LETTERS TO
THE EDITOR

Carbohydrate antigen 19–9 in cerebrospinal fluid and within malignant cells in a case of leptomeningeal carcinomatosis

Carcinoblastic antigen (CEA) concentrations in CSF hold promise as an indicator of metastatic leptomeningeal involvement by carcinoma. We describe a patient with leptomeningeal carcinomatosis showing a high concentration of carbohydrate antigen 19–9 (CA 19–9) but a normal CEA concentration in CSF despite equally positive immunostaining in the cytoplasm of tumour cells in CSF.

A 44-year-old man was admitted complaining of headaches and diplopia over 3 months. Neurologically, the patient was alert despite neck stiffness. Multiple cranial nerve dysfunctions were apparent, specifically bilateral lateral gaze palsy, inability to move his jaw due to masseter palsy, facial diplegia, left soft palate weakness, and absence of gag reflex on the left. Four limb ataxia was evident, and his gait was wide based and unsteady. Reflexes were symmetrically hypotonic in all extremities and pathological reflexes were absent.

Chest CT disclosed nodular, contrast enhancing, left upper lung densities. Gastric fibroscopy and abdominal CT were unrevealing. Non-contrast brain MRI was normal. On lumbar puncture, opening pressure was high (160 mm H2O). His CSF was xanthochromic and contained 9 cells/mm³, 117 mg/dl protein, and 48 mg/dl glucose. Cytological examination of CSF disclosed scattered large cells with irregularly shaped, polymorphic nuclei, sometimes with large cytoplasmic vacuoles characteristic of adenocarcinoma (fig 1 A, B). The CEA concentration (radioimmunooassay: Eiken, Tokyo, Japan) in CSF remained low (1.1 ng/ml), unlike that in serum (81.1 ng/ml (upper normal limit 2.5 ng/ml)). By contrast, the CSF concentration of CA 19–9 (enzyme immunoassay: Dainabot, Tokyo, Japan) was extremely high (61.4 U/ml), whereas that in serum remained nearly normal (39.4 U/ml (upper limit 37 U/ml)).

Weekly intrathecal methotrexate administration (10 mg) for 5 weeks failed to improve neurological deficits or lower CSF CA 19–9 concentrations (fig 2). Subsequently treatment was changed to weekly intrathecal cytarabine (30 mg) for 6 weeks, adding brainstem radiotherapy for the last 2 weeks. Headache and neck stiffness were relieved. The cranial nerve palsies and four limb ataxia remained unchanged.

Repeat CSF analysis disclosed the disappearance of identifiable tumour cells and a marked decrease in CSF CA 19–9 concentration, from 78.9 to 16.4 U/ml, whereas that of CEA in CSF remained at its previous low concentrations despite continuing high CEA in serum. Two weeks later, the patient became deaf and confused. Concentrations of CA 19–9 increased in the CSF, and the patient died 26 weeks after admission. Permission for postmortem examination was withheld.

Immunocytochemical studies of tumour cells in the CSF from the patient and two control patients with leptomeningeal carcinomatosis from squamous cell lung cancer were performed as follows. Cells obtained from CSF at initial lumbar puncture were collected on slides using cytopsin equipment. Cell preparations were stained using monoclonal antibodies against CA 19–9 or CEA, indicating production of the marker by the cells (fig 1 C, D). Tumour cells in CSF from the two control patients with squamous lung cancer were immunocytochemically negative for CEA, arguing against false positive staining in the patient.

On the assumption that tumour markers with a molecular weight similar to that of IgG should have similar filtration transfer properties at the blood-CSF barrier, the portion of carbohydrate antigen 19–9 produced was calculated in relation to IgG according to the equation:

\[
\text{CA 19–9 loc} = \frac{\text{CA 19–9 CSF}}{\text{CA 19–9 serum}} \times \text{CSF/serum albumin ratio}.
\]

\[
\text{CA 19–9 loc} = 0.7\times\frac{\text{CSF/serum albumin ratio}}{1000}\times\text{CA 19–9 serum}
\]

CA 19–9 loc (U/ml) was 59.6 initially, 7.4 at 8 weeks later, and 57.5 at 26 weeks after admission.

CA 19–9 is a monoclonal antibody defined carbohydrate antigen expressed by many carcinomas, which is useful for carcinoma

![Figure 1](image-url)
The most common type of hereditary motor and sensory neuropathy type 1A associated with sensorineural deafness

Hereditary motor and sensory neuropathy type 1A is caused by a duplication of the gene for peripheral myelin protein 22 (PMP 22), situated on chromosome 17p. We report on a patient with this genotype with bilateral sensorineural deafness. A 28-year-old man presented with progressive distal weakness, numbness, and progressive bilateral hearing loss. He had first noticed problems with running in his early teens and at the age of 13 had two operations to correct bilateral pes cavus. His walking tolerance gradually deteriorated to half a mile unaided. At the age of 26 he had been aware of diminished sensation in his feet and progressive bilateral hearing loss. Clinical history was unremarkable and he had not been exposed to any relevant drugs or toxins. There was no history of neurological problems among three siblings, his three children or the rest of his family. There was no parental consanguinity.

