LETTERS

Sub-acute presentation of Morvan's syndrome after thymectomy

A 70 year old male presented in February 2000 with persistent cough. Chest radiograph revealed a mediastinal abnormality. A computed tomography (CT) scan of the thorax confirmed an anterior mediastinal mass. CT guided mediastinal biopsy was performed but proved inconclusive. The patient declined further invasive investigation for 2 years. After follow up CT showed significant enlargement he underwent surgery in September 2002. An excellent post operative recovery was made. Histology confirmed a minimally invasive thymoma.

However, 6 weeks later he developed progressive proximal leg weakness, lethargy, and night sweats. He described a sensation like ''someone touching his legs'' and became agitated and restless at night. He was readmitted in November 2002 and on the first night became acutely confused and markedly disorientated with visual hallucinations.

On examination he was agitated and confused. His eyes opened spontaneously, there was no coherent verbalisation, and he withdrew to pain. He was apyrexial although there was marked hyperhidrosis and hypersalivation. Blood pressure was 120/70 mm Hg, and pulse was 98 bpm and regular. He had profuse diarrhoea although his abdomen was soft and non-tender. There were irregular myoclonic jerks of all four limbs predominating in his upper limbs as elbow flexion jerks. There was no startle reaction. Cranial nerve examination was unremarkable. Power and deep tendon reflexes were normal and plantar responses flexor. Intravenous phenytoin was administered with resolution of the myoclonic movements.

Laboratory investigations including electrolytes, auto-antibody screen, and anti-neuronal antibodies were unremarkable. Cerebral spinal fluid (CSF) was clear, colourless, and acellular, CSF glucose was 4.0 mmol/l (2.2–4.4) (serum 6.7), and CSF protein 0.25 g/l (0–0.40). Oligoclonal bands were negative in CSF and serum and no abnormality of the immunoglobulin G pattern was detected. CSF analysis for the 14-3-3 (prion) protein was negative.

Chest radiograph showed postoperative changes. Brain magnetic resonance imaging (MRI) disclosed multiple areas of periventricular and subcortical white matter signal change especially within the right parietal region, felt likely to represent diffuse cerebrovascular changes.

Serial electrocardiograms (ECGs) demonstrated sinus tachycardia. Serial electroencephalograms (EEGs) showed diffuse slowing only. Nerve conduction studies revealed mild motor conduction slowing (right median 49 m/s, right common peroneal 43 m/s). Sensory nerve amplitudes were small with normal velocities. Repetitive discharges were noted following evoked compound muscle action potential in upper and lower limb motor nerves. Doublet, triplet, and multiplet were recorded in abductor pollicis brevis, tibialis anterior, and extensor digitorum brevis indicating motor axon membrane instability compatible with neuromyotonia (fig 1).

Confusion, visual hallucinations, insomnia, anxiety, sweating, diarrhoea, a slurred dysarthria, and abnormal muscle activity fluctuated dramatically from day to day, but there was a steady overall deterioration. In a lucid interval he scored 68/100 using Addenbrooke's bedside testing of cognitive function (equivalent to a Mini Mental State Examination (MMSE) score of 18/30), performing poorly in orientation, attention/concentration, verbal fluency, and visuospatial abilities. He became chair bound despite little clinical weakness either proximally or distally, and later bed bound. Although never as prominent as on first admission, there was frequent muscle twitching, at best resembling myokymia, at worst multifocal myoclonus. He was transferred to a high dependency unit.

The diagnosis of Morvan's syndrome was based on the clinical phenotype and supported by the nerve conduction studies and the presence of antibodies to voltage gated potassium channel antibodies (VGKC) (165 pmol; normal <100 pmol), 10 weeks post-thymectomy.

At 10 weeks post-thymectomy he had 5 days of plasma exchange (PE). There was rapid improvement in orientation and memory and a cessation of abnormal muscle movements within 5 days. Prednisolone was commenced 40 mg daily and phenytoin continued. He made a dramatic clinical recovery, standing unassisted 10 days post-exchange and mobilising independently by 14 days, with no further muscle twitching. Addenbrooke's test 2 weeks post-PE revealed a score of 78/100 (MMSE 24/30).

Post-PE nerve conduction studies and EMG showed an increase in the motor conduction velocities (right median 56 m/s, right common peroneal 45 m/s) and resolution of the previous features of neuromyotonia. Repeat serum VGKC antibody levels at 1 and 4 months post-PE were within normal limit. EEGs both 2 and 6 months after treatment showed little improvement. MRI 6 months after treatment also showed no change.

At 8 months post-PE, on 10 mg prednisolone daily he remained asymptomatic aside from fatigue. His wife reported that apart from irritability his personality and memory were essentially back to normal, although on repeat Addenbrooke's he scored only 82/100. He has even returned to playing golf.

