Chronic inflammatory demyelinating polyneuropathy during treatment with interferon-α

Interferon-α (IFN-α) is widely used for the treatment of chronic viral hepatitis. There have been some reports concerning the development of autoimmune diseases, particularly thyroid disease, in patients under treatment with IFN-α. Disorders including autoimmune haemolytic anaemia, pernicious anaemia, thrombocytopenia purpura, systemic lupus erythematosus, Raynaud’s disease, parotiditis, and epididymitis have been reported. Some neurological problems have also been described; although most such adverse events have involved the CNS, several cases of peripheral nervous system involvement have been reported—namely, axonal polyneuropathy, neuralgic amyotrophy, multiple mononeuropathies, and myasthenia gravis. On the other hand, some authors have reported that IFN-α may be an effective alternative therapy in patients with chronic inflammatory demyelinating polyneuropathy (CIDP) who are refractory to conventional treatments. Two trials using IFN-α and IFN-β 12 have recently been published. We describe one patient who developed CIDP during IFN-α treatment.

A 29 year old man who had hepatitis C for 2 years, was started on IFN-α treatment. He had the usual related flu-like syndrome during the first month of treatment. Previously he had had some migraine headache episodes, but no other medical problems. After 4 months of treatment, he progressively developed paraesthesia and weakness in both feet. When he came to our hospital 4 months later, his condition had worsened. Neurological examination disclosed tetraparesis (proximal and distal) with 4/5 strength (Medical Research Council scale), generalised areflexia, and hypoaesthesia both in his hands and feet. EMG data are summarised in the table. Prolonged motor latency rather than conduction velocities, temporal dispersion of the compound muscle action potentials (CMAPs), marked prolongation of F wave latencies, and a reduction of sensory and motor CMAPs in both arms and the right sural nerve were found. These findings were consistent with a demyelinating polyradiculoneuropathy with a mild axonal degeneration. The protein concentration in CSF was 208 mg/dl, there were no cells. Immunoelectrophoresis was normal, and antiangioliside antibodies (GM1, GD1a, GD1b, GT1b) were absent. Serum biochemical studies, including HIV antibody determination, were negative. We ruled out the presence of cryoglobulins. Although IFN-α was discontinued, the disease continued to worsen; the maximal neurological deficit was reached 5 months from onset. The patient was given prednisone (60 mg/day) and progressively improved. One year later he had no symptoms and showed areflexia only on neurological examination. A further EMG showed appreciable improvement.

This is the first report of CIDP development during treatment with IFN-α. CIDP is an immune mediated disorder that usually responds to plasma exchange, intravenous gammaglobulin, or corticosteroids, although occasionally the disease is refractory to these therapies. In the past, some authors have reported improvement in patients with CIDP who were receiving IFN-α. The mechanism by which IFN induced improvement in these patients is uncertain, although it may be related to complex immunomodulating effects, possibly by reduction of proinflammatory cytokine concentrations (tumour necrosis factor and IFN-γ) which may have a role in the development of inflammatory demyelination. The relation between IFN-α and CIDP in our patient is uncertain. Whether IFN-α was the cause of CIDP or whether their relation was only coincidental remains uncertain. Nevertheless it seems clear that the treatment mentioned above did not prevent the development of this demyelinating disease with an immunological basis. IFN-α exerts complex immunomodulator effects, it can improve or worsen autoimmune diseases.

Although our findings could be coincidental, the data suggest caution, as IFN-α treatment might yield undesirable effects involving autoimmune phenomena.

Mª Eugenia Marzo
Mar Tintore
Oriol Fabregues
Xavier Montalban
Agustin Codina
Unit of Clinical Neuroimmunology, Department of Neurology, Hospital Vall d’Hebron, Barcelona, Spain
Correspondence to: Dr Xavier Montalban, Unit of Clinical Neuroimmunology, Department of Neurology, Hospital Vall d’Hebron, Psg Vall d’Hebron 119-129, Barcelona 08015, Spain. Fax 0034 3 4274700; email xmontal@ar.ub.es


Nerve conduction studies

<table>
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<th>Sensory:</th>
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<tr>
<th>F wave:</th>
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<td>Right common peroneal</td>
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Posteroventral pallidotomy can ameliorate attacks of paroxysmal dystonia induced by exercise

Paroxysmal exercise induced dystonia is a rare disorder classified as one of the paroxysmal dyskinesias. In this condition patients develop dystonia, mostly involving their feet, after prolonged exercise, usually walking or swimming. Treatment response is poor to botulinum toxin and antiepileptic drugs. For example, anticholinergic drugs, muscle relaxants, or acetazolamide. We recently noted the dramatic benefit of unilateral pallidotomy about attacks of paroxysmal exercise induced dystonia of the contralateral foot in one patient.

This 47 year old woman was followed up for over 15 years for a 10 year history of attacks of dystonia affecting her right foot, induced by exercise. At onset the attacks were mild and were induced by walking long distances. During an attack her right foot would invert for a few minutes making it difficult for her to continue walking or standing. The attack would subside within 2–3 minutes on resting. Two years after onset the attacks subsided and she was attack free for 3–4 years. Four years ago the attacks returned and got progressively worse, increasing in frequency and intensity. Over the past 2 years she could have an attack on walking even 10–15 steps. The attacks in the past few years not only made her right foot to stop but caused her to fall as the right leg would rise up in the air and flex at the knee and hip and there would be some involvement of the trunk causing her spine to twist to the left. Recently the toes of the left foot were also normally of attacks. She would never lose consciousness and the attacks would last 1–2 minutes and then subside. They never occurred in sleep. Internally the neurological examination was normal although posturing of the right foot could be induced by repeated prolonged passive flexion-extension movements of the right ankle. More recently she also began to have occasional spontaneous attacks. Investigations including repeated MRI of the head and spine were normal as were tests for Wilson’s disease and other causes of secondary dystonia. Examination of CSF gave normal results and disclosed no oligoclonal bands. The patient was negative for the common mitochondrial mutations. An EMG/nerve conduction study detected no evidence of a peripheral neuropathy and somatosensory evoked potentials were normal. Neurophysiologically confirmed cocontraction of agonists and antagonist muscle pairs in the right leg during an attack supporting an organic basis for the dystonia. Surface EEG during an attack and interictally disclosed no abnormality. The patient was tried on a variety of treatments including baclofen, levodopa, benzoxel, tetrabenazine, and acetazolamide without benefit. Different antiepileptic drugs were given individually or in combination (1g sodium...
Sudden appearance of invalidating dyskinesia-dystonia and off fluctuations after the introduction of levodopa in two dopaminomimetic drug naïve patients with stage IV Parkinson’s disease

Hypermotias (dystonia, dyskinesia) are, with fluctuating akinesias, the most debilitating disturbances appearing during the advanced course of Parkinson’s disease.1 The origin of these disturbances is controversial; as hyperkinesias are seen after long-term treatment with levodopa or dopaminomimetic drugs many researchers think that these motor fluctuations could be prevented by dopaminomimetic drug restriction,2 others think that hyperkinesias will appear anyway after enough years, independently of dopaminomimetic drug restriction—that is, the supersensitivity of striatal structures to external administration of dopaminomimetic drugs is an epiphenomenon.3

Ten years apart from one another we had the chance to observe two patients with Parkinson’s disease with prevalent akinetiform symptoms who came already in an advanced stage of Parkinson’s disease, classified as stage IV according to the Hoehn and Yahr scale.4 These patients had never been treated with dopaminomimetic agents (levodopa, dopamine agonists, anticholinergic drugs, and both developed dyskinesias and motor fluctuations when levodopa was increased to the amounts commonly used in patients with stage III–IV Parkinson’s disease for years.