General medical examination disclosed bilateral pes cavus, palpable greater auricular nerves, and evidence of previous spinal surgery. Otolaryngology examination showed bilateral sensorineural deafness (~40 dB at 6 kHz in both ears). Visual acuity, fundoscopy, and all other cranial nerves were normal. There was a typical essential tremor in the upper extremities. In the limbs there was symmetric distal wasting, worse in the lower limbs, with corresponding weakness. Deep tendon reflexes were absent. Pinprick and vibration sensation were impaired in both feet.

Laboratory investigations showed no evidence of any underlying systemic disorder. Protein concentration in CSF was 1.55 g/l. Wave I latencies were significantly delayed compared with laboratory controls. Interwave V 4.0 (0.23) 4.38 4.31

The following table shows the results of BAERs.

<table>
<thead>
<tr>
<th>Wave</th>
<th>Normal range</th>
<th>HMSN 1A (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Left</td>
</tr>
<tr>
<td>Wave I</td>
<td>1.7 (0.15)</td>
<td>2.22</td>
</tr>
<tr>
<td>Wave II</td>
<td>4.52 (0.30)</td>
<td>6.45</td>
</tr>
<tr>
<td>Wave V</td>
<td>5.70 (0.25)</td>
<td>6.60</td>
</tr>
<tr>
<td>Interwave I-V</td>
<td>4.0 (0.23)</td>
<td>4.38</td>
</tr>
</tbody>
</table>

Our two patients showed a motorsensory neuropathy a form to recognised criteria for a diagnosis of HMSN type 1 but more detailed clinical information on these patients is lacking. Perez et al suggested, in a small community study, that the incidence of deafness in a mixed group of HMSN 1 and HMSN 2 could be as high as 30%. Only the 73-year-old patient of Nicholson et al is definitely HMSN 1A, and it could be speculated whether at this age deafness is a coincidental symptom.

Nicholson et al have recently renewed interest in auditory abnormalities in patients with HMSN 1A. Our patient conforms to the pattern they found, with isolated delayed wave I latencies suggesting a problem in the distal VIIIth nerve, in which PMP 22 expression is known to occur. This is the first case report to provide incontrovertible evidence, with nerve biopsy and genetic analysis, of bilateral sensorineural deafness in a young patient with “a full house” phenotypically and genotypically for HMSN 1A.

Neurologists and otolaryngologists should be aware of this association, which may be commoner than previously thought.


**Chronic inflammatory demyelinating polyneuropathy accompanied by carcinoma**

We read the article by Antonie et al with interest. We have also reported on a patient with chronic inflammatory demyelinating polyneuropathy (CIDP) accompanied by hepatocellular carcinoma who showed improvement after intravenous methylpredonisolone injection. On the basis of this experience, we investigated 20 consecutive patients with pathologically established hepatocellular carcinoma in our hospital and found another patient with CIDP using the criteria of the Ad Hoc subcommittee of the American Academy of Neurology. This patient also had motor sensory neuropathy and showed improvement after intravenous methylpredonisolone injection. Our two patients showed a motorsensory neuropathy affecting the four limbs. Their CSF contained high concentrations of protein and the study of conduction velocities and biopsied nerves showed demyelination.
We did not find anti-GM1 antibodies in either patient. As discussed in Antonie et al. the association of carcinoma and primary demyelinating neuropathy has seldom been reported. However, the cases reported by Antonie et al as well as us suggest the possibility that weakness or clumness, which is sometimes seen in patients with car- cinoma may be caused by CIDP, and these symptoms should not be misinterpreted as representing general weakness caused by malignancies. Further investigation with larger numbers of patients may be useful in determining the mechanism.

KAZUO ABE
PUMINOBUSUGAI
Department of Neurology, Osaka University Medical School, 2–2 Yamadaoka, Suita, Osaka 565–0871, Japan

Correspondence to: Dr Kazuo Abe, Department of Neurology, Osaka University Medical School, 2–2 Yamadaoka, Suita, Osaka 565–0871, Japan. Telephone 0081 6 879 3579; fax 0081 6 879 3579; email abe@neurol.med.osaka-u.ac.jp


Frequency, causes, and consequences of burns in patients with epilepsy

The increased incidence of burns in people with epilepsy has long been recognised. Previous surveys (via questionnaires in clinic or burn unit admissions) have identified cooking, showering, and heaters as the most common causes. The duration of epilepsy and frequency of seizures have been recognized as the greatest risk factors, compounded by lack of awareness and education among people with epilepsy about the risk of burns. The aim of this study was to determine the frequency, causes, and consequences of burns and scalds in patients with epilepsy. The population comprised patients with chronic epilepsy who were resident at the Chalfont Centre for Epilepsy (CCE). The residential part of the CCE consists of a series of houses that provide for varying degrees of independence in terms of self care. There is also a short stay tertiary referral inpatient assessment facility and a medical and nursing unit on site where any injury is documented and assessed.

The daily records of the Medical and Nursing Unit for the year June 1995–6 were examined and any record of a burn extracted and followed until it was recorded as healed. The records for the day of the burn were then examined to determine the cause of the burn and whether it was seizure related.

The residential houses were divided into three groups according to the level of self care of the patients within each. Dependency was largely governed by physical infirmity rather than by severity of the seizure disorder.