Discussion

Since Morvan's original publication only a few cases have been described. The majority appear to be a paraneoplastic manifestation.[1 2] The discovery of VGKC antibodies in several of these cases, as seen in many cases with neuromyotonia,[3] has suggested that Morvan's syndrome may be an autoimmune disorder. Whether VGKC antibodies play a pathogenic role in the encephalopathy as they do in the peripheral nervous symptoms is as yet unclear. Others[1 2] have suggested that the VGKC antibodies may cross the blood–brain barrier and act centrally, binding predominantly to thalamic and striatal neurons[2] causing encephalopathic and autonomic features. The reversibility of the encephalopathy with plasmapheresis does suggest that the encephalopathy is also mediated by serum factors. Liguori *et al* reported the presence of weak CSF oligoclonal bands, absent in the serum, supporting a central immunological role.[2] There are also

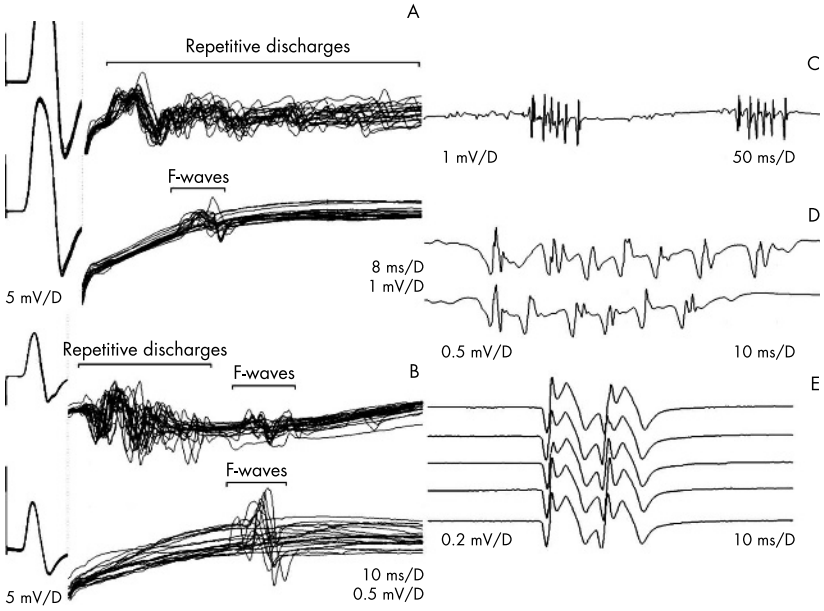

Figure 1 (A) Upper trace: recordings (superimposed) from abductor pollicis brevis following stimulation of the median nerve at the wrist. Note the repetitive discharges that completely obscure any F responses which may have been generated. Lower trace: following treatment the repetitive discharges have completely disappeared and normal F waves are now visible. (B) Similar to A; recordings before (upper trace) and after (lower trace) treatment from extensor digitorum communis following stimulation of the common peroneal nerve at the ankle. The repetitive discharges subside after 45 ms allowing the F responses to be seen. (C, D, E) Spontaneous bursts of neuromyotonic discharges in the form of multiplets (C and D) and doublets (E) with intraburst frequencies of up to 120 Hz. C and D are bursts of the same motor unit displayed at different sweep speeds.

reports of non-paraneoplastic limbic encephalitis associated with raised serum VGKC[4] suggesting that these antibodies may give rise to a spectrum of neurological disease presenting with symptoms arising peripherally, centrally, or both.[5] However in our case and the case reported by Lee *et al*[1] oligoclonal bands were absent in CSF and serum, and CSF immunoglobulin profiles were unremarkable.

The natural history of Morvan's is highly variable. Two cases have been reported to remit spontaneously. In one of these cases remission was associated with a fall in the serum level of VGKC antibodies. Others have required a combination of plasmapheresis and long term immunosuppression,[1 2] although in one of these cases the patient died shortly after receiving PE.[2] Other fatalities without remission have been described by, amongst others, Morvan himself. Cardiac involvement in some cases may increase vulnerability to sudden death.

Thymectomy has previously been a proposed treatment for Morvan's syndrome. This is the first reported case of Morvan's syndrome presenting post-thymectomy. Morvan's syndrome normally presents with a slow insidious onset over months to years.[1 2] Our case is unique in that presentation was over days, just weeks post-thymectomy, and responded to a single PE course with low dose immunosuppression. We hypothesise that surgery may have precipitated a rise in the serum VGKC antibodies levels, which were cleared by one course of PE resulting in remission as supported by the drop in serum VGKC levels. Although potentially a low risk of thymectomy, it is an important complication to recognise because of the dramatic reversibility to treatment.

