and the sensory nerve conduction velocity were 50·5 and 63·4 m/s for the right median nerve. There were no electrical responses from the right posterior tibial nerve or the right sural nerve.

Biopsy of the left sural nerve showed considerable reduction in the number of myelinated fibres. Electron microscopy showed a loss of unmyelinated fibres. Teased fibre studies and electron microscopy confirmed a primary disorder of the axons. There were amyloid deposits in the endoneurium and perineurium, and around vessels in the epineurium, which stained positively with Congo red and showed characteristic apple green birefringence under polarised light. Under the electron microscope, each fibril was 6–12 nm in diameter and 100–600 nm in length. Fibrils were parallel and tightly packed, forming a short bundle. These findings were in agreement with the characteristic structure of the amyloid fibrils in dialysis amyloidosis.[3] This amyloid substance was shown to be $\beta 2$ microgloublin by immunohistochemical staining (figure (A)). Amyloid A protein, prealbumin, and κ or λ chains of immunoglobulin were absent immunohistochemically (figure (B)). Our findings differed from other reports of primary and secondary amyloidosis, in which the amyloid fibrils were distributed in different directions without forming bundles.

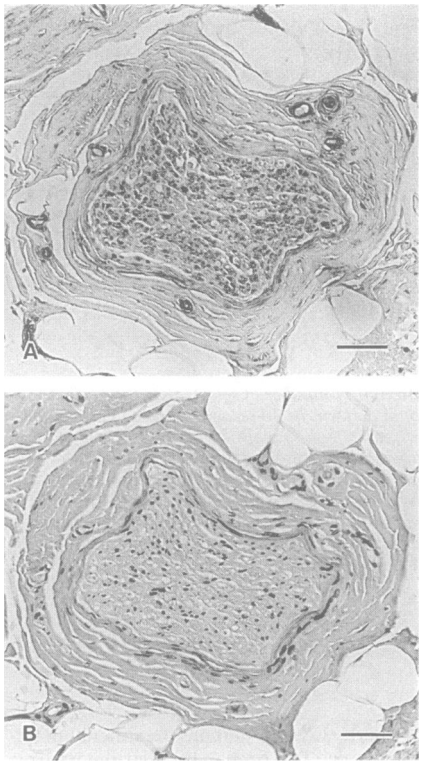
Peripheral neuropathy is an established complication of chronic renal failure. Although the metabolic derangement responsible for uraemic neuropathy is unknown, it is probably secondary to the accumulation of uraemic toxins. Because chronic haemodialysis stabilises peripheral nerve function in most patients with chronic renal failure, the occurrence of clinically evident neuropathy in patients on chronic haemodialysis has become uncommon. Muscle cramps and the restless legs syndrome, common symptoms of uraemic neuropathy,[4] were not present in our patient. Thus chronic renal failure was an unlikely cause of the neuropathy.

The mechanism of peripheral neuropathy in amyloidosis is not known, although several hypotheses have been suggested. In our case, the serum $\beta 2$ microglobulin concentration was very high, and the deposition of $\beta 2$ microglobulin as the amyloid substance was present in the sural nerve. If the patient had had primary amyloidosis, she would not have survived for 10 years and there would have been other signs of primary amyloidosis. The biopsy findings are compatible with those of amyloid neuropathy, either primary or familial, showing a predominance of axonal degeneration.[5]

We are grateful to Dr David L McIlwain and Dr Kiyoharu Inoue for their encouragement and helpful discussions, and Mr Shigeru Munakata, Mr Akira Sakuma, and Mr Kenichi Hasegawa for their technical assistance.

S ONO
Department of Neurology
T MOMOSE
T ARAI
M KANEKO
K KOIDE
The Third Department of Internal Medicine
K NAGAO
Department of Surgical Pathology,
Teikyo University School of Medicine,
Ichihara Hospital, Ichihara,
Japan

Correspondence to: Dr Ono, Department of Neurology, Teikyo University School of Medicine, Ichihara Hospital, 3426-3, Anesaki, Ichihara City, Chiba, 299-01, Japan.



Immunohistochemical staining with antiserum to $\beta 2$ microglobulin (A) and antiserum to amyloid A protein (B) of the sural nerve. The amyloid substance is positively stained with antiserum to $\beta 2$ microglobulin (bar = 50 μm).