Patient 1 was a 76 year old man living in the inner mountainous part of central Italy. When he came to us he was incapable of rising from his bed, head kept down, akinesia, flexed dystonic posture, and rigidity were rated 20 at motor examination with the unified Parkinson’s disease rating scale (UPDRS),5 modest 4–5 Hz tremor was present at the upper limbs, left and right intensity was rated 4 at the UPDRS, and utterances were feeble and incomprehensible. The total UPDRS score was 126 (SD 4).

It was possible to reconstruct his clinical history from relatives, and apparently his early stooped posture and akinetiform disturbances had appeared at least 10 years before, but was considered to be due to severe arthrosis and was treated with appropriate analgesics.

Brain MRI at admission was normal. Early treatment with 62.5 mg levodopa thrice daily+benserazide did not induce gastrointestinal intolerance but did not change his UPDRS score and was rapidly (4 days) increased to 250 mg levodopa four times daily+benserazide. Oromandibular dyskinesias, dystonic neck and trunk leftward rotations, and left leg dyskinesias were noticed 2 days after the 1.5 mg levodopa dosage was reached. Dystonic-dyskinetic movements appeared 20–30 minutes after the first (7.00 am) 250 mg levodopa+benserazide tablet, lasted through the day, and were painful, mostly in the levodopa intake. His UPDRS scores were 72 (SD 3) from 8.00 am to 2.00 pm, 88 (SD 3) from 2.00 pm to 8.00 pm. Dyskinesia-dystonia scores were 11 (SD 2) from 0.00 am to 1.00 pm and 13 (SD 2) from 2.00 pm to 10.00 pm. Because these dyskinetic-dystonic movements were not tolerated, the daily levodopa had to be reduced to 62.5 mg every 3 hours (total 375 mg/day).

With this treatment UPDRS scores were 86 (SD 4); oromandibular dyskinesias and
torsional dyskinesias were still present and rated 10 (SD 2). Bromocriptine up to 10 mg/day was not tolerated. During the next 2 years levodopa treatment could not be increased. His UPDRS scores were 89 at 2 weeks before his sudden death due to apparent cerebrovascular complications with cardiac arrest. A postmortem examination showed anteroinferior myocardial infarction, and normal brain structures with depigmentation of the nigral structure. Mesencephalic structures were cut into horizontal 7 mm thick sections and stained with haematoxylin and eosin; three Lewy bodies were found in 109 identified pigmented cells and cell loss was about 86% compared with age matched controls and literature reports.

Patient 2 was a 72 year old man from the same region of central Italy. He came to us akinetic and rigid, with a stooped posture and minor tremor of both upper limbs, and was confined to a wheelchair. Utterances were feeble and incomprehensible. His total UPDRS motor score was 93 for upper limbs, rest tremor was only 2. He had been incapable of walking during the past year, and spent his time on a chair, with both his relatives described the progressive deterioration in the past 10 years, from the stooped posture to progressive akinesia and language and walking deterioration. His disturbances were contributed to severe oculomotor disability, in comparison with other patients with Parkinson’s disease living in the same region, prompted the neurological consultation. This patient was treated with increasing doses of levodopa+benserazide after the first week with 125 mg thrice daily had not changed his UPDRS score. A 1.5 g daily dose of levodopa (in 6 administrations) was reached in the next week. Oromandibular dyskinesias and leftward torsional dystonias appeared in the same way.

He became able to walk unaided but tremor of the upper limbs was still present, at rest and during walking. His dyskinesias were uncomfortable, although not painful, and his stooped posture was only slightly modified (score 3 from 4). His UPDRS score during treatment was 57, tremor score was 4, and dyskinesias and dystonia score was 7 (SD 1). Treatment was then reduced to 0.2 g thrice daily+benserazide with 15 mg ropinirole (increasing in three weeks from 1.5 mg/day). With this treatment dyskinesias were reduced, UPDRS score for dyskinesias was 4 in the morning, 5 in the afternoon, and his hand was able to write and take his breakfast with salicylates in the morning. His UPDRS score during treatment was 65 (SD 4) in the morning and 79 (SD 2) in the afternoon. Brain MRI was normal.

In conclusion, both patients came to us with a levodopa responsive parkinsonism that had appeared, according to history reconstruction, at least 10 years before. Both could be considered at least in stage IV of the Hoehn and Yahr scale.1 Both had never been treated with dopaminomimetic drugs or with other drugs currently used in the treatment of Parkinson’s disease. In both patients dyskinesias and dystonias, accompanied by motor fluctuations throughout the day, appeared in the last week. After that these fluctuations worsened, and modified the akinesia and rigidity scores were reached. Reduction of levodopa dosage in patient 2 and introduction of a dopaminomimetic drug improved dyskinesia but the total UPDRS score was higher than the score obtained with 1.5 g/day levodopa.

These findings favour the hypothesis suggesting that hyperkinesic fluctuations are not dependent on prolonged dopaminomimetic drug administration but on the natural
Reversible hydromyelia in a synchronised swimmer with recurrent thoracic girdle pains

Synchronised swimming is considered a low impact, competitive aquatic sport for all ages, although stress related symptoms such as knee or shoulder pain are common. In favour of this viewpoint is the finding that MPTP exposed parkinsonian patients had severe loss of dopaminergic neurons and developed dyskinesias rapidly after starting levodopa therapy. Caveats about this conclusion must be placed, relative to the fact that both patients had prominently akinetic disturbances, and thus prevalent tremorogenic parkinsonisms might have different courses with different occurrences of complications during levodopa treatment.

MARCIO ONOFRJ
CRISTINA PACI
ASTRID THOMAS
Department of Oncology and Neuroscience, University of Chieti, Italy

Correspondence to: Professor Marco Onofrj, Clinica Neurologica, Ospedale Clinico Città “SS Annunziata”, Università “Gd’Annunzio”, Via Vestini, 66100 Chieti, Italy. Telephone: 0039 871 562019; email onofrj@ibmpune.unich.it or onofrj@phobos.unich.it


chemists and is used mainly as a rodenticide (rat poison). We report an unusual case of barium carbonate poisoning. The nerve and muscle electrophysiological studies were reported for the first time in barium carbonate intoxication.

A 19-year-old boy presented to a hospital emergency department with sudden onset tetraplegia. He was referred to our centre as a case of Guillain-Barré syndrome. The patient presented with tingling in the right upper arm, which was immediately followed by weakness in all four limbs. The weakness progressed and involved trunk muscles also within a few minutes. There was no history suggestive of bulbar or facial nerve involvement.

