone conductor that was used. The audiometric calibrator was not fully aware of the specific units in which bone conductors are generally calibrated but rather was influenced by the units of the sound level meter (suitable for air conducted sound). The calibration procedure is normally performed purely for testing hearing, in which case the precise units used are not strictly relevant (and under conditions which are quite different from those that the authors used). The authors have now purchased the required equipment to allow calibration of the B71, and have provided a guide to the force levels obtained.
Aciclovir induced posterior leucoencephalopathy

D Mahad, J Jarvis, P F Chinnery, D Mitra, A Gholkar and A Helldén

J Neurol Neurosurg Psychiatry 2005 76: 1308-1309
doi: 10.1136/jnnp.2004.059824

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LETTERS

‘Who came with you?’ A diagnostic observation in patients with memory problems?

The importance of obtaining collateral history when assessing patients attending the neurology clinic complaining of memory difficulties is well known.1-3 Patients developing amnesia in the context of Alzheimer’s disease may underplay their difficulties because of cognitive anosognosia, whereas those with purely subjective memory complaints (the ‘worried well’) may overemphasise difficulties. Memory complaint, preferably corroborated by an informant, is one of the suggested diagnostic criteria of mild cognitive impairment (MCI).1 Misdiagnosis of memory complaints may occur when no collateral history is available.4

For these reasons, all patients referred to my cognitive function clinic are sent, as part of their clinic appointment letter, a request asking them to bring a relative, friend, or carer from whom additional clinical information may be obtained; this is printed in bold type and in a separate paragraph. Despite this, some patients attend the clinic alone. A study was undertaken to measure the diagnostic value of this observation.

As part of an audit of referrals over a 2 year period (September 2002 to August 2004 inclusive), attendance or non-attendance of a relative or friend at each consultation was noted. Diagnosis of dementia was based on DSM-IV criteria, established by clinical interview, neuropsychological assessment and structural neuroimaging. Diagnosis of dementia subtype (Alzheimer’s disease, vascular dementia, dementia with Lewy bodies, frontotemporal dementia) and of MCI followed widely accepted diagnostic criteria. All patients had minimum follow up of 6 months.

Of 183 new referrals seen, 150 (82%; 95% confidence interval (CI) 76 to 88%) followed the written instruction in the clinic appointment letter and attended with a relative, friend or carer; the remaining 33 (18%; 95% CI 4 to 31%) attended alone. In this cohort, 90 patients were diagnosed with dementia and 93 were not demented; three had MCI. Of the 150 patients accompanied to the clinic, 90 (60%; 95% CI 52 to 68%) had dementia; of the 60 not demented, one had MCI. None of the 33 patients attending alone had dementia, although two had MCI.

Hence, if attending the clinic with a relative, friend, or carer (that is, following the instructions given in the appointment letter) were considered a diagnostic test for dementia, it would have a sensitivity of 100% (95% CI 96 to 100%; Wilson method), specificity of 35% (95% CI 26 to 46%), and positive and negative predictive values of 60% (95% CI 52 to 67%) and 100% (95% CI 95 to 100%) respectively. Positive likelihood ratio was 1.55 (95% CI 1.33 to 1.80, log method), judged unimportant, but negative likelihood ratio (0) was large.

Although not absolute, as those unaccompanied patients with MCI might yet evolve to dementia, the period of follow up for some patients is brief, and clinically established diagnoses may require revision (for example, when neuropathological data become available), these findings nevertheless support the belief that attending the neurology clinic alone despite written instructions to the contrary is a robust sign of the absence of dementia.5

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Competing interests: none

References

Laryngeal abductor paralysis can be a solitary manifestation of multiple system atrophy

Laryngeal abductor paralysis (LAP) and stridor are well known features that occur in one third of patients with multiple system atrophy (MSA).6 The pathogenesis of LAP is thought to be crico-arytenoid abductor muscle denervation,7 although there is a lack of consistent evidence of motor cell loss in the nucleus ambiguus.8 More recently, dystonia of the laryngeal abductor muscle has also been proposed.9 LAP/stridor usually occurs in the advanced stages of the disease, and is considered to be a poor prognostic feature.10 In contrast, some MSA cases have shown LAP initially, with most of these reported by otolaryngologists.6,7 However, there are no systematic surveys as to the extent to which MSA patients initially present with LAP. We describe the result of a survey of 200 MSA inpatients conducted in a neurology department.