- **Dependent (98 residents)—** all meals and hot drinks provided and help given with personal care.
- **Intermediate (94 residents)—** all meals provided, some residents make their own hot drinks and there is a variable level of independence with personal care.
- **Independent (111 residents)—** independent with regard to hot drinks, personal care, and some meals.

The number of residents in each category were calculated at the end of the year and remained relatively constant during the 1 year period. Seizures occurring in all patients were recorded prospectively in seizure diaries.

The number of seizures in the same 1 year period (June 1995 - June 1996) were calculated from the case records of the 303 residents. The number of seizures in the 28 bed assessment unit could not be calculated for the year, as there was a high patient turnover with a median stay of 32 days. The number of seizures from the residential houses were therefore extrapolated to allow for the number of patients in the assessment unit. No burns occurred in the assessment unit, which was classified as dependent with regard to the level of care made available to the inpatients.

A \( \chi^2 \) test was applied to the number of burns occurring in houses of differing levels of dependence to examine the significance of observed variation. This was then repeated correcting for the median number of seizures per person, in the three groups.

The results are shown in the table. Whereas the frequency of burns is regarded as accurate, the number of severe burns may not have been seen and recorded. Information as to whether an injury was seizure related or not was unavailable in three, and the cause of the burn was unavailable in two cases. Of the severe burns, one required skin grafting with healing occurring over 3 months and one patient attended an accident and emergency department, but was not admitted, and the burn took 4 months to heal. Most of the severe burns were complicated by methicillin resistant Staphylococcus aureus (MRSA), infection, but healed uneventfully. Two other patients had burns that were also complicated by an infection but without growth of a particular organism. One received antibiotics and recovered quickly, the other was initially treated only with topical therapy and took longer to recover.

Most burns were related to seizures (19 of 34). This was particularly true of the more severe burns (five of six). A total of 18 631 seizures were recorded during the year meaning that about one seizure in every 980 resulted in a burn and one in every 3105 seizures resulted in a severe burn.

Most burns were caused by hot water injuries (25 of 34). More severe burns were mostly caused by larger quantities of water. Cookers, hot pipes, and heaters were rare causes of burns in this study.

There were significantly more burns in the more independent houses \((p<0.05)\). The median number of seizures per person in the more independent houses was also greater as residents were placed in houses according to their physical disability rather than on the severity of their seizure disorder. Correcting for seizure frequency abolished the significance of the effect of level of dependence on the number of burns \((p>0.1)\).

Burns are a serious but underrecognised complication of epilepsy. Previous studies have used two different approaches. The first has been to give patients attending an epilepsy clinic a questionnaire about any burns ever sustained. This method relies on the memory of the patient involved and therefore biases recording towards serious injuries. These studies also gave little idea of frequency, as there was no time limit imposed. The second approach has been to consider patients with epilepsy admitted to burn units. This again restricts the survey to severe burns. Neither method gives any idea of frequency as there is no set population with no calculation of the number of seizures over a period of time, hence no idea of level of risk.

The residents at the Chalfont Centre for Epilepsy live as normal a life as their level of disability allows. This means that some residents are not exposed to the same risk of burns as those living in the community. A
A quartet of Down’s syndrome, Alzheimer’s disease, cerebral amyloid angiopathy, and cerebral haemorrhage: interacting genetic risk factors

Since 1993 the ε4 allele of apolipoprotein E (apoE) on chromosome 19 has been recognised as the major genetic risk factor for sporadic Alzheimer’s disease. Deposition of amyloid β protein (Aβ) protein in the cerebral cortex is a key feature of Alzheimer’s disease and may be of pathogenic importance. Sporadic cerebral amyloid angiopathy often coexists with Alzheimer’s disease and involves the deposition of Aβ protein in leptomeningeal and cortical blood vessels. Both conditions may occur in Down’s syndrome, presumably because of the increased expression of β-amyloid precursor protein (APP) associated with trisomy 21, the chromosomal location of the APP gene. Intracerebral haemorrhage is the principal, though uncommon clinical manifestation of cerebral amyloid angiopathy. Studies have suggested that the apoE ε2 allele and also the ε4 allele may occur more often in patients with cerebral amyloid angiopathy related haemorrhage. We report, to our knowledge, only the second case of cerebral amyloid angiopathy related haemorrhage in Down’s syndrome and suggest that the patient’s neuropathology and clinical manifestations were modulated by interacting influences of the APP and apoE genes.

A 46 year old man with Down’s syndrome was found dead in his bed. There were no suspicious circumstances. He had a long history of well documented seizures on 800 mg sodium valproate a day. One month before his death he had had a left lower lobe pneumonia, from which he recovered well with intravenous antibiotic. He was cognitively impaired and there was deterioration in behaviour in the last few years of his life, necessitating placement in care. There was no family history of dementia or intracerebral haemorrhage. He took no antiplatelet or anti-coagulant medication and was not hypertensive. A necropsy was performed.

The patient had a typical Down’s syndrome facies. No head injury was apparent. There was evidence of bronchopneumonia in the left lung. There was no significant coronary atheroma and no evidence of congenital heart disease. Neuropathological examination disclosed a small brain (940 g) with a blemished lower posterior frontal subarachnoid space overlaying the frontal and parietal lobes of the right cerebral hemisphere. Coronal sections disclosed a large haematoma 7 cm × 5.5 cm × 5.5 cm lying superficially in the hemisphere beneath the subarachnoid haemorrhage. The middle third of the right cerebral hemisphere was expanded with a 5 mm shift of the midline structures and a supracallosal hernia to the left. There was extensive secondary haemorrhage into the tegmen-

tum of the midbrain and upperpons, as a consequence of brainstem compression due to raised intracranial pressure.