Motor unit action potentials, cranial nerves, and sensory and cerebellar examination were normal. Examination of the motor system showed a power of 0/5 globally. No deep tendon reflex could be elicited. Surprisingly, with complete areflexic paralysis there was increased tone in the lower limbs. A diagnosis of Guillain-Barré syndrome was considered, but there were some pointers against this diagnosis. The onset and progression to tetraplegia was very rapid and the weakness started from the upper limbs followed by that of the lower limbs. Increased tone in the lower limbs was also not consistent with the diagnosis of Guillain-Barré syndrome.

Routine blood investigations at the time of admission, including serum electrolytes, were normal. Nerve conduction study showed normal distal latency of the compound muscle action potential and motor nerve conduction. Amplitude of the compound muscle action potential was low on proximal and distal stimulation. No conduction block, dispersion of compound muscle action potential, or F-wave response was recordable. Sensory conduction studies on median and ulnar nerves at both sides of the body were normal for distal latency and amplitude of sensory nerve action potential. No H-reflex was recordable on stimulation of posterior tibial nerves on both sides. The patient now disclosed that he had accidentally consumed barium carbonate (15 g) on the day before admission. He ingested barium salt by mistake thinking it as dieting food given to him by a slimming centre. Ingestion was followed immediately by profuse vomiting. One hour later, the patient had watery diarrhoea. Four hours later when taken to hospital where this stomach was washed out with magnesium sulphate solution. Blood investigations repeated 8 hours after admission showed normal blood counts, blood gas analysis, and renal and liver function tests. Serum potassium was normal. On day 2, the patient had watery diarrhoea. Four hours later, the patient had diarhea and vomited. On day 3, the patient had severe anaemia, toxic gastritis, and acute pancreatitis. She was alert without any mental disturbances. Laboratory data disclosed metabolic acidosis and hypokataemia of 126 mmol/l. She received bicarbonate and physiological saline intravenously to compensate for the metabolic disturbances. Serum sodium increased to 136 mmol/l within 3 days. On the third day she suddenly developed severe choreoathetotic movements.

Central pontine myelinolysis causes bilateral loss of deep sensitivity and pseudochoreoathetosis

Central pontine myelinolysis is characterised as symmetric and selective destruction of myelin sheath of the basis pontis. Central pontine myelinolysis often results from rapid increase of serum sodium concentration. Patients with central pontine myelinolysis often show symptoms such as conscious disturbances, tetroplegia, and pseudobulbar palsy. We present a case of central pontine myelinolysis due to compensation of hypernatraemia, resulting in acute onset of pseudochoreoathetosis and sensory disturbances.

A 39-year-old woman was submitted to a department of internal medicine of another hospital due to a long history of alcoholism, resulting in bad general condition accompanied by severe anaemia, toxic gastritis, and acute pancreatitis. She was alert without any mental disturbances. Laboratory data disclosed metabolic acidosis and hypokataemia of 126 mmol/l. She received bicarbonate and physiological saline intravenously to compensate for the metabolic disturbances. Serum sodium increased to 136 mmol/l within 3 days. On the third day she suddenly developed severe choreoathetotic movements.

Therefore she was transferred to our department of neurology. On the day of submission to our department she remained alert, but she had difficulties in swallowing and speaking. Examination of the cranial nerves showed bilateral ptosis and a dissociated nystagmus on the left side. We also found weakened corneal and pharyngeal reflexes. There was a general reduction of deep tendon reflexes and muscle tone. Muscle strength was normal. Involuntary movements were absent but angle positioning during hypnagogicREM sleep was choreoathetotic. She was unaware of the position of her limbs with closed eyes. We instructed her to watch her limbs and she was able to reach her nose with the finger. When investigating her sensitivity we found a complete loss of touching, vibration, and position sense in all limbs. Pannick sensation was unremarkable in the upper limbs, whereas testing of the legs caused a painful burning sense. Motor sensation and...
sensitivity of her face were normal. We excluded tabes dorsalis and vitamin B12 deficiency by laboratory tests. Cranial CT was normal. T2 weighted MRI showed a hyperintense lesion within the pons but no extrapontine myelinolysis (figure). Within 4 weeks the subject’s symptoms had nearly disappeared. Only a slight reduction of the vibration sense in all limbs persisted. Control MRI after 4 weeks disclosed an unchanged size of the patient’s pontine lesion. At that time nerve conduction velocities and somato-
sensory evoked potentials, which, due to technical reasons, were only performed after the patient’s recovery, were normal.

To our knowledge this is the first reported case of central pontine myelinolysis associated with acute onset of movement disorder and isolated affection of proprioceptive sensitivity. The appearance of parkinsonism, dystonia, or choreoathetosis in the course of central pontine myelinolysis are often looked on as symptoms of additional manifestation of extrapontine myelinolysis. The association with manifestation of central pontine myelinolysis remained speculative in some cases of delayed onset of movement disorders after central pontine myelinolysis. By contrast our patient showed an acute onset of pseudochoreoathetosis after manifestation of central pontine myelinolysis and MRI imaging in our subject disclosed no signs of extrapontine myelinolysis.

Our patient additionally showed an isolated loss of proprioceptive sensation. Disturbances of sensation are described as less severe symptoms of central pontine myelinolysis. Silver et al described an association of sensory ataxia and affection of vibration and position sense, but with reduced pinprick sensation. This case may imply a further extension of the pontine lesion or a possible extrapontine lesion, not detectable on MRI. Defebre et al reported two cases of central pontine myelinolysis with isolated affection of deep sensation. Isolated affection of the medial lemniscus of the brain stem or thalamic infarction may cause sensory ataxia and disturbances of deep sensitivity resulting in choreoathetotic movements. Therefore, we speculate that our patient’s pontine lesion caused sensory ataxia and subsequent pseudochoreoathetosis, because the movement disturbances appeared without delay after the onset of sensory defects. Moreover, the loss of proprioceptive sensitivity with spared thermal and pain sensation implies an isolated alteration of the medial lemniscus by sparing the spinothalamic tract. This finding suggests a lesion with a pontine site. We found no extrapyramidal lesion by MRI in our patient. In conclusion we hypothesise that the pontine lesion itself may be a possible cause of our patient’s pseudochoreoathetotic movements.

JENS FEDERLEIN
THOMAS POSTERT
HORST PRZUNTEK
THOMAS MÜLLER
Department of Neurology, Ruhr-University Bochum, St. Josef Hospital, Gudrunstrasse 56, 44791 Bochum, Germany

Correspondence to: Dr Thomas Müller, Department of Neurology, Ruhr-University Bochum, St Josef Hospital, Gudrunstrasse 56, 44791 Bochum, Germany.


T2 weighted MRI (A) sagittal, and (B) axial scan after acute onset of pseudochoreoathetosis: high signal in the central part of the pons.
Successful treatment of peripheral paraneoplastic neurological syndromes in small cell cancer

Immune mediated paraneoplastic neurological syndromes often become manifest before the underlying malignancy is detected. As a rule, these phenomena do not improve with antineoplastic treatment.1 We report on a case of a patient with small cell cancer with peripheral neurological symptoms that responded favourably to combination chemotherapy.

