An unusual case of Behçet’s disease presenting with bilateral internal carotid artery occlusion

Behçet’s disease (BD) is a multisystemic recurrent inflammatory disorder, which is originally described as a triad of oral and genital ulcerations with uveitis. As vasculitides of the vasa vasorum is the main pathological hallmark of BD, it is generally seen in the form of superficial thrombophlebitis or occlusion of major veins; however arterial obstruction and aneurysms may also be seen to a lesser extent. We present a patient with BD who developed bilateral internal carotid artery (ICA) occlusions.

Case report
A 43 year old, right handed male patient was referred to Ege University Neurology Department for evaluation of an acute onset right sided weakness, fever, headache, and difficulty with gait and speech in August 2001.

On admission, he was alert and fully oriented. His temperature was 38°C, pulse was regular (90/min), blood pressure was 150/80 mm Hg. His speech was severely dysarthric but he could name, repeat, read, and follow instructions. His cranial nerves and fundoscopic examination were normal. His gait was wide based and unsteady. He had four sided mild weakness, which was prominent on the right. Muscle stretch reflexes were normal but plantar reflexes were extensor bilaterally. His coordination was impaired in proportion to weakness in all four extremities. He had mild nuchal rigidity of the neck with positive Brudzniski’s sign. On physical examination, erythema nodosum like dark red, painful lesions were noticed on both anterior aspects of the legs. His ophthalmological examination did not reveal any signs of uveitis. He also complained of pain and fever in his scrotum, and urological examination showed swelling, induration, and marked tenderness of epididyma on both sides as the clinical findings of epididymitis.

His medical history showed that he had complained about recurrent oral aphthous lesions and aforementioned skin lesions for 8 to 10 years without medical consultation. He had no other medical history associated with BD. He was a moderate cigarette smoker for 20 years.

Laboratory tests were consistent with an inflammatory disease with a high erythrocyte sedimentation rate (100 mm 1st h) and C reactive protein (12.27 mg/dl; normal range 0–5 mg/dl) levels. CSF examination, serum immunoglobulin levels, platelet count, protein C, protein S, antithrombin III, C3 and C4 complement, rheumatoid factor, and lipid levels were within the normal range. Serum antineutrophil cytoplasmic and antineutrophil cytoplasmic and antinuclear antibodies were negative. ECG, 2D echo, chest radiograph, abdominal ultrasonography, and colour Doppler ultrasoundography of the lower extremity vessels were normal. Cranial magnetic resonance imaging showed diffuse cerebral atrophy and chronic ischaemic lesions in both cerebral hemispheres as well as the absence of the flow voids in both ICAs on T2 weighted axial images. Digital subtraction angiography (DSA) showed complete occlusion of the bilateral internal carotid arteries just rostral to the bifurcation (fig 1).

After consultation with the rheumatology clinic, a pathergy test was performed to confirm the diagnosis of BD and found to be positive. The patient was then transferred to the rheumatology clinic. He was treated with aspirin 300 mg/day, prednisolone 1 mg/kg/day, pentoxifylline 1200 mg/day, 750 mg pulse cyclophosphamide monthly for BD. He was also treated with oral antibiotics and analgesics for the episidymitis. Two months later, he had almost completely recovered.

Comment
Our patient had presented with unusual neurological findings for a classic stroke syndrome and MRI showed birehemispheric ischaemic lesions and bilateral ICA occlusion, which was also shown by DSA. It is known that cardiovascular risk factors, smoking, fibromuscular dysplasia, or moyamoya disease are frequently found as an aetiological factor in patients with bilateral ICA occlusion, whereas essential thrombocytopenia, giant cell arteritis, and BD are among the very rare causes.1, 2

Although our patient did not have cardiovascular risk factors except for smoking, he had been suffering from BD for about 10 years, which was not diagnosed before neurological presentation. His medical history, skin lesions, and urogenital findings supported with a positive pathergy test verified the diagnosis of BD according to latest diagnostic criteria for BD.3