We reviewed the case records of 200 consecutive ‘probable’ MSA patients who met the inclusion and exclusion criteria. They were 119 men and 81 women, mean age 60 years; 29 had the Parkinsonian form (MSA-P) and 171 the cerebellar form (MSA-C). Among these, eight patients (4%) (four MSA-P, four MSA-C) were shown to have stridor as the initial manifestation (table 1). Stridor was the solitary manifestation in six of the patients, though it was combined with minimal laryngeal signs in two of these six patients (inspiratory gash in one, hoarseness in one) and REM (rapid eye movement)-sleep related behavioural disorder (“night terror”) in one. In the remaining two patients stridor occurred together with bladder dysfunction or gait ataxia. In the former six patients, stridor was followed by bladder dysfunction in four, constipation in three, tremor/akinesia in one, ataxia in one, and postural hypotension in one. The average interval between the development of stridor and these later symptoms and signs was 3.3 years (range 1 to 6). The average interval between stridor and hospital admission was 5.4 years (1 to 10). In all eight patients, laryngoscopy confirmed that the stridor was caused by LAP. The grade of LAP at the first admission to our hospital (75 patients), according to Isozaki’s laryngoscopy classification,5 was moderate (abductor paresis during waking; paradoxical adduction during sleep) in three and severe (complete paralysis) in five. Among those patients, continuous positive airway pressure was introduced in three, laser incision of the vocal fold was carried out in one, and subsequent tracheostomy was necessary in five.

In the cases presented, it proved true that LAP/stridor can be a solitary manifestation of MSA. The interval between LAP/stridor and hospital admission was rather long (on average 5.4 years), suggesting that the progression of LAP was not very rapid in those patients. Although the initial presentation of LAP/stridor was not common (it occurred in only 4% of all MSA patients), it is clinically relevant because patients with LAP/stridor but without obvious neurological symptoms may see general physicians or otolaryngologists first. Laryngeal stridor also occurs because of local inflammation or tumours, or from distant causes that affect the vagal nerves, such as upper thoracic or nasopharyngeal carcinoma. If such conditions have been excluded, central neurological causes should be considered. Co-morbid bladder dysfunction (particularly urinary incontinence and post-voiding residual volume of more than 100 ml), postural and postprandial stridor, parkinsonism, and ataxia are all red flags suggestive of MSA.10 In our eight patients, bladder dysfunction was an early sign and was chronologically correlated with LAP/stridor; this finding is in line with a previous report.1 These atypical features for a local laryngeal lesion suggest that further studies of the brain are necessary to confirm the diagnosis of MSA.

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Table 1  Patients with multiple system atrophy who initially presented with laryngeal abductor paralysis/stridor

<table>
<thead>
<tr>
<th>Patient*</th>
<th>Years from the onset of illness</th>
<th>Laryngoscopy findings†</th>
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</thead>
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<tr>
<td></td>
<td>0</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13</td>
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<tr>
<td>1. 62/M</td>
<td>Laryngeal stridor</td>
<td>BD</td>
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<tr>
<td>MSA-P</td>
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<td>2. 74/F</td>
<td>Laryngeal stridor</td>
<td>Constipation, BD, PH, akinesia</td>
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<tr>
<td>MSA-P</td>
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<td>3. 83/F</td>
<td>Laryngeal stridor, inspiratory gasp</td>
<td>Atoxic gait, BD, constipation</td>
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<td>MSA-C</td>
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<td>4. 59/F</td>
<td>Laryngeal stridor, RBD</td>
<td>Atoxic gait</td>
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<td>MSA-C</td>
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<td></td>
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<tr>
<td>5. 62/M</td>
<td>Laryngeal stridor</td>
<td>Constipation, BD</td>
</tr>
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<td>MSA-C</td>
<td></td>
<td></td>
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<tr>
<td>6. 57/F</td>
<td>Laryngeal stridor, hoarseness</td>
<td>Hand tremor, Dysphasia</td>
</tr>
<tr>
<td>MSA-P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. 53/M</td>
<td>Laryngeal stridor, hoarseness, BD, erectile dysfunction, constipation</td>
<td>PH, decreased sweating, atoxic gait</td>
</tr>
<tr>
<td>MSA-P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. 63/F</td>
<td>Laryngeal stridor, atoxic gait</td>
<td>Admission: Hoarseness, akinesia; CPAP</td>
</tr>
<tr>
<td>MSA-C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Age, sex, diagnosis.  †Laryngeal abductor paralysis: + (mild), ++ (moderate), +++ (severe), Isozaki's classification.