At the time of admission the patient, a 66 year old woman, had had a combination of peripheral neurological symptoms for 3 months: (a) muscle weakness and muscle pain of the legs so that she could not walk unattended; (b) a numbness of both legs from the foot to the middle of the thigh; (c) dryness of the eyes and mouth; and (d) severe constipation.

Clinical examination showed a load dependent, proximally accentuated symmetric muscle weakness and hypoaesthesia of the legs. The patient was unable to stand or walk without support. The deep tendon reflexes of the arms were decreased on both sides and leg reflexes could not be elicited. No pathological reflexes were detectable. Analysis of CSF yielded normal values for protein content, cell number, and glucose. Besides a slightly increased erythrocyte sedimentation rate (35 mm in the first hour), standard laboratory values showed no abnormalities. Abdominal auscultation and CT were unremarkable.

Electrophysiological investigation (somatosensory evoked potentials of the tibial and median nerves, EMG, and electroneurography) showed normal amplitudes of P100 (tibial SEP), N10, and N13 potentials (median SEP) and polyphasic muscle action potentials. Nerve conduction velocities were on the border of the normal range for the motor peroneal and tibial nerves as well as for the sensory sural nerve. Stimulation of the ulnar nerve with 20 Hz yielded an increment of 60%. Besides a polynuropathic picture, the result of the electrophysiological examinations suggested Lambert-Eaton myasthenic syndrome.

Computed tomography showed a small metastasis of an undetectable primary tumour in a mediastinal para-aortal lymph node, which was immediately resected and histologically identified to be small cell cancer. As an autoimmune paraneoplastic origin of the neurological symptoms, particularly Lambert-Eaton myasthenic syndrome, was suspected, we measured autoantibodies against presynaptic voltage gated calcium channels by immunoprecipitating against presynaptic voltage gated calcium channels by immunoprecipitating

Table 1 Clinical, electrophysiological, and immunological variables before and after chemotherapy in a patient with small cell cancer

<table>
<thead>
<tr>
<th>Time of admission</th>
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<tr>
<td>Tumour diameter</td>
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<td>ANA titre on IgG</td>
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<tr>
<td>Anti-Hu titre</td>
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<tr>
<td>Pseudo-obstruction</td>
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<td>Ability to walk unattended</td>
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<td>Number of legs</td>
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<td>Antibodies against VGCC</td>
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<td>Electromyography at 20 Hz</td>
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ANA=antineuronal antibody; VGCC=voltage gated calcium channel.

As treatment with 3,4-diaminopyridine (10 mg every 4 hours) improved the muscle weakness but had no effect on constipation and the sensory disorders, these symptoms were thought to be unrelated to Lambert-Eaton myasthenic syndrome. Therefore, the anti-Hu titre was reduced to 1:32; immunoprecipitation for antivoltage gated calcium channel antibodies yielded 22.7 pM, which is within the normal range. Antineuronal antibodies were barely detected on sections of rat cerebellum at a serum dilution of 1:32. The anti-Hu signal was also clearly reduced on a western blot. The clinical, physiological, and laboratory findings before and after chemotherapy—that is, six months after admission—are summarised in the table. Combination chemotherapy brought about a considerable and unexpected improvement of two peripheral neurological syndromes (Lambert-Eaton myasthenic syndrome and anti-Hu syndrome with gastrointestinal pseudo-obstruction, muscle pain, and sensory deficits) and a reduced titre of autoantibodies in a patient with small cell cancer.

The results of treatment for paraneoplastic neurological syndromes are still discouraging, despite widespread use of chemotherapy combining antineoplastic and immunosuppressive activity. The reasons for the frequent failures may be irreversible loss of neurons due to autoimmune attack against the neoplasm without response. Therefore, all efforts should be directed at identifying the underlying malignancy. As soon as the presence of a tumour is confirmed, chemotherapy should be started to control its growth and to suppress autoantibody production, at least outside the CNS.

The skillful technical assistance of Mrs S Weier is gratefully acknowledged. We thank Drs P Eichhorn and M Wick for determination of antineuronal antibodies, Dr J Posner for determination of anti-Hu, Dr J Dalmau for critically reading the manuscript, and Ms B Jensen for copy editing it.

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VIKTOR ARBUSOW
Department of Neurology, Ludwig-Maximilians University Munich, Klinikum Großhadern, D-81366 Munich, Germany

RAYMOND D VOLTZ
Department of Neurology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021, USA

MICHAEL STRUPP
Department of Neurology, Ludwig-Maximilians University Munich, Klinikum Großhadern, D-81366 Munich, Germany

PETER SCHULZ
Department of Neurology, Ludwig-Maximilians University Munich, Klinikum Großhadern, D-81366 Munich, Germany

Correspondence to: Dr V Arbusow, Department of Neurology, University of Munich, Klinikum Großhadern, Marchioninistrasse 15, D-81377 München, Germany. Telephone 0049 89 7095 2585; fax 0049 89 7095 8883; email mstrup@GMP99M.fso.med.uni-muenchen.de


Cerebral disease with more prominent left sided cerebral involvement may be more closely associated with psychiatric phenomena; a comprehensive review of cerebral laterality in relation to psychosis has suggested that a special, although unclear, pathophysiology may be at work. A review of patients with treated Parkinson’s disease found an overall incidence of psychiatric side effects of 20% (range 10–50) in 908 patients treated in major studies.1

Psychosis—that is, hallucinations and delusions—occurred with a frequency of 4% and were more likely to occur with concurrent dementia, increasing age and use of higher doses of levodopa. It is assumed that the main precipitant of psychotic phenomena in Parkinson’s disease is dopaminergic excess secondary to treatment. Cognitive impairment, which has been reported to occur in as many as 29% of patients with Parkinson’s disease, associated with increased age and older age at onset, may also increase vulnerability to psychosis.

Asymmetry in Parkinson’s disease is said to remain unchanged over time,1 and patients with unilateral onset of Parkinson’s disease manifestations have greater degeneration of the contralateral substantia nigra at postmortem examination.2 If predominantly left sided pathology increases the vulnerability to psychiatric phenomena then initial right sided predominance of parkinsonian symptoms and signs might be a predictor of increased vulnerability. If initial right sided symptom predominance did indeed predict the subsequent development of psychotic phenomena (independent of cognitive decline, age, and medication) this might be clinically useful in identifying a patient subgroup in whom particular care is required in titrating medication.

A retrospective review of all cases notes of patients with Parkinson’s disease, identified by their presence on the specialist Parkinson’s disease nurse register in a district general hospital, was carried out (a) to evaluate the presence of psychotic symptoms using a checklist, (b) to record asymmetry of parkinsonism both current and at onset, and (c) to record handedness. Psychotic symptoms (delusions and hallucinations) were only noted when they occurred outside an acute confusional state. All patients had been diagnosed by one of two consultant neurologists. The level of medication, both current and while having psychotic symptoms, cognitive assessment, number of years of illness, and demographic variables were also recorded. Patients who had had a psychotic episode were compared with the remainder with respect to asymmetry of symptoms at onset of illness, age, duration of illness, medication levels and demographic variables. This was repeated with a subgroup of patients with no cognitive deficit. Logistic regression analysis (forward stepwise) was carried out with psychosis as the dependent variable.