Neurological involvement in BD has been reported to occur in 2.2% to 43% of cases in large series, either in the form of neuro-Behçet disease (parenchymal CNS involvement) or vascular-Beheçet disease (secondary or non-parenchymal CNS involvement) or both.2 Neuro-Behçet’s disease has a characteristic clinical picture with male predominance and typical cranial MRI findings of reversible inflammatory parenchymal lesions, attributable to small vessel disease, which may rarely be confused with those of MS.4 On the other hand, vascular-Beheçet’s disease is attributable to large vessel disease generally in the form of cerebral venous thrombosis and has limited symptoms with a better prognosis.5 Our patient’s neurological signs and symptoms were highly suggestive of neuro-Behçet; however CSF findings with acellularity and normal protein level and neuro-imaging studies showing ischaemic lesions and bilateral ICA occlusions supported a very unusual type of vascular-Beheçet.

Diffuse cerebral atrophy and survival with minimal or no neurological deficits in our patient is not infrequent in patients with bilateral ICA occlusion. This is explained by the adequate collateral flow provided by vertebrobasilar system and slow, gradual occlusion.6

Oclusive lesions in the bilateral ICAs, as seen in our patient, are extremely rare in BD and we suggest that this is a very unusual case of vasculo-neuro-Behçet’s disease. We also conclude that BD should always be remembered as an aetiological factor for bilateral ICA occlusions, especially in countries where the disease is highly prevalent.

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References
Miller-Fisher syndrome and Hodgkin's disease

Miller-Fisher syndrome (MFS) is a rare clinical entity classically regarded as a variant of Guillain-Barré syndrome (GBS) and is characterized by the clinical triad of ophthalmoplegia, ataxia and areflexia. In MFS, paralysis is restricted to extraocular and occasionally other cranial or bulbar muscles. We report on a patient with a relapsing Hodgkin's disease (type mixed cellularity, pathological stage IVB) who developed MFS. Conventional immunosuppressive and intravenous immunoglobulin treatments improved the neurological deficits. Millard and White (5) described a 27-year-old white man who had an eight year history of Hodgkin's disease (type mixed cellularity, pathological stage IVB) who had been receiving a salvage ESHAP regimen (etoposide VP-16 68 mg/day, methylprednisolone 500 mg/day, and cisplatin 42.5 mg/day for four days and cytosine arabinoside 3.4 g/day on the fifth day) since the first disease relapse four months before admission. He was admitted to the hospital for constitutional symptoms: fever, night sweats, fatigue, malaise, and weakness. There was no history of infection. General examination was unremarkable except for bilateral facial weakness. A laboratory workup including lymphocyte counts and increased levels of IgA and IgM antibodies to the GQ1b ganglioside in the cerebrospinal fluid protein and high titres of anti-GQ1b antibodies to the GQ1b ganglioside in the cerebrospinal fluid protein and high titres of anti-GQ1b antibodies. Serum immunoglobulin concentrations were increased (IgG: 19 g/l, normal 10.51 ± 2.9, IgA: 4.8 g/l, normal 1.65 ± 0.8). Gadolinium-enhanced brain magnetic resonance imaging of the head showed no abnormalities. There was neuropathological evidence of an axonal sensory neuropathy (sensory conduction in the right sural and median nerves was absent; motor and median motor compound muscle action potential 7.1 mV with a conduction velocity of 41.5 m/s). F wave latencies from the right posterior tibial, right common peroneal, right median, and ulnar nerves were minimally prolonged two days after onset but were within normal limits by three months. The patient presented moderate reduction of facial muscle action potentials. The blink response latencies were prolonged (1.5 ms, left: 1.3 mV, right: 1.4 ms, left: 1.2 mV). Blink R2 response latencies were normal (right: 29 ms, left: 29 ms). Masseter reflex was normal. The amplitude of the distal sensory evoked response was greatly reduced (upper extremity somatosensory evoked potentials to median nerve stimulation at the wrist). Brainstem auditory evoked potentials were normal. Intravenous immunoglobulin was given for five days at a dosage of 0.4 g/kg/day, starting 24 hours after the onset of symptoms. He gradually improved over the next two weeks. A follow up examination by our clinic found normal electrophysiological parameters were normalized, and IgA antibody titres to GQ1b were not detectable. Three months later, neurological examination and lumbar puncture results were normal, all electrophysiological parameters were normalized, and IgG antibody titres to GQ1b were not detectable. In Hodgkin's disease, the incidence of polyneuropathy is about the same as for the reticuloses in general—that is, approximately 1 or 2%. The major clinical picture of this patient was acute ataxia, ophthalmoplegia, and areflexia associated with increased cerebrospinal fluid protein and high titres of antibodies to the GQ1b ganglioside in the context of relapsing Hodgkin's disease, which suggests an autoimmune mediated neurological disorder. To our knowledge this is the first report on a patient with MFS evolving during a relapse of Hodgkin's disease. GBS and MFS occur in relation with conditions marked by an autoimmune mediated neurological disorder. To our knowledge this is the first report on a patient with MFS evolving during a relapse of Hodgkin's disease. GBS and MFS occur in relation with conditions marked by an autoimmune mediated neurological disorder. To our knowledge this is the first report on a patient with MFS evolving during a relapse of Hodgkin's disease. GBS and MFS occur in relation with conditions marked by an autoimmune mediated neurological disorder. To our knowledge this is the first report on a patient with MFS evolving during a relapse of Hodgkin's disease. GBS and MFS occur in relation with conditions marked by an autoimmune mediated neurological disorder. To our knowledge this is the first report on a patient with MFS evolving during a relapse of Hodgkin's disease. GBS and MFS occur in relation with conditions marked by an autoimmune mediated neurological disorder.
200 μV