AHI, apnoea hypopnoea index; BD, bladder dysfunction; CPAP, continuous positive airway pressure; F, female; HUT, head up tilt (60° for 10 min); M, male; MSA-C, cerebellar form of multiple system atrophy; MSA-P, parkinsonian form of multiple system atrophy; ODI, oxygen desaturation index (dips per hour); PH, postural hypotension; RBD, RBD sleep behavioural disorder; SAS, sleep apnoea syndrome.
Upon arrival his temperature was 36.4 °C, and his mental status declined. A head CT scan displayed new right fronto-parietal, right posterior cerebral artery (PCA) and left insula, right middle cerebral and anterior cerebral arteries, bilateral posterior cerebral arteries and left insular artery ischaemic infarcts. (B) In addition, a brain magnetic resonance imaging (MRI) scan shows right thalamic and left internal capsule lacunes, and the initial left occipital ischaemic infarct with haemorrhage. (C) A magnetic resonance angiogram showing no flow in the right internal carotid artery.

Figure 1 (A) Head computed tomography scan showing left parietal intraparenchymal, subarachnoid, and intraventricular haemorrhages, right middle cerebral and anterior cerebral arteries, bilateral posterior cerebral arteries and left insular artery ischaemic infarcts. In addition, a brain magnetic resonance imaging (MRI) scan shows right thalamic and left internal capsule lacunes, and the initial left occipital ischaemic infarct with haemorrhage. (A) Magnetic resonance angiogram showing no flow in the right internal carotid artery.

Disseminated Pseudallescheria boydii infection successfully treated with voriconazole

A 56 year old, right handed African-American man with past history of left knee osteoarthritis, remote intravenous drug use, remote alcoholism, and seropositivity for hepatitis C was admitted to a local hospital for fatigue, chest pain, 13.6 kg weight loss, night sweats, and vision loss. On examination, a loud systolic murmur was present. An electrocardiogram (ECG) displayed T wave alternans and a transoesophageal echocardiogram revealed severe mitral regurgitation with mitral valve vegetations, ruptured chordae tendineae, and left ventricular ejection fraction of 75%. He was diagnosed as having endocarditis and cyto-myelomycosis endophthalmitis, and was treated with ceftriaxone, vancomycin, ganciclovir, foscamet, aspirin, metoprolol, lisinopril, nifedipine, and intravenous enoxindol. He developed fever (39.3°C) and his mental status declined. A head computed tomography (CT) scan showed left occipital haemorrhage. His left leg was cold with pulses detectable only by Doppler. He was alert and oriented to person and place only, and recalled 1/3 items after short delay. His speech was fluent and well articulated. He had light perception on the right and was only able to count fingers centrally on the left. He displayed mild left leg weakness, normal reflexes and flexor plantar responses, mild right pronator drift, and diminished left sided proprioception. Ophthalmological examination disclosed bilateral vitreous infiltrates, retinal lesions, segmental retinal detachments, and scattered choroidal inflammation worse on the right. Fluconazole was added.

An ECG revealed a prolonged QT interval, Q waves in II, III, and AVF leads, and signs of left ventricular hypertrophy. The laboratory studies revealed a white blood cell count of 25 600/μl with 69% neutrophils, 23% lymphocytes, 6% monocytes, 1% eosinophils, and 1% bands; haematocrit, 30%; platelets, 207 000/μl; troponin T, negative; aspartate aminotransferase (AST), mildly elevated at 79 U/l and 99 U/l respectively (a finding attributed to active hepatitis C); alkaline phosphatase 96 U/l and the erythrocyte sedimentation rate (ESR) 26 mm/hr. Serological examination for human immunodeficiency virus (HIV) was negative.

A thoracoabdominal CT scan disclosed a 2 x 2 cm mass in the right subclavian and common carotid arteries and a right renal infarct. The left iliac artery was occluded. Intravenous heparin, in attempt to salvage the left leg, resulted in left parietal subarachnoid, intraparenchymal, and intraventricular haemorrhages. The causative organism was identified as Pseudallescheria boydii resistant to amphotericin, flucytosine, and fluconazole. On day 13 voriconazole was begun. He underwent urgent mitral valve replacement and left superior and profunda femoral, and iliac embolectomy. Heparin was discontinued, and he remained in prolonged coma. A head CT scan displayed new right fronto-parietal, right anterior cerebral artery (ACA), right posterior cerebral artery (PCA) and bilateral small cerebellar infarcts (fig 1A). A follow up brain magnetic resonance imaging (MRI) scan revealed several new small left frontal and parietal haemorrhages and ischaemic infarcts of the right thalamus, ACA, and PCA along with the left insula, basal ganglia, and parietal lobe (fig 1B). The right internal carotid artery was occluded (fig 1C). The findings were attributed to infectious emboli and haemorrhaging from myotic aneurysms.