1 Brown EA, Arnold JR, Gower PE. Dialysis arthropathy: complication of long term treatment with haemodialysis. *BMJ* 1986; **292**:163–6.
2 Fuchs A, Jagirdar J, Schwartz IS. Beta-2 microglobulin amyloidiosis (AB2M) in patients undergoing long-term hemodialysis. A new type of amyloid. *Am J Clin Pathol* 1987;**88**:302–7.
3 Shinoda T, Komatsu M, Aizawa T, *et al.* Intestinal pseudoobstruction due to dialysis amyloidosis. *Clin Nephrol* 1989;**32**:284–9.
4 Nielsen VK. The peripheral nerve function in chronic renal failure. II. Intercorrelation of clinical symptoms and signs and clinical grading of neuropathy. *Acta Med Scand* 1971;**190**:113–7.
5 Kyle RA, Dyck PJ. Amyloidosis and neuropathy. In: Dyck PJ, Thomas PK, Low PA, Poduslo JF, eds. *Peripheral neuropathy*. 3rd ed. Philadelphia: Saunders, 1993:1294–309.

Subacute cerebellar degeneration and Lambert-Eaton myasthenic syndrome associated with antibodies to voltage-gated calcium channels: differential effect of immunosuppressive therapy on central and peripheral defects

Several reports have described a neurological disorder in patients with cancer, manifesting as subacute cerebellar degeneration (SCD) and Lambert-Eaton myasthenic syndrome (LEMS).[1–3] Autoantibodies, possibly directed against voltage-gated calcium channels (VGCCs), may play a part in the pathogenesis of this syndrome.[4–6] We report a patient with non-Hodgkin's lymphoma who developed SCD and a LEMS-like neuromuscular disorder. Onset of these symptoms was associated with very high amounts of anti-VGCC antibodies in the patient's serum and CSF. We describe here the differential response of neuromuscular, but not cerebellar, symptoms to immunosuppressive treatment and the associated changes in titres of anti-VGCC antibodies in the serum. This patient (patient 6) was included in a previous report.[2]

A 55 year old woman was well until July 1989 when she noted right supraclavicular adenopathy. A biopsy showed non-Hodgkin's lymphoma. A staging procedure for metastatic disease was negative. The patient underwent radiation therapy to the neck one month later. She was then well for the next three months when she noted the onset of slurred speech. In January 1990, she developed worsening dysarthria as well as diplopia, ptosis, vertigo, nystagmus, and a clumsy gait. An edrophonium test was negative and multiple brain MRI scans were normal. Lumbar puncture showed clear CSF under normal pressure. There were 9 mononuclear cells/mm^3, normal CSF protein, and negative cytology. Oligoclonal bands were noted with a normal CSF IgG index. Serum antiacetylcholine receptor antibody and antiPurkinje cell antibody (Yo) were negative. A clinical diagnosis of SCD was made.

In June 1990 there was onset of proximal muscle weakness affecting the upper and lower extremities without sensory change or sphincter dysfunction. There was no evidence of autonomic dysfunction. Mental state was normal. Ptosis, disconjugate gaze, and nystagmus were seen bilaterally. Other cranial nerves were normal. Motor examination showed normal bulk and tone without fasciculations. Strength was 4/5 in proximal upper and lower extremity muscles. Distal muscles were 5/5. No improvement of strength was noted with exercise. Sensory examination showed mildly decreased vibration sensitivity in the lower extremities with normal pain, temperature, and position sensation. There was moderate dysmetria in the upper and lower extremities. Gait was wide based with poor tandem walking. Romberg's sign was absent. Deep tendon reflexes were normal in the upper extremities and mildly reduced in the lower extremities. The plantar responses were flexor bilaterally.

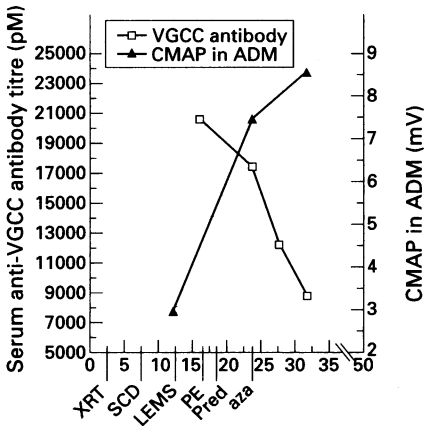
Repeat oncological evaluation was unrevealing. Brain MRI was normal without cerebellar atrophy. Serum protein electrophoresis and tests for HIV, creatine phosphokinase, B12, folate, venereal disease, antiacetylcholine receptor antibody and anti-DNA antibodies were negative or normal. Tests for serum anti-Yo, Hu, and Ri antibodies were negative. Oral prednisone was started at 100 mg every other day in September 1990 and azathioprine (150 mg per day) was added in May 1991.