Histological examination of sections of cerebral neocortex stained by silver impregnation (modified Bielschowsky’s stain) disclosed numerous non-branching, sparse neuritic plaques. There were scanty neurofibrillary tangles. The age related neuritic plaque score and history of dementia gave a “definite” neuropathological diagnosis of Alzheimer’s disease according to the criteria of the Consortium to Establish a Registry for Alzheimer’s disease (CERAD). In sections from the haematomata wall there was extensive acute ischaemic necrosis in addition to the haemorrhage. Immunohistochemistry for Aβ protein (Dako mouse monoclonal antibody raised to residues 8–17 of Aβ protein) confirmed the presence of multiple plaques within the cortical ribbon and showed severe amyloid deposition in many blood vessels within the cortex and overlying meninges. Some blood vessels had narrowed lumens and others displayed a “double barrel” appearance, typical findings in cerebral amyloid angiopathy associated with Alzheimer’s disease.

There was microscopical evidence of previous haemorrhage in the form of multiple small intracortical glial scars with haemosiderin pigment in macrophages. In the sections examined there was no evidence of fibriinoid necrosis.

The apoE genotype of the patient was ε2/ε4, determined by analysis of DNA extracted from formalin fixed paraffin embedded brain tissue as described previously.

Only once before has a cerebral amyloid angiopathy related haemorrhage been reported in a patient with Down’s syndrome and Alzheimer’s disease. Indeed an analysis of death certificates listing Down’s syndrome as the underlying or a contributing cause of death did not document intracerebral haemorrhage among 793 cases examined from the United States during 1976. This seems surprising as Down’s syndrome is associated with both Alzheimer’s disease and cerebral amyloid angiopathy, the second predisposing to intracerebral haemorrhage. The studies on our patient may suggest some reasons why the expected quartet of features is a rare but aetiologically related occurrence.

Patients with Down’s syndrome have a shorter life expectancy because of excess mortality from haemorrhages, congenital heart defects, and respiratory tract infections. Although there is “premature” Alzheimer’s disease in patients with Down’s syndrome, predisposition to these other conditions can have an early fatal outcome.

Our patient was predisposed to Alzheimer’s disease not only because of his extra copy of the APP gene, but also because of his apoE ε4 allele. By the age of 40, virtually all patients with Down’s syndrome have neuropathological changes characteristic of Alzheimer’s disease. The increased dosage of the APP gene has been shown to produce increased serum concentrations of APP and the Aβ major form of APP—Aβ40 and Aβ42. The ε4 allele increases the risk of dementia in patients with Down’s syndrome. Indeed the combination of Down’s syndrome with the ε4 allele leads to very high deposition of Aβ protein in plaques. Possession of the ε4 allele also predisposes to deposition of Aβ protein in the cerebral leptomeningeal and cortical vasculature. Evidence currently suggests that the ε2 allele, although protective against Alzheimer’s disease, pre-
disposes to haemorrhage due to cerebral amyloid angiopathy.\textsuperscript{1,2} We previously found more than a threefold overrepresentation of both the $e2$ allele and the $2/4$ genotype in patients with cerebral amyloid angiopathy related haemorrhage and speculated that whereas $e4$ is a risk factor for deposition of $\beta$ protein in blood vessel walls, $e2$ is a risk factor for haemorrhage from amyloid laden blood vessels.\textsuperscript{3} Although $e2$ and $e4$ alleles are neither necessary nor sufficient for cerebral amyloid angiopathy related haemorrhage, these apoE alleles seem to be major susceptibility polymorphisms for cerebral amyloid angiopathy ($e4$) and cerebral amyloid angiopathy related haemorrhage ($e2$). Because the $e2$ allele is only 8% of the apoE alleles in the population, including the subgroup of patients with Down’s syndrome, it does not commonly coexist with the more closely related conditions of Alzheimer’s disease, cerebral amyloid angiopathy, and Down’s syndrome to produce cerebral haemorrhage.

In conclusion, we suggest that in this patient with Down’s syndrome, three copies of the APP gene, possession of the apoE $e4$ allele, and age (46 years) predisposed to Alzheimer’s disease and cerebral amyloid angiopathy whereas the apoE $e2$ allele predisposed to haemorrhage from the amyloid laden blood vessels.

MOMcC is supported by a Patrick Berthoud fellowship.