On day 38 of hospitalisation the patient’s coma resolved. He was eventually able to follow simple commands, and sit and stand, although expressive aphasia and left hemiparesis remained. His vision improved to 20/800 on the left. He was subsequently discharged to a long term care facility.

Discussion

Pseudallescheria boydii (anamorph or asexual phase: Scedosporium apiospermum) is a ubiquitous saprophytic fungus commonly found in soil, manure, decaying vegetation, and polluted water. Its commonest clinical presentation in the USA is as mycetoma, a chronic limited subcutaneous infection in immunocompetent individuals engendered by minor trauma, and is characterised by grain formation and local tissue destruction.1,2 Although endocarditis and endophthalmitis have been described,3 lung, bone, joint, or central nervous system (CNS) involvement is more typical of this organism.4 Infections are classically acquired through penetrating trauma5 or massive inoculation through inhalation, such as may occur in near drowning in stagnant or polluted water.6 Disease subsequently results from contiguous extension and haematogenous dissemination. It is likely that our patient acquired his infection through prior intravenous drug use, resulting in endocarditis with secondary dissemination to eye, kidney, extremities, and brain.

Among the various types of invasive fungal disease attributable to P. boydii, survival rates

References


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Figure 1  Tonic oculomotor tilt reaction in patient 1. Note sustained head tilt and concurrent vertical divergence of the eyes (skew deviation). T2 weighted axial magnetic resonance imaging of the brain showed acute infarcts in middle cerebellar peduncle and lateral inferior pontine tegmentum. There is conjugate leftward torsion of the eyes (that is, counterclockwise from the patient’s point of view). Fundus photography showed 25° extorsion of the left eye and 12° intorsion of the right eye. There was no caloric response on the left side. Pure tone audiometry showed 65 dB sensorineural hearing loss on the left side. The subjective visual vertical with binocular viewing was tilted 17 degrees to the left (that is, counterclockwise from the patient’s point of view).

The second patient was a 58 year old woman with type 2 diabetes mellitus and hypertension who developed severe vertigo, hearing loss, tinnitus on the left side, dysarthria, and imbalance. She had bilateral gaze evoked nystagmus with a horizontal-rotatory component. There was left peripheral facial weakness and numbness, dysmetria of the left limbs, and gait ataxia. Pure tone audiometry showed a 65 dB sensorineural hearing loss on the left side. Fundus photography showed 14° extorsion of the left eye and 3° extorsion of the right eye. Prismatic testing showed a skew deviation with a right hypertropia of 20 prism diopters in primary gaze (fig 1). Magnetic resonance imaging (MRI) including diffusion images showed acute infarcts in the left middle cerebellar peduncle and the left lateral inferior pontine tegmentum (fig 1).

References


Ocular tilt reaction and anterior inferior cerebellar artery syndrome

The oculomotor tilt reaction (OTR) is an eye-head postural reaction consisting of ipsilateral head and neck tilt, skew deviation, and ocular torsion. OTR indicates either a unilateral peripheral vestibular deficit (inner ear or vestibular nerve) or a unilateral lesion of brain stem pathways from the vestibular nuclei to the interstitial nucleus of Cajal in the rostral midbrain.

The anterior inferior cerebellar artery (AICA) supplies the lateral inferior pontine tegmentum and middle cerebellar peduncle, vestibulocochlear nerve including the root entry zone, inner ear, and anterior inferior cerebellum. Although there has been one report of skew deviation owing to an AICA infarct, the clinical features of the OTR have not previously been documented. We describe two patients with AICA infarction, each of whom had ipsiversive OTR—one with complete OTR, the other with skew deviation and tonic ipsiversive ocular torsion.

The first was a 58 year old man with long standing hypertension who presented with sudden vertigo and imbalance. On neurological examination, he had bilateral gaze evoked horizontal nystagmus, left peripheral facial weakness and numbness, dysmetria of the left limbs, and gait ataxia. There was no caloric response on the left side. Pure tone audiometry showed 65 dB sensorineural hearing loss on the left side. The subjective visual vertical with binocular viewing was tilted 17 degrees to the left (that is, counterclockwise from the patient’s point of view). Fundus photography showed 25° extorsion of the left eye and 12° intorsion of the right eye. He had a skew deviation with a right hypertropia of 20 prism diopters in primary gaze (fig 1). Magnetic resonance imaging (MRI) including diffusion images showed acute infarcts in the left middle cerebellar peduncle and the left lateral inferior pontine tegmentum (fig 1).