The case notes of 100 patients were reviewed. There were 51 men and 49 women in the sample. Fifty one patients were right handed, four were left handed, and in 45 handedness was unknown. Dementia was noted in 30 patients, and psychotic episode in 14. The association between psychosis and cognitive decline was also confirmed. Details of illness, for the whole sample and the cognitively intact subsample, with psychosis as the dependent variable were compared with the remainder with psychosis as the dependent variable. Logistic regression analysis (forward stepwise) was carried out with psychosis as the dependent variable.

Comparison of side of onset with psychosis provided support for our a priori hypothesis that right sided onset of parkinsonian symptoms having psychotic symptoms, although this was not significant (χ²=3.0, df=1, p=0.09; table). Presence of psychosis was significantly associated with presence of cognitive decline. Eighteen out of 38 in the cognitively impaired group were psychotic by comparison with 12 out of 62 in the cognitively intact group (χ²=13.5, df=1, p<0.003). Presence of psychosis was also associated with duration of illness (t=2.69, df=36, p<0.02). There were no significant differences between the psychotic symptom group and the other patient groups in age, age at onset of symptoms, and dosage of current medication. Comparative dosage of levodopa and selegiline are shown in the table. Benzhexol, bromocriptine, pergolide, and orphenadrine were taken by 10, 14, 13, and seven patients respectively, and showed no differences between the groups. Furthermore there were no significant differences in the dosage of antiparkinsonian medication and the dose noted when undergoing a psychotic episode.

Cognitive decline was associated with increasing age but was not related to age of onset or dosage of medication. Patients with cognitive decline (n=38) were removed from the analysis, right sided onset of symptoms was significantly related to the presence of psychosis (χ²=5.0, df=1, p<0.03) in the remainder. In this subsample there were no significant differences between left and right side onset for age, duration of illness, or dosage of different medication.

Logistic regression analysis of the total sample, with psychosis as the dependent variable, confirmed the association between psychosis and cognitive decline (χ²=3.89, p=0.003) and increased duration of illness (t=2.64, p<0.02). There were no other significant contributing variables, although side of onset was the strongest associated variable remaining (r=1.69, p<0.09). However, when the logistic regression was repeated with the subsample without cognitive decline, right sided onset was the only variable significantly associated with psychotic symptoms (r=2.30, p<0.03).

Our results show only a trend, in the sample as a whole, linking right sided symptoms at onset and the subsequent development of psychosis; perhaps unsurprising in view of the confounding effect of cognitive impairment. In the cognitively intact subsample there was a significant association with right sided onset of symptoms of Parkinson’s disease. This suggests that damage to left hemispheric structures involved in Parkinson’s disease is associated with a predisposition to psychosis. Our results do not support an iatrogenic dopaminergic excess as a cause of psychosis; this may be because of subsequent dosage adjustment, or the explanation may lie in asymmetric upregulation of dopamine receptors and supersensitivity to dopaminergic therapy at equivalent doses of medication.

The limitations of using retrospective data are well recognised and the possibility of mild cognitive dysfunction not being detected in the cognitively intact group needs to be recognised. However, this preliminary study provides support for our a priori hypothesis that right sided predominance of neurologically deficit at the onset of Parkinson’s disease predicts the subsequent development of psychosis.
We thank Dr Margaret Barrie and Dr Rodney Walker for permission to review cases of patients under their care. We thank Vanessa Brigham, specialist Parkinson's disease nurse, for access to her case register.

SUKHWINDER S SHERGILL
Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London, UK

ZUZANA WALKER
CORNELIUS LE KATONA
Department of Academic Psychiatry, University College London Medical School, London, UK

Correspondence to: Dr SS Shergill, Clinical Research Fellow, Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK.

1 Flor-Henry P. Cerebral basis of psychopathology. Bristol: John Wright; 1983.

Cerebral venous sinus thrombosis associated with 2010A mutation of the prothrombin gene

Predisposing factors can be identified in up to 80% of patients who develop cerebral venous thrombosis (CVT).

1 In many patients risk factors are acquired but 10 to 15% of patients may have inherited tendencies to thrombosis. Deficiencies in protein C, protein S, or antithrombin are reported in large series. The recently identified factor V Leiden mutation (FVR506Q) giving rise to activated protein C resistance is one of the most prevalent genetic mutations currently identified (10% to 15% of the white population), and it is now known to be an important risk factor for cerebral venous thrombosis.

2 All of these thrombophilias, and particularly by the factor V Leiden mutation, are compounded by other factors such as the oral contraceptive pill, pregnancy, pueperium, or immobility.

3 Prothrombin is a precursor of the serine protease thrombin and is a key enzyme in the process of haemostasis. Recently, a single nucleotide substitution (G to A) at position 20210 in the 3' untranslated region of the prothrombin gene encoding prothrombin has been identified. Its heterozygous state, 2010A, is a risk factor for the development of deep vein thromboses, and it has recently been implicated in the development of superior sagittal sinus thrombosis in a woman taking the oral contraceptive pill.

4 We report the development of extensive cerebral venous thrombosis in a patient, without other risk factors, who was found to be heterozygous for this newly identified genetic mutation.

A 46 year old man had headaches for 2 weeks which became acutely worse and were associated with vomiting and dizziness. His conscious level fluctuated but was progressively deteriorating. He had a generalised tonic-clonic seizure and a history of a spontaneous deep vein thrombosis. There was no family history of CVT.

He was obtunded with bilateral papilloedema. There were no focal signs except for a right extensor plantar. Unenhanced brain CT was normal but a lumbar puncture disclosed a pressure of 34 cm of CSF with 28 000 red blood cells, 40 white blood cells/mm³ and a protein concentration of 1.5 g/l with normal glucose. A repeat brain CT with contrast showed diffuse swelling in the posterior fossa, with supratentorial and infratentorial haemorrhages and high attenuation around many of the venous sinuses. Brain MRI disclosed extensive thrombosis of the superior sagittal sinus, the straight sinus, and both transverse and sigmoid sinuses. There was haemorrhage in the left cerebellar hemisphere and haemorrhagic lesions in the left parietal and both cerebellar hemispheres.

Full blood count and biochemistry were normal. The erythrocyte sedimentation rate was 24 mm in the first hour and C reactive protein was 2.1 mg/l (normal-0). Autoantibodies including antinuclear antibodies were negative. Treponemal pallidum haemagglutination test and rapid plasma reagin tests were negative. The prothrombin time and activated partial thromboplastin time were normal. A thrombophilia screen was performed 24 hours after starting heparin (table). Initial antithrombin activity was reduced at 70% but was normal when repeated 4 months after the initial presentation; however, the patient was found to be heterozygous for the 2010A prothrombin gene mutation. This was identified using the polymerase chain reaction (PCR) of exon 14 and the 3'-untranslated region of the prothrombin gene, followed by restriction digestion by Hind III. The mutant allele then appeared as an extra DNA fragment on agarose gel electrophoresis. The presence of the 20210A allele was subsequently confirmed by PCR using factors. To the list of inherited thrombophilias as a cause of CVT seem to be rare in the absence of other factors, with only the patient with protein S deficiency in the series of Deschients et al and other occasional cases4 having no other predisposing factor.