200 ms

Computer. Frequent cramps occurred in the fingers and toes. There was painful tension in the calves, the feet, and the hands. The patient also complained of excessive sweating. These symptoms had progressively worsened. One year before presenting to us, he developed ptosis of the right upper eyelid, rapidly followed by vertical and horizontal diplopia. These symptoms were fluctuating with worsening in the evening. Repetitive stimulation of the facial nerve showed a decremental response, symptoms and signs disappeared after injection of prostigmine, and anti-AChR antibodies were found. It was concluded that the patient had ocular myasthenia and the patient was treated with oral methylprednisolone. Improvement was rapid and after a few weeks treatment was stopped. Two weeks before presentation, the patient again complained of right palpebral ptosis and diplopia. The symptoms were responsive to pyridostigmine bromide. The medical history was remarkable for ophthalmal migraine, arterial hypertension, and hypercholesterolaemia. Treatment consisted of fenofibrate and metoprolol. The family history was non-contributory.

Full blood count, serum creatinine, glucose, antinuclear antibodies were negative at a titre of 1:80. Prostate specific and carcinoembryonic antigens were negative. Both ACHR antibodies (26 nmol/ml, normal values less than 0.5 nmol/ml) and VGKC antibodies (1091 pmol/l normal values less than 100 pmol/l) were detected. Computed tomography of the chest was normal.

Nerve conduction studies showed evidence of a severe right-sided carpal tunnel syndrome, but otherwise they were normal. Needle electromyography revealed myokymic discharges in distal muscles of upper and lower extremities (fig 1). These discharges consisted of bursts of motor unit potentials, appearing as doublets, triplets, or multiple units with intraburst frequencies of 40 to 100 Hz. Burst recurrence was irregular with an interburst frequency of 5–8 Hz. There was evidence of mild chronic denervation with slightly reduced recruitment in distal muscles.

Anti-VGKC antibodies are found in approximately 40% of patients with acquired neuromyotonia,24 they are also found in patients with other neuromuscular hyperexcitability syndromes, such as cramp fasciculation syndrome, acquired rippling muscle syndrome, facial myokymia.25 In a significant proportion of these patients, coexistence of myasthenia gravis and neoplastic disorders, thyomina in particular, is observed.26 About 20% of all reported neuromyotonia patients had thyomina; 70% thereof also had myasthenia gravis and anti-AChR antibodies and 20% had anti-AChR antibodies without overt myasthenia gravis. The absence of anti- striated muscle antibodies and of radiological evidence of mediastinal tumour in a patient with neuromyotonia of nine years duration illustrates that the association of autoimmune neuromyotonia and myasthenia gravis can occur without thyomina.