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now showed 1° of extorsion of the left eye, indicating that the left eye had been extorted by 13° at the first examination (that is, by 14° minus 1°) and 9° of extorsion of the right eye, indicating that at the first examination the right eye had in fact been intorted by 6° (that is, by 3° minus 9°).

Comment

Most earlier reports of AICA infarction have focused on the brain stem or cerebellar findings. Recently, there have been several reports describing the clinical importance of inner ear symptoms, vertigo and/or sudden deafness. However, a detailed description of OTR as a sign of AICA infarction has not been reported previously. OTR, a sign of vestibular dysfunction in the roll plane, is characterised by a triad of conjugate ocular torsion, skew deviation, and head tilt. It results from destructive or irritative lesions of central or peripheral graviceptive vestibular pathways. Although head tilt is a common component of OTR, skew deviation with conjugate ocular torsion often occurs without head tilt in our patient. Thus the pathophysiology of a partial OTR (that is, skew deviation and conjugate ocular torsion without head tilt) is the same as that of a complete OTR, and skew deviation with conjugate ocular torsion is sufficient for the diagnosis of OTR.

In addition to lesions of the central and peripheral vestibular pathways conveying graviceptive signals, lesions of the cerebellum may also result in OTR. Skew deviation is commonly seen with cerebellar infarction. Mossman and Halmagyi described two patients with cerebellar stroke, presumably in the territory of the posterior inferior cerebellar artery, who had tonic conjugate ocular torsion without associated head tilt. These investigators speculated that interruption of nodular inhibitory projections to graviceptive neurons in the ipsilateral vestibular nuclei may have accounted for the contraversive conjugate ocular torsion. Sensorineural hearing loss and canal paresis to caloric stimulation on the left side clearly indicated involvement of the peripheral audiovestibular system. Ipsiversive OTR with acute posterior inferior cerebellar artery infarction. Stroke 2002;33:2807–12.


Video assessment of rTMS for Tourette syndrome

In a recent study, a subjective 1 Hz repetitive transcranial magnetic stimulation (rTMS) over left motor or premotor cortex failed to improve tics in patients with Gilles de la Tourette syndrome (GTS) as determined by self assessment scores.1 However, video ratings of this study had not been analysed. Here, we present the results of blinded analysis of the video of GTS patients who participated in the previous study. We show that rTMS has a placebo effect and confirm that low intensity motor or premotor rTMS does not have a specific effect on tics in GTS. In a placebo controlled cross-over study of 16 patients with GTS, threshold 1 Hz rTMS (2400 stimuli delivered on 2 consecutive days) were applied under three conditions: a 30° head tilt, a 30° head tilt and a 30° head tilt with a 40° head tilt.

In conclusion, this is the first report of well documented OTR with AICA infarction. The ipsiversive OTR in these patients probably resulted from infarction of the inner ear or the root entry zone of the eighth nerve.

Acknowledgements

This study was supported by grants of the Oriental Medicine R&D Project (03-PJ9-PG6-S002-0001), Ministry of Health and Welfare, Republic of Korea.

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References


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Table 1 Mean differences (before and after rTMS) and confidence intervals of clinical scores

<table>
<thead>
<tr>
<th>Score</th>
<th>Motor rTMS</th>
<th>Premotor rTMS</th>
<th>Sham rTMS</th>
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<tbody>
<tr>
<td>MRVS total score</td>
<td>1.5</td>
<td>1.1</td>
<td>0.4</td>
</tr>
<tr>
<td>95% CI</td>
<td>-0.8 to 3.8</td>
<td>-0.5 to 2.8</td>
<td>-1.2 to 2.0</td>
</tr>
<tr>
<td>AYVS total score</td>
<td>4</td>
<td>2.1</td>
<td>0.3</td>
</tr>
<tr>
<td>95% CI</td>
<td>-0.3 to 8.3</td>
<td>0.2 to 4.0</td>
<td>2.6 to 3.1</td>
</tr>
<tr>
<td>AYVS motor score</td>
<td>1.1</td>
<td>1.4</td>
<td>0.8</td>
</tr>
<tr>
<td>95% CI</td>
<td>-1.3 to 3.5</td>
<td>0.5 to 0.9</td>
<td>-0.9 to 2.4</td>
</tr>
<tr>
<td>AYVS vocal score</td>
<td>2.9</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.4 to 5.3</td>
<td>-1.1 to 2.6</td>
<td>-2.4 to 1.4</td>
</tr>
</tbody>
</table>

AYVS, Adapted Yale Video Scale; CI, confidence interval; MRVS, Modified Rush Video Scale.
appears to be a valid and comprehensive tool to assess tic severity in GTS patients, but it needs to be evaluated further.