MARK O MCCARRON
JAMES A R NICOLL
DAVID I GRAHAM
Department of Neuropathology, Institute of Neurological Sciences, Southern General Hospital NHS Trust, Glasgow, UK

Correspondence to: Dr Mark McCarron, Department of Neuropathology, Institute of Neurological Sciences, Southern General Hospital NHS Trust, Glasgow G51 4TF, UK. Telephone 0044 141 201 2998; fax 0044 141 201 2998; email mmcran18@clinmed.gla.ac.uk


Chhabra hydrocephalus shunt: lessons for gravitational valves

Overdrainage is a significant clinical problem after shunting for hydrocephalus as confirmed by the UK Shunt Registry.\textsuperscript{4} Various devices have been developed to reduce the rate of CSF drainage in the upright position which have been assessed by the UK Shunt Evaluation Laboratory.\textsuperscript{5} The average price of a shunt varies from £175 to £650 in the United Kingdom. Surprisingly, the prices are higher in the developing countries.\textsuperscript{5} However, some local lower cost constructions are available and are reported to function well.\textsuperscript{6}

The Chhabra shunt is a low cost device, developed and manufactured in India, that incorporates a gravitational siphon preventing mechanism. In the vertical position one, two, or three (depending on performance level) stainless steel weighting balls press on a sapphire ball which closes the CSF flow aperture, increasing the shunt’s opening pressure (figure (A)). In the horizontal position the opening pressure is theoretically equal to zero mm Hg, as the balls fall away. A similar principle is applied in constructions of other “gravitational” shunts—namely, the Cordis horizontal-vertical LP valve, the newly designed dual-switch Miethke valve (Germany) and the Fuji, another low cost valve (Philippines).

We tested a sample of two Chhabra medium pressure shunts (containing two balls) using a 2 week evaluation protocol.\textsuperscript{1} Our main aim was to investigate the impact of posture (horizontal-vertical) on shunt pressure-flow performance. We also investigated how the fluctuations in proximal pressure, simulating the presence of naturally occurring waves of intraventricular pressure, may alter shunt function. Such waves may occur not only due to heart and respiratory function but also due to body movements during walking, jogging, etc.

The figure (B) shows two typical pressure-flow performance curves recorded in the horizontal and the vertical position. They represent two almost straight parallel lines. Their slopes depict the low hydrodynamic resistance of the shunt (1.3 mm Hg/ml/min) This is much lower than the physiological resistance to CSF outflow, which normally lies within the range 6–10 mm Hg/ml/min.\textsuperscript{7} The average operating pressure determined for the vertical shunt position was around 7 mm Hg and for the horizontal position it was 0.6 mm Hg. The area between these lines represents the possible operating range in all the intermediate body positions. Therefore, we conclude that the operating pressure of the shunt varies with the body position, as intended.
The main problem with this valve arises when the patient moves upwards and downwards. Such a situation has been simulated by the addition of a pulsating waveform of variable amplitude to the proximal pressure (frequency was controlled from 90 revolutions/min to 5 min). As a result, the lower end of the pressure-flow performance curve was consistently twisted to the left (towards lower pressures, figure (B)). In vivo, variations in intraventricular pressure, produced by an increased magnitude of the pulse waveform or repeated body movement, may accelerate the drainage rate, in some cases possibly leading to overdrainage. The above phenomenon is probably a common feature of all gravitational valves, which should always be implmented with caution, taking into account the usual risk factors for serious consequences from overdrainage (than cerebral mantle and a high brain compliance) and the possible lifestyle of the patient after surgery.

Contrary to other gravitational valves, the Chhabra shunt does not have any valve working with the weighting balls that would prevent the reflux of CSF from the peritoneal cavity to the ventricle. Therefore, CSE flux is possible, undoubtedly in the upside down position (albeit at a lower rate).

The behaviour of the valve in a strong magnetic field (1.5 T) does not exhibit any alarming variation. However, the artefact on MRI may be considerable.

In conclusion, the intentions of the designers of the Chhabra shunt to make it operate at a higher operating pressure in the vertical than the horizontal body position were confirmed during this evaluation. The shunt has a repeatable pressure-flow performance that does not differ from the performance of more expensive valves manufactured by the big western corporations. However, because the shunt has a very low resistance to flow, overdrainage may be a problem depending on the patient’s life activities. As a CSF from the peritoneal to the ventricular cavity is possible.

We are very grateful to Mr R Hayward and Dr P Mital for providing us with Chhabra shunts for evaluation. We thank the Department of Health Medical Devices Agency for funding the laboratory.

Mittal for providing us with Chhabra shunts for use from the performance of more expensive valves manufactured by the big western corporations. Therefore, CSE flux is possible, undoubtedly in the upside down position (albeit at a lower rate).

The behaviour of the valve in a strong magnetic field (1.5 T) does not exhibit any alarming variation. However, the artefact on MRI may be considerable.

In conclusion, the intentions of the designers of the Chhabra shunt to make it operate at a higher operating pressure in the vertical than the horizontal body position were confirmed during this evaluation. The shunt has a repeatable pressure-flow performance that does not differ from the performance of more expensive valves manufactured by the big western corporations. However, because the shunt has a very low resistance to flow, overdrainage may be a problem depending on the patient’s life activities. As a CSF from the peritoneal to the ventricular cavity is possible.

We are very grateful to Mr R Hayward and Dr P Mital for providing us with Chhabra shunts for evaluation. We thank the Department of Health Medical Devices Agency for funding the laboratory.

The UK Shunt Evaluation Laboratory and Academic Neurosurgical Unit, Addenbrooke’s Hospital, Cambridge, UK.