Acute attacks and brain stem signs in a patient with glutamic acid decarboxylase autoantibodies

Glutamic acid decarboxylase (GAD) is a major autoantigen in type 1 diabetes mellitus and stiff-man syndrome. Patients with progressive cerebellar ataxia and GAD autoantibodies (GAD-Ab) have been reported,27 and the pathogenetic role for GAD-Ab in suppressing cerebellar γ-aminobutyric-acid (GABA)-ergic transmission has been discussed. We present a woman who eventually developed progressive cerebellar ataxia, but had stroke-like episodes and brain stem involvement during her clinical course.

A 63 year old woman suffered dizziness of sudden onset accompanied by nausea and vomiting. Her physician found horizontal, gaze evoked nystagmus. A few days later, she noticed transient horizontal diplopia, after which spontaneously all her symptoms gradually subsided. Two months later, she experienced intermittent vertigo when she turned her head and then unsteadiness of gait. Her past medical and family histories were unremarkable. On examination, she was fully conscious and had no general physical abnormalities. There was coarse horizontal nystagmus, coarser on the left side. On phonation, her posterior pharyngeal wall shifted rightward, indicating paralysis of the constrictor muscles of the left side of the posterior pharyngeal wall (signe de raidsou, Verne). She had ataxia in her left arm and leg and walked throwing the left leg outward. Although lesion in the left dorsal cortical lower brain stem was suspected, MRI and MR arteri and venous images were unremarkable. A routine blood examination, as well as glucose tolerance and thyroid function tests, detected no abnormalities. CSF analysis was normal with negative oligoclonal IgG bands and a
patients with progressive cerebellar ataxia have type I diabetes mellitus, the high serum by acute onset, exacerbations, and such signs progressed, accompanied by a gradual rise in independent gait returned. Ataxia, however, Abs titre decreased to 4700 U/ml, and left position of the plasmapheresis course, her GAD-

title was 496 U/ml. Intrathecal GAD-Ab titre may present with episodes that resemble multiple sclerosis or recurrent brain stem encephalitis.


cells because motoneurons in the nucleus ambiguous receive GABA mediated inhibition. 1 As speculated by Honnorat et al, 2 high GAD-Ab titre would merely reflect the presence of a more complex immune reaction against the nervous system. In this context, the subacute and atypical ataxia with high GAD titre raises the possibility that the GAD-Ab might have been a paraneoplastic phenomenon. Sillevis Smitt et al reported reversible cerebellar ataxia attributable to antibodies against a glutamate receptor in two patients with Hodgkin’s disease.3 At present, however, follow up examinations of this patient showed no evidence for malignancy. The case of our patient suggests that progressive ataxia with high GAD-Ab titre may present with episodes that resemble multiple sclerosis or recurrent brain stem encephalitis.

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References

High concentrations of sVCAM-1 and sICAM-1 in the cerebrospinal fluid of patients with intracerebral haemorrhage are associated with poor outcome