The identification of an inherited thrombophilia in a patient with CVT should not, therefore, preclude a search for other provoking factors. To the list of inherited thrombophilias should now be added the newly identified 2010A prothrombin gene mutation.

Table: Results of thrombophilia screening

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Laboratory normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin gene (2010A) mutation</td>
<td>Heterozygous</td>
<td>Negative</td>
</tr>
<tr>
<td>Factor V Leiden mutation</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>Antithrombin III activity (%)</td>
<td></td>
<td>85</td>
</tr>
<tr>
<td>Antithrombin III (4 months later) (%)</td>
<td></td>
<td>66</td>
</tr>
<tr>
<td>Protein C activity (%)</td>
<td></td>
<td>79</td>
</tr>
<tr>
<td>Protein S free antigen (%)</td>
<td></td>
<td>87</td>
</tr>
<tr>
<td>Protein S total antigen (%)</td>
<td></td>
<td>3.05</td>
</tr>
<tr>
<td>Activated protein C resistance ratio</td>
<td>4.1</td>
<td>0.0–1.4</td>
</tr>
<tr>
<td>IgG anticardiolipin antibodies (GPL U/ml)</td>
<td>1.3</td>
<td>0.0–1.6 MPL U/ml</td>
</tr>
<tr>
<td>IgM anticardiolipin antibodies (MPL U/ml)</td>
<td>1.16</td>
<td>0.9–1.1</td>
</tr>
<tr>
<td>Russell’s viper venom ratio 50/50</td>
<td>1.01</td>
<td>0.9–1.1</td>
</tr>
<tr>
<td>Platelet neutralisation ratio (%)</td>
<td>1.16</td>
<td>0.0–1.2</td>
</tr>
</tbody>
</table>

Cell membranes, the clinical presentation of CVT, is slower than that of arterial thrombosis. The thrombotic tendencies arise when concentrations are less than 60% of normal. The initial concentration was probably secondary to the acute thrombosis or treatment with heparin. Repeat testing after 4 months showed normal concentrations, hence we think that antithrombin deficiency is unlikely to be implicated in this patient’s CVT. There were no other risk factors for venous thrombosis in our patient, unlike the recently reported patient with sagittal sinus thrombosis, who was taking the oral contraceptive pill.

Activated protein C resistance due to the factor V Leiden mutation is the most common hereditary thrombophilia associated with CVT, although in most cases it is also associated with an acquired prothrombotic tendency, such as the oral contraceptive pill. In a recent study of 40 patients with CVT, Activated protein C resistance with the Leiden mutation was found in four patients, proving C deficiency in one, and normal in another.1 Isolated hereditary thrombophilias as a cause of CVT seem to be rare in the absence of other factors, with only the patient with protein S deficiency in the series of Deschients et al and other occasional cases4 having no other predisposing factor.

The identification of an inherited thrombophilia in a patient with CVT should not, therefore, preclude a search for other provoking factors. To the list of inherited thrombophilias should now be added the newly identified 2010A prothrombin gene mutation.
Pseudo-Argyll Robertson pupil of patients with spinocerebellar ataxia type 1 (SCA1)

A pseudo-Argyll Robertson pupil is a neurological sign indicating a normal near reflex but the absence of a light reflex (light-near dissociation), a lack of miosis, and pupil irregularity. It has been reported in patients with diabetes mellitus, multiple sclerosis, Wernicke’s encephalopathy, sarcoidosis, tumors, and hemorrhage. Although the appearance of pseudo-Argyll Robertson pupil is very similar to Holmes-Adie pupil, the first is distinguishable from the second by the location of lesions and pharmacological response. The responsible lesion in pseudo-Argyll Robertson pupil is in the central region, whereas that of Holmes-Adie pupil is peripheral. Dilute pilocarpine constricts the pupils of patients with Holmes-Adie pupil, but it is not effective in patients with pseudo-Argyll Robertson pupil. We present a patient with spinocerebellar ataxia type 1 (SCA1) and her asymptomatic younger brother who both exhibited pseudo-Argyll Robertson pupil.

Patient 1 was a 21 year old woman who complained of gait instability in 1996. Thereafter, she noticed difficulties in speech and in the fine movement of her hands. Her mother had similar disturbances since her 20s and died of pneumonia at the age of 35. The condition of our patient deteriorated gradually, and she was admitted to our hospital in April, 1997. Neurological examination showed bilateral mydriasis (7.0 mm in diameter) and light-near dissociation (figure). Although the light reflex was absent, the near reflex was normal. The extraocular movements were saccadic and the upper gaze of both eyes was slightly limited. Optokinetic nystagmus was absent. Her tongue showed atrophy and fasciculation. The distal muscles of the limbs were slightly weak, although muscle tone was normal. The deep tendon reflexes were augmented in her upper and lower limbs. Babinski’s and Chaddock’s signs were positive on both sides. The sensory system was normal. Her speech was ataxic; slight limb ataxia was detected in the hands; and her gait was wide based and ataxic. Blood and urine laboratory findings were normal. Her pupils reacted to 1% pilocarpine, but not to 0.2% pilocarpine. Brain MRI showed remarkable atrophy of the cerebellum and a slight atrophy of the pontine tegmentum. **“Technetium-hexamethylpropyleneamine oxime (****Tc-HMPAO) SPECT disclosed a hypoperfusion of the cerebellar vermis,pons,and basal ganglia.**

Patient 2 was a 20 year old man, the brother of patient 1. He consulted our clinic for examination, although he had not experienced any neurological problems. He received dialysis three times a week because he had renal failure due to pyelonephritis. On examination, he presented pupillary abnormalities which were similar to those of patient 1 (mydriasis; 6.5 mm, light-near dissociation). Although the light reflex was absent, the near reflex was normal. His upward gaze was slightly limited. Fasciculation was noted on his tongue. The distal portion of the upper limbs was slightly weak and the deep tendon reflexes in the limbs were slightly accentuated. Babinski’s sign was positive in both feet, although there were no signs of spastic or ataxic movement in his limbs and in his gait. Their father showed no abnormalities on neurological examination.

Blood was collected for molecular studies with informed consent from both patients and their father. Total DNA was extracted by the phenol/chloroform method from peripheral blood leucocytes. To detect CAG expansion in the SCA1 region, we performed a polymerase chain reaction (PCR) with Rep-1 (5’ AACTGGAAATGTGGGCAGTCTGAG 3’) and Rep-2 (5’ AACTGGAAATGTGGGCAGTCTGAG 3’) according to Orr et al.** The products of PCR were separated by electrophoresis (2% agarose) with ethidium bromide staining. Patients 1 and 2 showed the CAG repeat expansion in the SCA1 gene. A sequencing analysis for patient 1 indicated a CAG repeat number of 60/27 (Dr Igarashi, Niigata University).