Electrophysiological evaluation in August 1990 showed normal motor and sensory nerve conduction velocities and distal latencies. Repetitive stimulation of the ulnar nerve at 2 Hz recording from the abductor digiti minimus showed a 28% decrement with post-tetanic potentiation of 90%. Stimulating the peroneal nerve and recording from the extensor digitorum brevis there was a 28% decrement and post-tetanic potentiation of 600%. Compound muscle action potential amplitude (baseline to negative peak) obtained with supramaximal stimulation was 3 mV in the abductor digiti

minimus (normal >2·8 mV) and 0·66 mV in the extensor digitorum brevis (normal >2·5 mV) (figure). A follow up examination one year later again showed normal motor and sensory nerve conduction. Repetitive stimulation of the ulnar nerve at 3 Hz recording from the abductor digiti minimus showed a 17% decremental response and post-tetanic potentiation of 30%. Compound muscle action potential amplitude of the abductor digiti minimus was 7·5 mV.

Antibodies to N-type calcium channels were assayed in the Institute of Molecular Medicine laboratories, Oxford, using ^{125}I-w-conotoxin-labelled human neuroblastoma (SKN-SH) cells.[5] Titres are expressed as pM, values >30 pM being considered positive.[5] The Figure shows serum anti-VGCC antibody titres at four time points after the diagnosis of SCD. The titre was also measured in a CSF sample taken about six months after presentation. This titre was 42 pM; correcting for the IgG concentration of 0·02 mg/ml gave a normalised titre of 2100 pM/g IgG.[2] A progressive decline in the serum anti-VGCC antibody titre was noted, concurrent with the increase in amplitude of the abductor digiti minimus compound muscle action potential amplitude, over the next 18 months (figure). Two years after initiation of immunotherapy, the patient showed improvement of gait and strength, although diplopia and cerebellar dysfunction persisted.

This patient shows the clinical features of SCD and the clinical and electromyographic features of LEMS. Prior reports have shown a positive effect of plasma exchange and immunosuppressive treatment in patients with LEMS,[5 7] including a fall in the titre of anti-VGCC antibodies with immunosuppressive treatment associated with improved electrophysiological measures of disease activity.[5] With immunosuppressive treatment our patient showed improvement in neuromuscular, but not cerebellar, symptoms and this improvement was associated with decreasing serum titres of anti-VGCC antibodies (figure).



Serum anti-VGCC antibody titre and compound muscle action potential amplitude in the abductor digiti minimus (ADM) with regard to the onset of SCD and LEMS. XRT = radiotherapy; CMAP = compound muscle action potential; pred = predisore; aza = azathioprine; PE = plasma exchange.

The finding of raised antibody titres to VGCC in patients with LEMS, and in patients with SCD associated with LEMS, raises the possibility that the two disorders are due to autoantibodies of similar specificities.[1 2 8] The presence of anti-VGCC antibodies in both serum and CSF in our patient is consistent with this hypothesis. The development of SCD in only a subset of patients with LEMS suggests that if both are due to the same autoantibody, the ability of the antibody to enter the CNS may differ between patients. This could be due to higher serum titres of anti-VGCC antibodies in patients with SCD and LEMS, or to intrathecal antibody production as occurs in multiple sclerosis.[9] The second possibility is supported by the presence of oligoclonal immunoglobulin bands in the CSF.

The lack of effect of immunosuppresive treatment on the symptoms due to SCD, by contrast with those due to LEMS, may be because of irreversible damage to Purkinje cells. Alternatively, the immunosuppressive regimens used to date may be ineffective in attenuating the immune response within the CNS. This could be because antibody forming cells making pathogenic antibody have taken up residence inside the blood-brain barrier, where they may be less accessible to immunosuppressive treatment. It is also possible that cerebellar neurons are affected differently by anti-VGCC antibodies than presynaptic terminals at the motor endplate. Neurons express a number of subtypes of VGCCs,[10] some of which are expressed preferentially by cerebellar Purkinje cells.[11]

The pattern of combined central and peripheral nervous system involvement in this patient, together with increased antibody titres to VGCCs and a differential response of neuromuscular symptoms to immunosuppression, suggests that VGCC antibodies may play a differential role in the pathogenesis of the peripheral and central deficits in LEMS and SCD.