Intracerebral haemorrhage (ICH) accounts for approximately 10% of strokes and is a life threatening condition with a 30 day mortality rate of about 45%.1 The adhesion molecules cerebrospinal fluid and serum concentrations of adhesion molecules can be used as prognostic markers for the clinical outcome of patients with ICH. 2 3 They have been correlated with acute inflammatory and blood-brain barrier dysfunction.3 4 In this study, we investigated whether ventricular cerebrospinal fluid (CSF) and serum concentrations of adhesion molecules can be used as prognostic markers for the clinical outcome of patients with ICH. 2 For this purpose, we studied prospectively 10 patients with acute ICH and ventricular tamponade. Estimated blood volume of the ICH was between 40 and 60 ml in all patients. Initial intubation and mechanical ventilation due to coma were required in all patients. All of them were being treated at the neurological intensive care unit after neurosurgical application of a ventricular drainage to treat acute hydrocephalus. Paired serum and CSF samples from the ventricular drainage were obtained within eight hours after the first symptoms attributed to ICH and within three hours after operation. Concentrations of soluble ICAM-1 (sICAM-1) and sVCAM-1 were determined by enzyme linked immunosorbent assay (ELISA). In corresponding clinical examinations, the Scandinavian stroke scale and Glasgow coma scale scores were determined. The patients were categorized into two groups: patients who survived (n = 6) and patients who died (n = 4) from cerebral causes within eight weeks after the onset of ICH. Patients with prior cerebrovascular diseases and patients who subsequently died of non-cerebral causes were excluded from this pilot study. Data were analysed using the SPSS statistical program (SPSS, Chicago, Illinois, USA). The Wilcoxon test was applied to compare the two patient groups. The two patient groups (survivors versus non-surviving) did not differ statistically with regard to age, sex, location and size of ICH, and initial Glasgow coma scale and Scandinavian stroke scale scores. As fig 1 shows, the CSF concentrations of sICAM-1 and sVCAM-1 were below 13.7 ng/ml (mean (SD) 8.7 (4.7) ng/ml) and of sVCAM-1 below 35.4 ng/ml (11.5 (13.1) ng/ml) in the group of patients who survived (n = 6). However, in patients with a lethal outcome (n = 4), initial ventricular CSF concentrations of sICAM-1 were above 18.3 ng/ml (25.5 (9.3) ng/ml) and of sVCAM-1 were above 44.5 ng/ml (76.8 (45.0) ng/ml). These differences were significant for the CSF concentrations of sICAM-1 (p < 0.01) and of

Figure 1 Ventricular cerebrospinal fluid concentrations of [A] soluble intercellular adhesion molecule-1 (sICAM-1) and [B] soluble vascular cell adhesion molecule-1 (sVCAM-1) in two groups of patients who had intracerebral haemorrhage with ventricular tamponade. The patients are categorised into two groups: patients who survived (n=6) and patients who died (n=4) from cerebral causes within eight weeks after the onset of intracerebral haemorrhage.

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sVCAM-1 (p < 0.01). However, the concentrations of adhesion molecules in serum did not differ significantly (non-surviving: 444 (152) ng/ml for sICAM-1, 1422 (465) ng/ml for sVCAM-1; surviving: 463 (110) ng/ml for sICAM-1, 1147 (382) ng/ml for sVCAM-1).

This is the first study to investigate soluble adhesion molecules in CSF and serum in patients with ICH with ventricular tap. We found a strong correlation between clinical outcome and the concentrations of soluble adhesion molecules in the CSF of patients with acute ICH and ventricular drainage. Moreover, we found more than threefold increases of sICAM-1 and of sVCAM-1 in the CSF of patients with lethal outcome as compared with CSF in patients with acute ICH and ventricular drainage. However, based on our results, it can be speculated that these cells are already inside the ventricular CSF and thus out of reach of these antibodies. With these data of only 10 patients, it cannot finally be concluded whether the increased soluble adhesion molecules in CSF are indicators of the fatal process or are responsible for the initiation of secondary brain damage.

Acknowledgements
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plasma lactate were both 2.1 mmol/l and oligoclonal bands were not found. DNA was extracted from a blood sample and analysed for mtDNA mutations using standard procedures and was negative at positions 3243, 8344, 8993, 3460, and 14484, but with a homoplasmic mutation at position 11778.

Our patient had the mutation most often associated with MS-like CNS lesions and visual loss in women. Brain stem lesions have been previously described in a patient with visual loss, complete ophtalmoplegia, and bilateral tinnitus. However, to our knowledge, this is the first description of LHON in association with brain stem lesions presenting with respiratory arrest and loss of involuntary ventilation (Ondine’s curse). The high signal tract, which are part of the ventral and dorsal respiratory groups respectively, and would seem well placed to account for loss of respiratory control during sleep with well preserved capacity for volitional respiratory manoeuvres while awake. Ondine’s curse produced by lesions of these structures and their tract, through a variety of causes has been widely described. However, the exact nature of CNS lesions in patients with mitochondrial cytopathy remains obscure.

Our patient tolerated NIPPV. She improved on this regimen such that 123 days after starting NIPPV, she was able to take a few steps with a Zimmer frame and had successfully weaned off NIPPV support. This patient provides a further example of the broad manifestations of mitochondrial disease.