We conclude that left motor or premotor low intensity 1 Hz rTMS does not improve tics in GTS patient as assessed by blinded video scoring. Further studies, perhaps using higher intensity rTMS, longer rTMS trains, or bilateral stimulation, are needed to delineate the usefulness of rTMS in GTS patients. In these studies, blinded and independent video rating should be used.

Acknowledgements

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Competing interests: none declared

Figure 1 Video scores before and after each intervention (means and standard error of the mean). (A) Modified Rush Video Scale (MRVS) total score; (B) Adapted Yale Video Scale (AYVS) total score; (C) AYVS motor score; (D) AYVS vocal score.

References


A case of superior cerebellar artery syndrome with contralateral hearing loss at onset

Deafness is rare in ischaemic stroke but sometimes occurs as a result of lower pons infarction. The main cause of such deafness is occlusion of the anterior inferior cerebellar artery (AICA); occlusion of the superior cerebellar artery (SCA), which perfuses the higher pons, causes SCA syndrome and also results in deafness but is extremely rare.1 In the present report, we describe a patient with SCA syndrome, whose initial complaint was contralateral hearing loss.

Case report

A 64 year old male with untreated hyperglycaemia and hypertension was admitted 4 h after the sudden onset of deafness in his right ear. Hearing loss was the only complaint and other neurological signs were absent. Right sensorineural hearing loss was revealed by a hearing test (fig 1A). After several examinations including stapedial reflexes and speech discrimination, an initial diagnosis of sudden deafness was made. However, 8 h later the patient complained of diplopia, vertigo, and nausea. Impaired abducens function in the right eye and bilateral lateral gaze nystagmus were observed. Finger-nose and heel-knee tests suggested left cerebellar ataxia. Hence, a diagnosis of SCA syndrome was made, and argatroban, an anti-coagulant, was administered. Diffusion weighted magnetic resonance imaging (MRI) 12 h after onset showed infarctions in the left cerebellum (fig 1B) and lateral superior pons (fig 1C). Magnetic resonance angiography showed loss of blood flow in the lower basilar artery (fig 1D). Respiratory failure developed 4 h later, and the next day the patient also showed right hemiparesis and Horner’s syndrome. Bilateral cortical blindness was also present. A diagnosis of SCA syndrome with hemiparesis and cortical blindness was made. A fluid attenuated inversion recovery (FLAIR) image 2 weeks later showed an enlarged infarction in the left cerebellum, and a new infarction in the right cerebellum, dorsal pons, and bilateral occipital lobes (fig 1E). The patient’s symptoms remained unchanged 3 months later.

Discussion

SCA syndrome shows ipsilateral cerebellar ataxia and Horner’s syndrome, contralateral superficial sensory disturbance and hearing loss, as well as nystagmus toward the impaired side, vertigo, and nausea.2 Fibres from the contralateral auditory nucleus join the lateral lemniscus, pass into the brain, and terminate in the hearing centre. Therefore, impairment of the lateral lemniscus on one side causes hearing loss on the other. In SCA infarction, the ischaemic lesion occurs in the area where fibres from the nucleus have already crossed, and therefore sensory hearing loss is observed in the contralateral side.

We describe a rare case of SCA syndrome which began with deafness in one ear. Although deafness sometimes occurs as a result of brainstem infarction, most cases of ipsilateral hearing loss are due to AICA infarction.3 To our knowledge, the study by Doyle et al is the only previous report of hearing loss due to contralateral SCA infarction.4 Amarenco et al described a large series of SCA syndrome cases, where no patient showed contralateral deafness.5 The present report presents a important finding regarding symptoms of ischaemic stroke, and suggests that hearing loss, although rare, can be the first symptom. It is necessary to carefully observe patients with sudden deafness.

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Figure 1 (A) Right sensorineural hearing loss. ‘o’ and ‘x’ indicate air conduction without masking in the right and left ears, respectively. ‘[’ and ‘]’ indicate bone conduction with masking in the right and left ears, respectively. (B, C) Axial diffusion weighted MRI images (B, C) 12 h after the onset of deafness. Note high signal intensity at the left cerebellum (B, arrow) and left lateral territory of the superior cerebellar artery: a clinical and pathological study of 33 cases. Neurology 1990; 40: 1385–90.