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doi: 10.1136/jnnp.2003.031401

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Urinary retention associated with mild rhombencephalitis

The importance of the pontine tegmentum as the micturition centre responsible for urinary voiding has been well established from animal studies.[1] A cliniconeuroradiological study showed that the nuclei involved are the pontine reticular nucleus and the reticular formation, located adjacent to the locus ceruleus and the medial parabrachial nucleus.[2] This micturition centre, which is thought to coordinate detrusor sphincter activity during micturition, probably conveys its efferent fibres through the bulbospinal pathway to the spinal parasympathetic nucleus.

We describe a patient with suspicion of mild viral rhombencephalitis presenting with acute urinary retention because of a lesion affecting the dorsal tegmentum of the medulla and the pontomedullary junction bilaterally. Reports on urinary retention caused by bulbar lesions other than stroke and tumours are rare but emphasise the importance of this often neglected association.

Case report

A 34 year old Nepali construction worker, with no past medical history, presented with suprapubic pain because of acute urinary retention and was admitted for observation. In the weeks before admission he had complained of mild headache and dizziness. The headache responded well to paracetamol. There was no history of orogenital ulcers, and he had received no recent vaccinations.

On admission, he was conscious and alert, with normal cognitive examination. There was no neck stiffness. Fundoscopy, pupil reflexes, accommodation, and vertical and horizontal eye movements were normal. Bulbar function was intact. There was generalised hyperreflexia, including the jaw jerk, with equivocal plantar responses. There was no indication of spinal cord or cauda equina syndrome on sensory examination. Coordination and gait were normal. He had urinary retention (550 ml), which was managed with an indwelling catheter. General examination revealed an afebrile patient with normal vital signs. Skin testing for tuberculosis was negative. Peripheral blood analysis showed normal findings: the erythrocyte sedimentation rate was 4 mm/h and the white blood cell count was 8500/μl (60% neutrophils and 27% lymphocytes). Magnetic resonance imaging (MRI) of the spinal cord including the cauda equina was normal. However, MRI of the brain stem revealed a symmetrical bilateral abnormal high signal on T2 weighted images in the medulla and pontomedullary junction (fig 1). Cerebrospinal fluid (CSF) analysis revealed features of aseptic meningitis (105 cells/mm^3 with 96% lymphocytes and 4% neutrophils, and normal protein, glucose, and IgG). Serum autoantibody, viral serology tests, and CSF smear and cultures did not contribute to the diagnosis. Neurophysiological investigations (visual evoked and somatosensory evoked potentials) were normal. A urogram showed an atonic bladder. Organic obstructive urological disease was excluded radiologically, and no urological cause for the urinary retention could be identified. On the basis of the neurological findings, there was involvement of the pyramidal tracts and the micturition centre or its efferent pathways. The differential diagnoses included mild viral rhombencephalitis, acute demyelinating disorder (multiple sclerosis or acute disseminated encephalomyelitis), or an underlying autoimmune disorder (for example, neuro-Behçet disease). Three weeks after admission, the neurological symptoms gradually disappeared. Repeat CSF analysis and spinal MRI were normal. MRI of the brain stem revealed regression of the hyperintense lesions on the T2 weighted images.

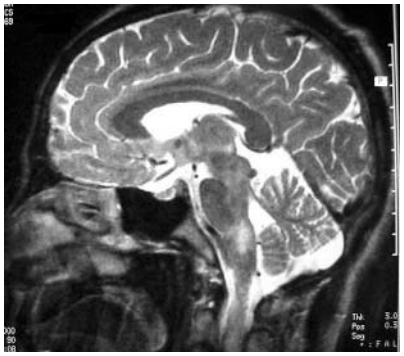

Figure 1 Magnetic resonance imaging of the brain stem (sagittal view). T2 weighted images on admission show hyperintense focus in the tegmentum of the medulla oblongata, extending from the pontomedullary junction downward.

Comment

Although this patient was likely to have suffered from a mild, probably viral rhombencephalitis, the true diagnosis remains unclear. We speculate that parainfectious demyelination or direct viral invasion was likely to have been the cause of the patient's neurological presentation. Intriguingly, a similar case was reported by Komiyama *et al*, in which a 30 year old man had urinary retention, mild horizontal gaze paresis, and hypaesthesia around the mouth and fingers.[3] In their case, the MRI findings revealed several amorphous lesions in the pons and cerebellum, in addition to a well defined lesion in the right dorsolateral tegmentum of the upper pons. CSF analysis showed a mild increase in protein but only 3 cells/mm^3. In contrast to their patient, the lesions in our case were bilateral and extended from the medulla to the pontomedullary junction, but showed a similar rate of disappearance (four weeks).

Brain stem control of micturition has been reviewed by Sakakibara and Fowler.[4] Urinary retention is extensively described in patients with brain stem tumours or strokes. In the series of patients with brain stem tumours, the majority of the lesions were located in the pons and medulla, while in patients with