**Acknowledgement**

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**References**


### Table 1: Frequency of relapse of Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) following various immunisations

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>GBS Patients</th>
<th>Relapses</th>
<th>CIPD Patients</th>
<th>Relapses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>211</td>
<td>8 (3.8%)</td>
<td>46</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Tetanus</td>
<td>105</td>
<td>6 (5.7%)</td>
<td>23</td>
<td>2 (8.7%)</td>
</tr>
<tr>
<td>Typhoid</td>
<td>50</td>
<td>3 (6.0%)</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Polio</td>
<td>42</td>
<td>4 (9.5%)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>37</td>
<td>3 (8.1%)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>20</td>
<td>1 (5.0%)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Rabies</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>15</td>
<td>0</td>
<td>6</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td>BCG</td>
<td>8</td>
<td>2 (25.0%)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>12</td>
<td>2 (16.7%)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>16</td>
<td>1 (6.2%)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Cholera</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rubella</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>5</td>
<td>2 (40.0%)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Measles</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Smallpox</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mumps</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Some patients had received more than one vaccine.

The Guillain-Barré Syndrome Support Group, a British patient organisation, posted 3000 questionnaires to its members, asking them to identify their illness, record all immunisations administered after their illness, and describe any symptoms within six weeks of immunisation suggestive of recurrence of GBS or worsening of CIDP.

All but one of the patients who reported neurological symptoms after immunisation were contacted by telephone to confirm their history and to grade their symptoms using the modified Rankin scale. For the patient who could not be contacted by telephone, the patient’s consultant neurologist provided the information. Questionnaires were sent to the general practitioner for each patient who reported a “relapse” to confirm which vaccine had been administered.

A total of 1144 patients (37%) completed the questionnaires, of whom 927 had had GBS, 179 had CIDP, and eight were excluded because they had other diseases. Of the 927 patients with GBS, 311 had received immunisations since having GBS. Eleven (3.5%, 95% confidence intervals (CI) 1.8%, 6.2%) reported symptoms including increased fatigue, weakness, numbness, and paraesthesiae, but these were usually mild and no patient required hospitalisation or treatment.

In two cases symptoms came on within 24 hours of immunisation and all but one developed symptoms within one week of immunisation. One patient reported symptoms rendering him unable to walk unaided for two weeks, which increased his modified Rankin scale score from grade 2 to 4.

Influenza, tetanus, and typhoid were the most common immunisations associated with a relapse after GBS but the number of patients who reported symptoms was small compared with the total numbers receiving each of these vaccines (table 1). Although the results suggest that some vaccines that are administered less frequently (such as diphtheria) may be associated with a higher relapse risk, the numbers were small and most of these vaccines were administered at the same time as other vaccines.

Of the 311 patients with GBS who had received vaccines after having GBS, 29 had also received a vaccine in the six weeks before the onset of their initial illness. Two of these patients (6.9%, 95% CI 0.8%, 22.8%) had a recurrence of symptoms after a second, different, vaccine was subsequently administered.

Of the 179 patients with CIDP, 65 had been immunised after disease onset. Five reported worsening of neurological symptoms following immunisation. In three the symptoms were similar to a typical relapse of their CIDP, but only one of these patients required treatment within two months of immunisation. The other two patients with CIDP were immunised when already experiencing mild neurological symptoms, which then worsened, so that their modified Rankin scale scores had increased from 4 to 4 and they became dependent on a walking stick and unable to drive.

Of the patients with CIDP who experienced a relapse after immunisation, two relapses occurred among 23 patients who received the tetanus vaccine, giving a risk of relapse of 8.7%. Two of 46 (4.3%) patients with CIDP had relapses after influenza vaccine, of whom one had simultaneous pneumococcal meningitis. Two of six (33%) patients, including the last mentioned, experienced relapses after pneumococcus vaccine. Seventeen patients with CIDP had no symptoms of relapse following immunisation with typhoid vaccine. Between one and seven patients with CIDP had no
Hypoglycaemia induced by phenytoin treatment for partial status epilepticus