The UK Shunt Evaluation Laboratory and Academic Neurosurgical Unit, Addenbrooke’s Hospital, Cambridge CB2 2QQ, UK. email zc200@medschl.cam.ac.uk

The clinical manifestations in our patient et al (GalNAc-GD1a), a terminal trisaccharide bind to N-acetylgalactosaminyl GD1a (GalNAc-GD1a), a terminal trisaccharide identical to that of GM2. Jacobs et al did not test whether IgM anti-GM2 antibodies react with GalNAc-GD1a. By contrast, Kasunoki et al reported that a patient with Guillain-Barré syndrome had IgM antibody activity against both GalNAc-GD1a and GM2, but in whom no result of anti-CMV antibody was present. We had a patient with Guillain-Barré syndrome subsequent to acute cytomegalovirus hepatitis who had IgM antibodies both to GM2 and GalNAc-GD1a. We investigated whether the IgM anti-GM2 antibodies cross react with GalNAc-GD1a.

Three days after an episode of stomatitis, a 32 year old man noticed left sided facial weakness and dysaesthesia distally in his feet. Over a day, the facial weakness extended to the right side and dysaesthesia progressed to the limbs. He developed progressive weakness of the limbs on day 4, and the next day was unable to stand. On day 5, the patient presented with facial diplegia, severe limb weakness, and moderate reduction of superficial sensation distally in all four limbs. The respiratory muscles were slightly affected. Deep tendon reflexes were absent. Liver enzyme concentrations were raised slightly. Protein concentration in CSF was 109 mg/dl and cellularity was normal. High IgM anti-CMV antibody titres were found in both serum and CSF by enzyme linked immunosorbent assay (ELISA). An electrophysiological study suggested that the predominant process was demyelination involving the motor nerves. Right ulnar sensory nerve action potential was absent. Visser et al reported that patients with Guillain-Barré syndrome with associated cytomegalovirus were young and often developed severe sensory loss with facial nerve involvement and respiratory insufficiency. They also reported a strong correlation between cytomegalovirus infection and severe sensory loss. The clinical manifestations in our patient were similar to those reported by Visser et al.

Thin layer chromatography with immunostaining showed that the serum IgM from our patient reacted strongly with GM2 and GalNAc-GD1a, but not with GM1, GD1a, GD1b, or GT1b (fig 1). ELISA confirmed that his serum had high titres of IgM antibodies to GM2 (1:25 600) and to GalNAc-GD1a (1:12 800) on day 4. Plasmapheresis was performed on days 5, 6, 24, 27, and 29, he was able to walk without assistance on day 60, but his facial diplegia showed slow improvement. The IgM anti-GM2 (1:800) and anti-GalNAc-GD1a (1:800) titres in this patient were significantly reduced on day 39. In the absorption study his serum was added to separate wells coated with individual ganglioside antigens (GM2, GalNAc-GD1a, GM1, and GD1a). The absorption rate was calculated from (1−(optical density at 492 nm in the well with serum with absorption treatment)/(optical density in the reference well with serum without absorption treatment)). No IgM anti-GM2 antibody was absorbed by GM1 or GD1a (fig 2). By contrast, IgM anti-GM2 antibody was absorbed by GalNAc-GD1a. Larger studies are needed to confirm whether (1) some patients with Guillain-Barré syndrome after CMV infection have IgM anti-GalNAc-GD1a antibody and (2) that the anti-GalNAc-GD1a antibodies cross react with GM2.

This research was supported in part by grants in aid from the Ono Medical Research Foundation, Uehara Memorial Foundation, Ciba-Geigy foundation (Japan) for the Promotion of Science, the Nakabayashi Trust for ALS Research, the Ryouchi Naito Foundation for Medical Research, and a Research Grant for Neuromuscular Diseases from the Ministry of Health and Welfare of Japan.

MASAGO TSUKAGUCHI
YUMI TAGAWA
HIROAKI TAKEUCHI

Third Department of Internal Medicine, Kagawa Medical University, Kagawa, Japan

NOBUHIRO YUKI

Department of Neurology, Dokkyo University School of Medicine, Tochigi, Japan

Correspondence to: Dr H Tsukaguchi, Third Department of Internal Medicine, Kagawa University, Ikenobe 750-1, Miki, Kagawa, 761-0793, Japan.


Electrophysiological recordings in bilateral hemifacial spasm

Hemifacial spasm typically consists of unilateral involuntary spasms of the mimic muscles innervated by either facial nerve. There is some controversy whether mechanical irritation of the facial nerve entry zone by vessels in the cerebellopontine angle or hyperexcitability of the facial nerve nucleus is the main cause of this problem. The mechanism underlying the bilateral occurrence of spasms has not been investigated so far; either hyperexcitability of a facial nerve nucleus spreading to the contralateral side or independent mechanical irritation of both nerves might be involved. We report a patient with predominantly left sided spasms, electrophysiological diagnosis of bilateral facial spasm, the clinical course after surgical treatment according to MR evidence of elongated vertebral and basilar arteries, and implications of electrophysiological recordings on the pathogenesis of bilateral hemifacial spasm.