Pupillary reactions are divided into light reflexes and near reflexes. The light reflex pathway reaches the Edinger-Westphal nucleus through the pretectal nucleus. The near reflex consists of both the convergence reflex and the accommodation reflex. Their pathways are different from that of the light reflex until they reach the Edinger-Westphal nucleus. Therefore, it may be that the lesion for light-near dissociation is located between the pretectal nucleus and the Edinger-Westphal nucleus. Although the pupillary diameter is reduced in the Argyll Robertson pupil, mydriasis was seen in our patients. A patient with similar pupillary abnormalities (pseudo-Argyll Robertson pupil) has been reported by Olsen et al. The causative disorder of the patient reported by Olsen et al was congenital ocular motor paralysis. They attributed the pupillary abnormalities to the aberrant reorganization of the oculomotor nerve. In Holmes-Adie pupil, the reaction to a parasympathomimetic agent (0.2% pilocarpine) can usually be confirmed. Our patient 1, however, did not respond to 0.2% pilocarpine. Therefore, there was no denervation supersensitivity in the post-ganglionic parasympathetic nerve fibre after the ciliary ganglion. The most plausible explanation for the mydriasis in our patients is the dysfunction of the pre-ganglionic parasympathetic nerve fibre connecting the ciliary ganglion and the Edinger-Westphal nucleus. It is conceivable that the near reflex is maintained through a different pathway. Dasco et al have divided the Edinger-Westphal nucleus into the rostral and caudal portion, with the rostral portion relating to the light reflex and the caudal portion relating to the near reflex.

Patients with SCA1 present mydriasis and occasionally the absence of a light reflex. However, light-near dissociation has not been reported in any of these patients. Gilman et al have reported a postmortem case of SCA1 in which they found neuronal loss and a marked gliosis of the periaqueductal grey matter as well as a neuronal loss of the Edinger-Westphal nucleus. These pathological changes may cause light-near dissociation. Further detailed examinations of the pupillary abnormalities in SCA1 patients are eagerly anticipated.

KAZUNORI MABUCHI
HIROAKI YOSHIKAWA
MASAHARU TAKAMORI
Department of Neurology, Kanazawa University School of Medicine, Kanazawa, Ishikawa, Japan

HIDEHIRO YOKOJI
Department of Neurology, Noto General Hospital, Japan
Correspondence to: Dr Hiroaki Yoshikawa, Department of Ophthalmology, Kanazawa University School of Medicine, Kanazawa, Ishikawa, Japan


“Non-neuroleptic malignant” syndrome

We report on a patient with the clinical and biochemical features of the so-called neuroleptic malignant syndrome, occurring more than a decade after her last exposure to neuroleptics, while taking the cyanoxyrolone zopiclone. We consider possible mechanisms underpinning the development of this clinical syndrome in the light of these findings and current models of basal ganglia dysfunction.

A 62 year old woman was found collapsed at home. On admission to hospital she was alert, eye opening and moving limbs spontaneously, but her affect was flat and she was unable to give any account of herself. She was pyrexial (38.9°C) and clinically dehydrated with a pulse rate of 110/min and a blood pressure of 90/60 mm Hg. She was mute and afebrile with a jaw tremor, but there was no muscle tenderness. There was profound axial and limb rigidity with opisthotonic posturing, and that our patient may have had increased brain GABA activity as a result of zopiclone (with or without nitrazepam) treatment, resulting in increased pallidodialamatic inhibition and enhanced conduction in the indirect pathway, whereas reduced pallidodialamatic inhibition, results in hyperkinesia. For this model, it is of note that a selective loss of indirect pathway GABA/enkephalinergic neurons influencing basal ganglia output through a sequence of connections involving the external segment of the globus pallidus and the subthalamic nucleus, providing a negative feedback to the subthalamic nucleus and the ventral tegmental area. In this model, GABAergic basal ganglia output through the indirect pathway is increased; for example, hypokinesia is thought to result from increased pallidodias- thamic inhibition and enhanced conduction in the indirect pathway, whereas reduced pallidodios thamic inhibition, results in hyperkinesia. For this model, it is of note that a selective loss of indirect pathway GABA/enkephalinergic neurons is found in Huntington’s disease, and that GABAamimetics (propranolol) have been reported to improve onset fluctuations in Parkinson’s disease. Hence, in the light of this model, we suggest that our patient may have had increased brain GABA activity as a result of zopiclone (with or without nitrazepam) treatment, resulting in increased pallidodialamatic inhibition and enhanced conduction in the indirect pathway, and producing profound hypokinesia in the absence of recent neuroleptic treatment.

A J LARNER, SARAH C SMITH, SIMON F FARMER Department of Neurology, St Mary’s Hospital, Praed Street, London, W2 1NY, UK

Correspondence to: Dr A J Larnar, National Hospital for Neurology and Neurosurgery, Queen Square, London, WCIN 3BG, UK, Fax 0171 829 8720.


Corpora amylacea in hippocampal sclerosis

I read with pleasure the short report of Van Paesschen et al. This finding perhaps may raise some interest again in corpora amylacea as well as in the pathology of temporal lobe epilepsy. As I studied corpora amylacea for about 25 years I call the attention of the authors to the first—but important—finding of Ramsey who published in her article in 1965 a case of a 35 year old man who had intractable temporal lobe epilepsy. Surgical intervention was performed with temporal lobe resection including 3 cm of hippocampus. The pathologist’s report stated that the tissue seemed histologically normal except for a few areas of pyknosis and shrinkage of neurons and a decrease in the number of neurons in hippocampus. The presence of corpora amylacea without gliosis was noted and was especially prominent in the hippocampus. The diagnosis was “mild probable cortical atrophy of the temporal lobe with corpora amylacea in the hippocampus.”

I studied the occurrence of corpora amylacea in 1407 cases of various diseases with special reference to the so called predisposition sites of corpora amylacea, and I sometimes found large numbers of corpora amylacea in the hippocampal area and other regions with and without special pathology, even in young people. The conditions which favor the development of corpora amylacea vary greatly (aging, chronic vascular—hypo—diseases, ALS, multiple sclerosis, dementias, etc) as well as various pathogenetic mechanisms promoting formation, which included chronic hypoxia, neuronal degeneration, external hydrocephalus—as a consequence of local cortical atrophy—diabetes mellitus, and other processes which induce stress states expressed by strong HSP 60 positivity in our investigations. So the corpora amylacea formation really is an epiphenomenon in different diseases, as Van Paesschen et al state.

Letter

R F Gledhill
Department of Neurology, MEDUNZA and Gu-Rankuwa Hospital, South Africa
Correspondence to: Professor R F Gledhill, Department of Neurology, PO Box 108, Medunsa 0204, South Africa. Telephone 022 12 521 4136/4209; fax 0027 12 521 4758/560 0086.

Evers replies:
The figures in table 1 were indeed incorrect and the correct figures from the original data are 8 µV before haemodialysis and 24 µV after haemodialysis.