A 22 year old woman was admitted at our epilepsy unit in status epilepticus. On examination, seizures were characterised by a confusional state with little response to external stimuli, and recurrent, brief, tonic motor manifestations lateralised to the left side. Family history was negative for epilepsy and metabolic disorders. Full term birth was uncomplicated and first psychomotor developmental milestones were normal. In the past medical history there was no sign of any metabolic disturbance and no reports of cognitive dysfunction or personality disturbances. At the age of 16, the patient presented with epilepsy, which was characterised by two types of seizures: global tonic seizures, which occurred yearly, and brief episodes of loss of contact without any other manifestations, which were rare. The patient was treated for many years with 20 mg of clonazepam twice daily. The awake EEGs that were performed routinely during the years of treatment with clonazepam showed normal background rhythm with rare epileptiform discharges, characterised by irregular 2–3 Hz spike and wave complexes that were localised to both frontal–central regions. Magnetic resonance imaging of the brain, which was performed at the age of 18 years, showed no abnormalities.

On the day of admission at the epilepsy unit, the patient had an urgent EEG that revealed continuous, rhythmic spikes or spike and wave complexes over both frontal–central regions with right predominance. Emergency drug treatment with intravenous lorazepam 4 mg was performed twice with a 15 minute interval, but there was no change in the clinical status. Therefore, after 30 minutes, intravenous phenytoin 1000 mg was given by infusion over a period of 20 minutes, and then an infusion of 750 mg of phenytoin was set up for a period of 24 hours. Clinical symptoms and EEG abnormalities rapidly improved and completely resolved after 40 minutes from the start of the administration of phenytoin.

Nine hours later, while the medical observation was still ongoing, the patient developed an episode of severe mental clouding of consciousness, which was preceded by prodomal symptoms, including tachycardia, sweating, light headedness, and irritability. On examination, there was reduction of alertness, confusion, and tachycardia; there were areas of intermedial pupil diameter and reactive to the light. No focal neurological signs were observed. EEG monitoring did not show any abnormalities. Emergency blood tests revealed severe hypoglycaemia (<20 mg/dl). Prompt correction of the hypoglycaemia was obtained by the intravenous infusion of 50 ml of 50% glucose, and a consequent recovery of consciousness occurred. Phenytoin infusion was then withdrawn and oxcarbazepine was titrated. In the following days no further episodes of hypoglycaemia were noticed. The patient was therefore investigated with the oral glucose tolerance test, which showed normal levels of plasma glucose, immunoreactive insulin, and immunoreactive insulin/plasma glucose, and with insulin suppression test which did not show evidence of pancreatic insufficiency.

Comment

We have described a patient who experienced a severe episode of hypoglycaemia induced by intravenous phenytoin, which was administered at the doses recommended for the treatment of status epilepticus. It is known that phenytoin interferes with glucose metabolism. Indeed, it may inhibit the release of glucose stimulated insulin and induce a consequent hyperglycaemia. The ability of hypoglycaemia to escape from the inhibitory effects of phenytoin on insulin secretion or an increased sensitivity of the tissues to insulin. The striking finding of our case is that the hypoglycaemia is induced by a therapeutic dose of phenytoin, and, to our knowledge, this is the first case of severe hypoglycaemia during treatment with phenytoin for status epilepticus. In this case we have indeed excluded a different aetiology of the hypoglycaemia. In particular, a possible effect on glycaemia produced by status epilepticus, has been considered not relevant, because the status epilepticus was partial and resolved nine hours before the onset of hypoglycaemia. However, we cannot rule out hypoglycaemia when a therapeutic dose of phenytoin was administered is unclear, and further studies are needed to fully investigate the effects of phenytoin on carbonhydrate metabolism.
α-Synuclein is a presynaptic protein highly and broadly expressed in the brain but its normal function is unknown.\(^1\) and its association with sporadic Parkinson's disease (PD) is not clear. However, studies have suggested that \(\alpha\)-synuclein remains unknown. Lee \(\alpha\) et al recently reported that overexpression of \(\alpha\)-synuclein in human neuroblastoma cell line retards cell death induced by serum withdrawal or hydrogen peroxide. This suggests that the dose of \(\alpha\)-synuclein may influence neuronal viability. Thus, in Japanese, allele 1 may be associated with high expression or low degradation of \(\alpha\)-synuclein.

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