BOOK REVIEWS

Myology, third edition


This is the third edition of an established two volume text covering all aspects of human muscle disease. Since the second edition in 1994 rapid advances in the molecular genetic understanding of a range of muscle diseases have occurred. Indeed some diseases, such as muscle channelopathies, have only been fully recognised as distinct entities during this period. These huge advances are reflected in a complete and up-to-date revision. Myology contains 70 chapters divided into three parts: Part 1, Scientific basis of muscle disease; Part 2, General approaches to neuromuscular disease; and Part 3, Diseases of muscle. All chapters are well constructed and written by authorities in each field. It is likely to be parts 2 and 3 that are of most interest to the readers of the JNPP. Part 2 is full of practical information. In particular the chapters on clinical examination and electrodiagnosis will be of interest to clinicians frequently encounters patients with neuromuscular symptoms and will also be valuable for trainees. Also in part 2 is an informative chapter on the evolving clinical uses of imaging in the investigation of muscle disease. It seems clear that MRI is going to play an increasing role in the evaluation of muscle diseases in the future. Part 3 contains comprehensive chapters on all of the known human muscle diseases. More genes have been discovered in the area of muscle disease than in virtually any other area within neurology in the past few years. This is reflected in the fact that 21 of the 30 chapters describing individual muscle diseases are given over to genetic disorders, including the muscular dystrophies, congenital myopathies, muscle channelopathies, genetic inclusion body myopathies, and the metabolic myopathies. I found it difficult to fault any of these chapters. The continuing challenges involved in understanding the molecular pathogenesis of and in treating the inflammatory myopathies are well covered. The final seven chapters of part 3 cover disorders of neuromuscular transmission, neuropathies, and neuromopathies. Myology the third edition must have been a mammoth task to produce and the editors are to be congratulated. I think there is plenty of accessible information, of practical use for clinicians and trainees dealing with muscle disease. I can thoroughly recommend this text.

Essential Neurology, 4th edition


Lecture Notes: Neurology, 8th edition


What constitutes the “core knowledge” of neurology that all medical students should reasonably be expected to learn? This is a question that Lecture Notes: Neurology (LNN) and Essential Neurology (EN)—two stalwarts of the medical student library—continue to grapple with in their latest editions.

EN, longer but with fewer chapters than LNN, tackles subjects in greater depth (and hence claims to be a review text for MRCP), whilst LNN has greater breadth, with suggestions for extra reading and key points summarising each chapter. Both texts incorporate case histories, somewhat more successfully in EN if only because the answers are physically separate, encouraging readers to pause and think about each presentation. Illustrations seem more integral to the text in EN, but this volume does have some surprising typographical gaffes—for example, Brown-Séquard, L’Hermitte; Angell Robertson with a hyphen. I enjoyed reading about “messy breakfast syndrome” and “Kellogg’s epilepsy” which, like “flying saucer syndrome”, are variant names for juvenile myoclonic epilepsy. Considering my experience of general neurological clinics, I would have valued more discussion in EN on “neurologically unexplained symptoms”, which seem so frequent, and a specific section on neurofibromatosis, the commonest monogenic disorder that I see, albeit rarely.

How should the undergraduate neurology text develop, assuming that it is not wholly superseded by internet browsing? Should there be more emphasis on expert consensus diagnostic criteria and management guidelines, rather than succinct qualitative descriptions of neurological conditions, facilitating pattern recognition, and their treatment? Should there be greater reference to the evidence base (and its inadequacies)—for example, citing of systematic reviews? These are issues to be addressed by the authors in future editions, but for now one has no hesitation in recommending either of these volumes to medical students, or both, since it would be invidious to choose one as “better”.

A J Larner

A historical dictionary of psychiatry


Edward Shorter is Professor of History of Medicine at the University of Toronto and this 338 page volume is claimed to be the first “Historical Dictionary of Psychiatry”. As always in alphabetical order, discovery of individual entries is easy and an index takes us to words embedded in the text, more in encyclopaedia fashion.

Neurology without physical signs? The neurologist may still feel this is adequate definition of psychiatry, particularly nowadays with so many publications that bring together works in

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2 Mills CK. Hemianesthesia to pain and temperature and loss of emotional expression on the right side, with ataxia of the upper limbs on the left. The symptoms probably due to a lesion of the thalamus or superior peduncles. J Nerv Ment Dis 1908; 35: 331–2.


the fields of neurology, psychology, and psychiatry (take, for example, Adam Zeman’s *Consciousness, a User’s Guide*). Thus *Gustati* merits its long entry and the wholeness of this book is enhanced by a guide to pronunciation of difficult names that is embedded in the text and thus for example, helpfully, we are given *Hö-kä* for Alfred Erich Hoche. This is a sort of bilingual glossary that guides the writer and is a standard work the writer should have at his side. Several individuals in the Menninger family are grouped together and give us insight into the medical achievements of father and sons. Neurologists will not be surprised to find Jung and Kraepelin, and happily also stumble upon James Parkinson, Charcot, and Wernicke, each wearing his psychiatry hat. The electrical circuitry that binds our specialties includes an entry on Hitzig. Lest all this history become too much, the entries on anxiety and phobias cover a substantial seven pages. This volume will assist neurologists, psychologists, and psychiatrists in their quest for learning; medical authors should find it very handy indeed.