J M GOLDSTEIN
S G WAXMAN
T L VOLLMER
Department of Neurology, Yale University School of Medicine, New Haven, CT, USA
B LANG
I JOHNSTON
J NEWSOM-DAVIS
Neurosciences Group, Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK

Correspondence to: Dr JM Goldstein, Department of Neurology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510-3289, USA

1 Blumenfeld AM, Recht LD, Chad DA, DeGirolami U, Griffin T, Jaeckle KA. Coexistence of Lambert-Eaton myasthenic syndrome and subacute cerebellar degeneration: differential effects of treatment. *Neurology* 1991;**41**:1682–5.
2 Clouston PD, Saper CB, Arbizu T, *et al.* Paraneoplastic cerebellar degeneration. III. Cerebellar degeneration, cancer, and the Lambert-Eaton myasthenic syndrome. *Neurology* 1992;**42**:1944–50.
3 O'Neill JH, Murray NMF, Newsom-Davis J. The Lambert-Eaton myasthenic syndrome: a review of 50 cases. *Brain* 1988;**111**: 577–96.
4 Lang B, Newsom-Davis J, Prior C, Wray D. Antibodies to motor nerve terminals: an electrophysiological study of a human myasthenic syndrome transferred to mouse. *J Physiol* 1983;**344**:335–45.
5 Leys K, Lang B, Johnston I, Newsom-Davis J. Calcium channel autoantibodies in the Lambert-Eaton myasthenic syndrome. *Ann Neurol* 1991;**29**:307–14.
6 Lennon VA, Lambert EH. Autoantibodies bind solubilized calcium channel-w-conotoxin complexes from small cell lung carcinoma: a diagnostic aid for Lambert-Eaton myasthenic syndrome. *Mayo Clin Proc* 1989; **64**:1498–1504.
7 Newsom-Davis J, Murray NMF. Plasma exchange and immunosuppressive drug treatment in the Lambert-Eaton myasthenic syndrome. *Neurology* 1984;**34**:480–5.
8 Oguro-Okano M, Griesmann GE, Wieben ED, Slaymaker SJ, Snutch TP, Lennon VA. Molecular diversity of neuronal-type calcium channels identified in small cell lung carcinoma. *Mayo Clin Proc* 1992;**67**:1150–9.
9 Cutler RWP, Watters GV, Hammerstad JP. The origin and turnover rates of cerebrospinal fluid albumin and gamma globulin in man. *J Neurol Sci* 1970;**10**:259.
10 Miller RJ. Multiple calcium channels and neuronal function. *Science* 1987;**235**:46–52.
11 Llinás RR. The intrinsic electrophysiological properties of mammalian neurons: insights into central nervous system functions. *Science* 1988;**242**:1654–64.

Benign thalamic cyst presenting with contralateral postural tremor

Postural or action tremors have several aetiologies, but intracranial masses are rarely implicated as a cause. We present a young girl with a cystic mass of the right thalamus whose sole presenting complaint was a unilateral postural tremor affecting the left upper and lower limbs.

An 11 year old girl presented with involuntary movements of the left upper limb for seven months and the left lower limb for five months. She had no history of weakness of these limbs, gait disturbance, or symptoms of raised intracranial pressure. On examination she had no papilloedema or weakness of any of her limbs. There was a coarse postural tremor (6–8 Hz) of the outstretched left upper limb, which was more prominent in the distal muscle groups. On attempting to stand or walk, the left lower limb also manifested the tremor; it was most evident in the ankle and foot. The tremor was accentuated slightly with movement of the limbs and seemed to have a greater amplitude while nearing the target in the finger to nose test. The tremor was abolished when the limbs were at rest and when the patient was asleep. She had no nystagmus or gait ataxia and had a normal muscle tone and a normal speech. There was no dystonic posturing or sensory abnormalities.

CT of the head showed a large, well defined, rounded, non-enhancing, hypodense mass occupying the right thalamus with the same density as CSF. The lateral and third ventricles were normal sized. MRI suggested the presence of fluid in the mass with an intensity similar to that of CSF (figure (A), and (B)). A CT guided stereotactic aspiration of the cyst yielded 45 ml of clear, colourless fluid. As there was no enhancing wall a target was not chosen for biopsy. Post operative CT showed pronounced reduction in the size of the cyst with no blood within or outside it. Analysis of the fluid showed protein 47 mg/dl, sugar 33 mg/dl, and 2 lymphocytes per mm^3. The fluid was centrifuged and the sediment examined for cysticercus scolices, hydatid sand, and malignant cells, all of which were negative. A diagnosis of a benign epithelial (ependymal) cyst was made.[1] There was a dramatic improvement in her symptoms in the immediate postoperative period with virtual cessation of the tremors.