S Evers
Department of Neurology, University of Münster, Albert Schweitzer Strasse 33, D 48129 Münster, Germany

Traumatic distal femoral neuropathy

We read with interest the recent report by Padua et al on a body building champion with an isolated mononeuropathy of a distal branch of the femoral nerve in body building champion. The hypothesis of needle injury was not considered in the article, but in the case report, the patient described the intense cramp that had not been noticed with previous biopsies. The site of the biopsy was 5 cm lateral to the mid-point between the patella and the anterior superior iliac spine. Over subsequent months lasting of the distal lateral vastus lateralis muscle was noted. An EMG 3 months after injury showed increased insertional activity, fibrillation potentials, and positive sharp waves with no activation of motor unit potentials in the distal fibres of the vastus lateralis muscle. A further EMG 6 months after the biopsy showed evidence of reinnervation. In our patient, the distal mononeuropathy was traumatic, and clearly related to the needle biopsy. A distal motor branch of the femoral nerve as identified in the anatomical studies of Padua et al was traumatised by the biopsy. It does raise the possibility of an alternative mechanism for the patient of Padua et al which was not considered in the article, and can be difficult to verify by clinical history alone. The use of anabolic steroids is very prevalent among body builders with the lateral thigh being a common site of administration. Direct injection could have traumatised the nerve, and may also explain the lack of any improvement with time. It is also noted in the illustration of the unaffected leg, that a small dimple is present in the skin at a site where the distal motor branch may be vulnerable, although this is significantly more distal than the biopsy site in our patient. This may, however, be an indicator of previous injections to the lateral thigh.

PETER I. SILBERT
Department of Neurology, Royal Perth Hospital, Perth, Western Australia

ROD MOORE
Sports Medicine, St John of God Hospital, Murdoch, Perth, Western Australia

BRIAN DAWSON
Department of Human Movement, University of Western Australia, Perth, Western Australia
Correspondence to: Dr P Silbert, Department of Neurology, Royal Perth Hospital, GPO Box X2213, Perth, Western Australia. Telephone 0061 9 9224 2593; fax 0061 9 93817488; email: psilbert@opera.internet.net.au


The authors reply:
We are grateful for the response of Silbert et al. In our paper we described an isolated mononeuropathy of a distal branch of the femoral nerve and hypothesised that stretching and compression of the nerve had probably occurred during strenuous exercise. We agree with the possibility of a traumatic nerve lesion due to needle injection and we have knowledge of some cases of this kind of nerve injury in body builders, but in the case reported in the article, we specifically asked the patient if drug injection was taken in the area of the thigh. He replied that he had never used this kind of drug administration. Moreover, our patient did not refer to any pain in the thigh, whereas in the case of Silbert et al an “intense cramp” was felt by the subject. Concerning the figure, detailed clinical examination of both thighs had been performed and no suspected “dumping” was seen. We think that the effect in the figure could rather be due to the hypertrophy of a nearby muscle and as noted it is distal to the site of the femoral nerve branch.

For these reasons, the hypothesis of needle injury was not considered in the article, but we agree that in the case of body builders, a needle injury (for anabolic drug injection) must always be suspected.

LUCA PADUA
PIETRO TONALI
Ist Neurologia

ROBERTO PADUA
Ist Ortopedia, Università Cattolica

LUCA PADUA
A/R Osp Faraonfiati, Iola Tiberna, Roma, Italy

BOOK REVIEWS


It has sometimes been said, perhaps unfairly, that radiosurgery has been a treatment looking for a successful application. This volume, the second in the series on radiosurgery, attempts, in some parts more successfully than others, to refute that suggestion. The technique was first established by Lexsell, using a collimated cobalt source ("the gamma knife"). In the United Kingdom, the Stereotactic Radiosurgery Centre in Sheffield has been treating patients since 1985. The published results for treatment of arteriovenous malformations have been good and its place in the non-operative management of cerebral arteriovenous malformations is now secure. Radiosurgery has now become the treatment of choice for appropriately sized and located malformations. However, increasingly refined techniques of endarterial obliteration for vascular lesions have also been developing apace in parallel, and it seems likely that the combined use of both techniques will in future make it increasingly rare for us to have to undertake surgery for these often demanding lesions.

The main drawback of the "gamma knife" technique of radiosurgery has been the enormous capital outlay required for the equipment. In the United Kingdom there is only one machine and this has perhaps inhibited a wider application of the technique in the management of intracranial malignancy. The greater availability of machines in the United States, and the commercial pressures to retain the appropriate return on investment, has led to a wider range of applications in the United States and the results of some of these are published in this book. The development of fractionated stereotactic radiotherapy using relocatable stereotactic frame and a linear accelerator has shown that it is possible to achieve good results with this technique and some of these are also published here. In the United Kingdom we are beginning to identify a much wider range of applications for this technique and, in the not too distant future, we should expect a whole range of reports of its use in malignant brain tumours, recurrences, melanomas, and other metastatic lesions. However, for the moment the literature is rather sparse and it remains to be seen whether the technique in future will also become the treatment of choice for these rather dismal conditions.

The place of radiotherapy in general, and stereotactic techniques in particular, for benign lesions, such as acoustic neuromas and meningiomas, in my view remains uncertain despite some rather encouraging results published here. At this stage it is perhaps sensible to proceed with caution until the long term effects are clearer. With regard to the future, the rapid advances in imaging techniques using MRI, the various new variants of CT, and the PET machine, offer the tantalising possibility of being able to identify both the anatomical and functional pathology to be targeted for treatment. With the merging of these exciting new technologies it may at last be possible to make some real progress in improving the outcomes for CNS tumours.

DAVID HARDY


This well produced book joins a small group of books which actually show some of the measures now used in clinical research. There are many, many measures, and each book can only show a selection. This book would be helpful to anyone who is interested in learning about measures of disease severity and outcome, although it might not be the best in any particular circumstance.

Everyone should read the introduction to this book, written by Dr Herndon. It is full of common sense. It also emphasises the most important point of all, and I repeat it here: "...the most important question in designing or choosing a scale is how well it is suited to the task at hand in terms of validity, efficiency, sensitivity and specificity ...". If only every researcher would read, remember, and act on this one statement then neurological research would advance greatly.

The book is then primarily structured around diseases. This is useful to anyone interested in a specific disease, but means that many non-specific areas of measurement are not covered. The chapters cover most of the common and important neurological diseases: multiple sclerosis; amyotrophic lateral sclerosis; head injury; stroke; movement disorders including Parkinson’s disease; epilepsy; and dementia. Many of the chapters follow a similar layout, but there are exceptions. Most seem to be written by people who have direct experience of the scales, and indeed there is much original and useful data relating to the assessment of progression in motor neuron disease in that chapter. There are two more general chapters. The first covers paediatric developmental scales, and I think that this is the only similar book to cover this area. The second covers the measurement of the outcome from rehabilitation. The best chapters are those covering multiple sclerosis; amyotrophic lateral sclerosis; movement disorders, and dementia. The chapter on stroke is much less comprehensive, and contains some errors in references (for example, to the Hamrin Activity Index), and the chapter on head injury stands out as containing much less useful information.

The book gives considerable useful information about many of the scales mentioned, and certainly would help anyone who was unfamiliar with the field. The references are reasonable, although sometimes inaccurate and quite often statements are made without reference, which can be irritating especially as references do exist to support most statements. Overall this book is good, and complements the other books available well. It will be especially helpful to those interested in the current "hot" diseases, multiple sclerosis, amyotrophic lateral sclerosis, and Parkinson’s disease.

DERICK WHITE