*The Auditory Cortex, A Synthesis of Human and Animal Research*

Edited by Reinhard Konig, Peter Heil, Eike So far, so good. Part II ("Coding of sounds"),

...with its heavy-duty electrophysiology, is more of a challenge; and yet the coding of sounds is a problem of the most fundamental scientific and philosophical interest. How on earth is it possible to reconstruct the world we hear from the one-dimensional flutter of two membranes? Part III ("Plasticity, learning and cognition") addresses the interface between the brain and experience. Confronted with a chapter about ferrets, perhaps the clinician will master an initial rising sense of alarm by recalling that this is the science that made possible the cochlear implant and may yet explain how cocktail parties work (or fail).

If neurologists should learn something here about bats, barn owls, or ferrets, it can’t hurt. This book is a bracing corrective to the error, too often implicit in clinical practice as in daily life, that the eyes (human eyes, at that) are the sole windows of the brain. To paraphrase that poem of Kemp’s, the unguessed glories of the auditory cortex remind us that the five-sensed cane of mind is, after all, five-sensed.

*Mechanism and management of headache, seventh edition*


As a general rule, it is safe to assume that any textbook entering a seventh edition does so on its merits and must be worth reading. The latest edition of the classic *Mechanism and Management of Headache* by Lance and Goadsby does not disappoint. It is occasioned not just by the passage of time but also by advances in the field of headache that make a new edition necessary. Among these, the long-awaited revision of the International Classification of Headache Disorders is the most important, as it has created some entirely new headache entities and significantly altered criteria for others. New information about the structural consequences of seemingly benign headache disorders – iron deposition in the brainstem, the increased prevalence of clinically silent ischaemic brain lesions in migraineurs, for example – and impressive gains in understanding of the basic pathophysiology of headache also demand explication for practising physicians. So too do new “hot topics” such as the possible connection between patent foramen ovale and chronic daily headache. The book begins with an historical overview of headache that serves as a useful reminder of just how far we have come from the days when holes were drilled in the skull to relieve headache. Throughout the book, photographs have been updated or replaced, and in general are clearer than those in previous editions. Horner’s syndrome, third nerve palsy, and other physical findings are nicely and usefully illustrated, and are a true asset to the chapter on examination.

Not unexpectedly, the chapters dealing with headache classification and pathophysiology have undergone the most extensive revision. Updated, timely information about natural treatments has also been added, reflecting the reality of patient interest and enthusiasm for such things. A new table on clinical stratification of acute, specific migraine therapies has been added to the treatment chapter, and other tables in this chapter are more carefully organised, larger, and more readable than those in previous editions. A small oversight is the retention of the older term “tension headache” in many places – perhaps done to save space, but if so at the expense of the subtle but important implications conveyed by the longer term “tension-type.”

*Reference*


*Oxford handbook of psychiatry*


*Psychiatry, third edition, Oxford core texts*


The *Oxford Handbook of Psychiatry* is a wonderful little book. The “little” applies to its size...
and not its stature, as it is actually over 900 pages long and packed with a wealth of useful and interesting information. There has clearly been a tremendous amount of effort put into its production including the piloting of various versions with local SHOs. Although it is aimed primarily at the SHO, it would be a useful book for psychiatrists of all levels because it is so comprehensive. It provides discrete chapters for each type of psychiatric disorder, which contain key facts about the illness with a focus on management, both immediate and long term. These are preceded by several chapters on assessment and followed by a number of chapters devoted to specific considerations such as ethics and therapeutics in specific circumstances requiring a general knowledge of psychiatry. The information is very well laid out in easily digestible sections. There are also more highlighted lists and tables than previous editions that serve to emphasise important information or provide ready reference to aspects of assessment and management. This improved version is highly recommended to the non-specialist.

D J Mahad, A Helldén, J Jarvis, et al. Aciclovir induced posterior leucoencephalopathy (J Neurol Neurosurg Psychiatry 2005;76:1308–9). The authors of this letter were mistakenly grouped according to their affiliations. The correct ordering of the authors is: D J Mahad, A Helldén, J Jarvis, D Mitra, A Gholkar, P F Chinnery.

E Joyce

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