Electrophysiological recordings in bilateral hemifacial spasm

Hemifacial spasm typically consists of unilateral involuntary spasms of the mimic muscles innervated by either facial nerve. There is some controversy whether mechanical irritation of the facial nerve entry zone by vessels in the cerebellopontine angle or hyperexcitability of the facial nerve nucleus is the main cause of this problem. To our knowledge, only two cases of bilateral hemifacial spasm have been described in some clinical detail but without electrophysiological recordings. The mechanism underlying the bilateral occurrence of spasms has not been investigated so far; either hyperexcitability of a facial nerve nucleus spreading to the contralateral side or independent mechanical irritation of both nerves might be involved. We report a patient with predominantly left sided spasms, electrophysiological diagnosis of bilateral facial spasm, the clinical course after surgical treatment according to MR evidence of elongated vertebral and basilar arteries, and implications of electrophysiological recordings on the pathogenesis of bilateral hemifacial spasm.

This 60 year old male patient presented with a history of gradually increasing left eye twitching over the past few years. He did not notice involvement of other facial muscles or of associated symptoms such as hearing deficits, vertigo, or headache. Visual inspection showed frequent clonic involuntary synchronous contractions of his left orbicularis oculi and left orbicularis oris muscles. On voluntary contraction of the orbicularis oculi muscle, there was some synkinesis of the left orbicularis oris.
muscle and vice versa. There was no weakness of facial muscles or other neurological deficit. Four channel surface EMG recording from facial muscles was performed to ascertain the suspected diagnosis of left hemifacial spasm. Recordings gave evidence of irregular and asynchronous spasms of left and right facial muscles with higher frequency, amplitude, and longer duration on the symptomatic left side (fig 1A). Blink reflex recordings with stimulation of either supraorbital nerve showed bilateral R2 components also involving the orbicularis oris muscles of both sides (fig 1B); latencies of R1 and R2 components were in the normal range. Magnetic resonance imaging showed a grossly distended vertebral and basilar artery approaching first the right cerebellopontine angle and later in its course also the left cerebellopontine angle before taking its normal median position in its rostral segment (fig 2). This extraordinary course suggested a possible mechanical irritation of both facial nerves.

The patient thus had a neurovascular decompression on the symptomatic left side. During surgery, close contact of the basilar artery with nerve entry zones of the left facial and vestibulocochlear nerve was found. After interposition of a piece of ilon sponge, spasms of the left facial muscles disappeared almost completely leaving a slight left facial nerve paresis which cleared completely over the next months without functional deficit. There was a partial hearing loss on the operated side. Electrophysiological control recordings 4 months after surgery showed a reduction of the amplitude of compound muscle action potentials recorded from the left orbicularis oculi muscle. There was also a loss of facial synkinesis on the operated side, whereas spontaneous spasms and synkineses of the right facial muscles remained unchanged or even slightly increased (fig 1A). Right sided spasms have become more prominent also during clinical investigation; they have, however, so far not bothered the patient enough to warrant an additional contralateral operation.

Bilateral twitching of facial muscles most commonly occurs in blepharospasm; this focal dystonia may occasionally mainly present by contractions of the orbicularis oculi muscle of only one side as experienced by our patient. Even more so, in patients with bilateral hemifacial spasm a dystonic aetiology may be erroneously attributed and lead to unsuccessful treatment. Needle EMG recordings can be helpful in discriminating these diseases by showing unphysiologically high frequent discharges of motor units in hemifacial spasm. Needle EMG recordings can be helpful in discriminating these diseases by showing unphysiologically high frequent discharges of motor units in hemifacial spasm. With surface electrodes, simultaneous electrophysiological recording from facial muscles of both sides can differentiate this disorder from

---

Figure 1  Four channel surface EMG recording from orbicularis oculi and oris muscles. (A) Spontaneously occurring spasms of facial muscles. EMG bursts are synchronous on each side (representing synkinesis) but asynchronous with regard to the contralateral side. Before surgery, bursts are more frequent, of higher amplitude and duration on the clinically symptomatic left side. After surgery, spasms occurred only on the right side at increased frequency. (B) Blink reflex with electrical stimulation of the right supraorbital nerve. Before surgery, R1 components appear in both muscles on the stimulated side, R2 components are seen synchronously on both sides thus also involving the contralateral orbicularis oris muscle (same phenomenon also with stimulation on the left side). After surgery, synkinesis of the orbicularis oris muscles has disappeared. Arrow=wave of stimulation.
the rare bilateral hemifacial spasm by showing synchronous twitching of the muscles innervated by each facial nerve but asynchrony of muscle twitching between right and left facial muscles. In normal subjects and on the unaffected side of patients with unilateral hemifacial spasm R2 components of the electrical blink reflex are restricted to both orbicularis oculi muscles, but additional facial muscles are usually involved in patients with hemifacial spasm. This synkinesis of other muscles, which was found in this patient bilaterally, could be due to ephaptic transmission at the nerve entry zone or to facial nerve nucleus hyperexcitability; the immediate postoperative disappearance of synkinesis and abnormal R2 spread found in this case would thus be compatible with either suppression of ephaptic transmission at the nerve entry root or reduction of secondary facial nerve nucleus hyperexcitability. Both the asynchrony of spontaneous muscle bursts and the persistence or even increase of spasms on the less affected side after contralateral successful surgery in our case suggest independent trigger mechanisms on both sides most probably due to bilateral nerve entry zone irritation by aberrant vessels. Even with irritation of the nerve entry root being the probable primary cause, hyperexcitability of brain stem nuclei may also play a part; the reduced contralateral R2 component of the orbicularis oris muscle of the side contralateral to surgery (fig 1B) might be due to a loss of facilitatory effect of the operated side on the generation of this response.

A SCHULZE-BONHAGE
A FERBERT

Neurologische Klinik, Städtische Kliniken Kassel, Germany

Correspondence to: Professor A Ferbert, Klinik für Neurologie, Städtische Kliniken Kassel, Mönchebergstrasse 41–43, D-34125 Kassel, Germany.


CORRESPONDENCE

Depression and its relation to lesion location after stroke

The documentation of a 20% prevalence of depression after stroke1 has important therapeutic implications for patients with significant ischaemic heart disease and/or cardiac arrhythmia coexisting, either coincidentally or in an aetiopathogenic role, with stroke illness. In such patients therapeutic choices now need to be governed by the recognition that, despite comparable therapeutic benefit, adverse cardiac events such as sinus tachycardia, severe angina, and ventricular ectopy, are more likely to occur after tricyclic drugs such as nortriptyline, than after selective serotonin reuptake inhibitors such as paroxetine (p<0.03).1 Whereas nortriptyline causes a sustained increase in heart rate and a reduction in heart rate variability,2 the second being a marker of increased cardiac mortality risk,3 no such sequence occur after paroxetine.

O M P JOLOBE
Department of Medicine for the Elderly, Tameside General Hospital, Fountain Street, Ashton under Lyne, OL6 9RW, UK


MacHale replies:

We wholeheartedly agree with Jolobe’s comments on the need to treat depressive illness after stroke with appropriate antidepressants that have a low risk of cardiovascular side effects. Other studies using trazodone1 and other selective serotonin reuptake inhibitors such as citalopram2 have shown that these are safe and effective in the treatment of this condition. Unfortunately, the problem remains that the vast majority of patients with depressive illness after stroke remain untreated. Despite clear evidence of negative effects on recovery in functional status and cognitive performance3 it has been shown that inadequate and insufficient efforts at treatment had not influenced the prevalence of depression up to 5 years after stroke.1 The first important step therefore seems to be to encourage clinicians to recognise and treat depression after stroke, the second need to educate them about which are the appropriate medications to prescribe.

SIOBHAN MACHALE
Department of Psychological Medicine, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh EH3 9YW, UK


BOOK REVIEWS


Downloaded from http://jnnp.bmj.com/ on November 4, 2016 - Published by group.bmj.com
In Soho, there used to be a restaurant called Fatso’s. Here you could eat as many bowls of different pastas with creamy sauces as you could manage for a fixed price. I feel sure that I made a major contribution to its bankruptcy, quite soon after opening. Now, as well as eating different pastas with creamy sauces, I have evolved myself to increased risk of epilepsy, cerebral calcifications, dementia, peripheral axonal neuropathy, schizophrenia, anxiety, and depression. For these are some conditions apparently associated with coeliac disease and the risk of coeliac disease seems to be greatest in those consuming large amounts of gluten in wheat products, especially pasta. The most interesting chapter tracks the early stock, and I am sure I have encountered the same phenomenon in the process of writing an introduction to the literature. I came away hoping as a source to which to refer with comprehensive access in topographical and pathogenesis of coeliac disease. The neurology of this area is only just being uncovered and the remainder of the book is occupied by papers and case reports that introduce the possible range of the disease. The papers are illustrated by some good quality scans, and clinical and pathological photographs. The book should be useful to neurological therapists, and paediatric psychopharmacologists, who have not created a new science. Instead it provides a basis for the remainder of the book. This book is written mainly by an assistant professor of communication disorders, with contributions from 28 speech therapists, psychologists, doctors, physiotherapists, occupational therapists, and educators from different centres across the United States. It focuses on neurological disease and therapy, and has been compiled by 27 contributors who have been exposed to the Mayo Clinic experience over the past 30 years. The book consists of 18 chapters starting with pathophysiological and pharmacological concerns before considering the epidemiology, clinical presentation, investigations, and management of each chapter. Each chapter is written from a personal experience point of view, but is backed up by reference to the key literature in the subject. The chapter on the epidemiology of subarachnoid haemorrhage considers the difficulties in studying such patients, including access to selection bias and referral populations, etc., and I found this particularly useful. The Mayo Clinic is recognised for its surgical excellence of neurovascular conditions, and the authors have written the book to facilitate successful rehabilitation after subarachnoid haemorrhage, a subject which is often missing in textbooks of this type.

In summary, I found that this addition concerning subarachnoid haemorrhage is a useful addition to the neurovascular bookcase. I would recommend it to those with a mild surgical, neurological, or rehabilitation interest in neurovascular disorders.
Carbohydrate antigen 19–9 in cerebrospinal fluid and within malignant cells in a case of leptomeningeal carcinomatosis

YOSHIHIRO SATO, YOSHITAKA OHTA, MASAHIDE KAJI, KOTARO OIZUMI and MASAHIDE KAJI

J Neurol Neurosurg Psychiatry 1998 65: 402-403
doi: 10.1136/jnnp.65.3.402

Updated information and services can be found at:
http://jnnp.bmj.com/content/65/3/402

These include:

References
This article cites 4 articles, 1 of which you can access for free at:
http://jnnp.bmj.com/content/65/3/402#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes