Table Physiological and therapeutic response profile

Patients	Motor conduction studies			Anti-GM1 Titres before/after therapy	Manual Muscle Score before/after therapy	Simplified Barthel Index before/after therapy
	Velocity	Temporal dispersion	Conduction block			
1	NV	NV	M (0.6), U (0.4), P (0.5)	103/120	50/35	50/35
2	NV	NV	R (0), T (0.5), P (0.4)	630/612	135/140	55/55
3	NV	NV	NV	132/164	150/140	78/78

NV = at or within 15 % normal values.

U = ulnar, R = radial, M = median, T = tibial, P = peroneal.

Values in brackets are the ratios proximal/distal motor action potential area.

oral chlorambucil resulted in no significant improvement.

All patients had weakness and wasting, with electrophysiological evidence of denervation-reinnervation in one or more extremities that was not attributable to focal nerve or roots lesions. No upper motor neuron signs (bulbar dysfunction, spasticity, brisk reflexes) or cranial nerve dysfunction were seen. No patient had sensory signs or electrophysiological evidence of a peripheral neuropathy involving sensory fibres. Laboratory, enzyme and biochemical, including serum immunoelectrophoresis, CSF and neuroimaging studies were carried out to exclude other conditions which may cause motor neuron signs.³

Patient 1 was a 62 year old woman with asymmetrical tetraparesis who had progressive weakness, suggestive of a left sciatic neuropathy, for six years. She experienced cramps and fasciculations, right sciatic neuropathy for two years, and radial and median neuropathies for one year. The progression was not slowed by prednisone 1.5 mg/kg per day for five weeks. Examination revealed asymmetrical generalised weakness and muscle wasting, distal in the upper extremities (grade 3 to 4+) and distal greater than proximal in the lower extremities (grade 0 to 4). The tendon reflexes were decreased or absent. She was then given oral chlorambucil 0.15 mg/kg per day over a period of six months, without modifying the progression of the disability.

Patient 2 was a 67 year old man who had progressive weakness with wasting and cramps involving the right upper limb for four years. Two surgical explorations of the radial nerve were carried out, without evidence of entrapment. Six months before admission he developed cramps and weakness of his right lower limb. Examination revealed multifocal weakness, wasting and fasciculations in the distribution of the right ulnar, radial and axillary, left radial and right sciatic nerves. Reflexes were decreased or absent. The symptoms and signs were not modified by prednisone, 1.5 mg/kg per day for two months. He was then given oral chlorambucil 0.15 mg/kg per day for six months, without modifying the symptoms.

Patient 3 was a 37 year old man who experienced left hand clumsiness, progressive weakness and wasting with cramps of his forearm for two years. Examination revealed that left deltoid, biceps and triceps (MRC grade 4), wrist extensors and flexors (MRC grade 3), finger extensors and flexors and intrinsic hand muscles (MRC grade 0) were weak and amyotrophic, with active fasciculations throughout. Tendon reflexes were absent in the left upper limb. He was treated with chlorambucil, 0.15 mg/kg per day for 6 months, without improvement.

Strength testing was quantified using a manual muscle test score, based on the Medical Research Council scale. Flexion and

extension at the ankle, wrist, elbow, hip, knee, and shoulder abduction were tested bilaterally. The patient's ability to perform motor activities of daily living skills was rated using a simplified Barthel index. Motor function was tested at the start of oral chlorambucil and at one, three and six months apiece.

The presence of anti-GM1 antibodies in sera was measured before and after treatment by ELISA using purified ganglioside antigens, as previously reported:¹ titres greater than or equal to 100 units were considered as "high" in our laboratory.

Multisegmental motor nerve conduction studies were performed with percutaneous supramaximal stimulation while recording the compound muscle action potential with TECA 4 mm disc electrodes. Determination of conduction block and temporal dispersion was made based upon the criteria of Feasby *et al.* F-wave latencies from at least 10 responses were recorded following stimulation at the wrist or ankle. Using surface electrodes, sensory nerve action potentials were recorded orthodromically. Needle examination was performed using standard DISA concentric electrodes.

The physiological and therapeutic profiles of the 3 patients are presented in the table. All patients showed evidence of a multifocal neuropathy involving motor fibres but sparing of sensory axons. This was shown as asymmetrical and variable conduction block along motor axons in patients 1 and 2, prolongation of F-wave latencies and reduction of the CMAPs amplitude. Axonal loss was found in all patients, was prominent in patient 1, as shown by denervation potentials at rest, and voluntary motor unit potentials indicative of chronic denervation-reinnervation.

Relative strength and simplified Barthel index measurements were not improved and both parameters declined or were stabilised over time. By ELISA assay, the levels of anti-GM1 measured after treatment with chlorambucil were not modified.

Treatment was well tolerated, without haematological side effects but patients 1 and 2 developed transient haemorrhagic cystitis.

Our study was designed to assess the efficacy of chlorambucil in the treatment of multifocal motor neuropathy syndrome presenting as a progressive, multisegmental weakness with wasting, fasciculations and cramps and anti-GM1 antibodies. Our patients were similar to several previously reported cases of selective motor neuropathy, with or without electrophysiological evidence of conduction block.^{2,5} Recent data have suggested that antibody responses to gangliosides are probably T-cells independent responses of B cells and that prednisone is ineffective in suppressing antibodies.^{2,5} Cyclophosphamide has been shown to be effective but in view of the danger of serious toxicity, therapy with this agent is limited.⁵

We therefore elected to use chlorambucil, an immunosuppressive drug with some B cell specificity but with fewer side effects.

Clearly, our results demonstrate that chlorambucil is not an alternative drug that can be recommended. Chlorambucil lacked a therapeutic effect as judged in the absence of improvement in the manual muscle test score and simplified Barthel index. Moreover, chlorambucil did not reduce significantly the titre of anti-GM1 antibodies. The duration of therapy seems to have been sufficient in our cases, because improvement in strength began within two to five months in the reported improved patients.⁵

In summary, we feel that the use of chlorambucil is not effective in patients with lower motor syndrome and anti-GM1 antibodies. Whether other regimes of immunosuppression other than cyclophosphamide or the administration of parenteral immunoglobulins that have been shown to be effective in other neuropathies, such as chronic inflammatory demyelinating polyneuropathy should be used, remains to be investigated.

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Unilateral vestibular paralysis as the sole manifestation of mumps

A 36 year old man noted sudden rotational vertigo with nausea, vomiting and postural imbalance. The next day clinical and electro-oculographic findings confirmed a left vestibular paralysis. There was spontaneous horizontal-rotatory (counterclockwise) nystagmus to the right enhanced by Frenzel's lenses and increasing on gaze to the right. Stance and gait were unsteady with a tendency to fall to the left. The left horizontal semicircular canal was unresponsive to stimulation with warm (44°C) and cold (30°C) water. The audiogram was normal.

Body temperature was normal. White blood cells were elevated ($15000/\text{mm}^3$) and became normal ($5800/\text{mm}^3$) within 3 days. CSF analysis revealed 19 white cells/ mm^3 (with 85% lymphocytes and 3% plasma cells), normal glucose, lactate and protein content without IgG oligoclonal bands. The EEG was normal. On day 2, serum antibody testing (ELISA) revealed positive mumps virus IgM titres up to a dilution of 1:320 and negative IgG (for dilutions $\geq 1:40$). CSF antibody testing was negative (for dilutions $\geq 1:10$). On day 51, mumps virus IgG titres (ELISA) in the serum were positive for dilutions up to 1:640 and negative for IgM (for dilutions $\geq 1:40$). There was complete clinical recovery within 7 weeks and thermic stimulation showed improved vestibular function on the left (hyporesponsiveness of 43%). CSF was normal.

Sudden deafness with or without abnormal caloric responses is a possible complication of epidemic parotitis.^{1,2} Several investigators³ have suggested that subclinical mumps infections without parotitis may produce sudden unilateral hearing loss sometimes with vertigo in adults, but the relationship of the mumps infection proven by positive blood serology and the onset of symptoms was not clear.

In our patient, hearing was spared and only unilateral vestibular paralysis accompanied the serologically proven acute mumps infection. This condition has not been described previously. The Kilham strain of the mumps virus and a neurotrophic mumps strain (isolated from the CSF of a child with mumps meningitis) may infect the endolymphatic structures of the labyrinth.⁴ Neurons of the vestibular and cochlear ganglia were regularly infected by the Kilham strain but only occasionally by the neurotrophic strain.⁴ Infections of the labyrinthine endolymphatic structures or of the vestibular ganglia may be followed by vestibular paralysis and such a mechanism seems most likely in our patient.

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Ataxic hemiparesis with cheiro-oral syndrome in capsular infarction

Ataxic hemiparesis (AH) is defined as an unusual combination of ipsilateral pyramidal and cerebellar signs. AH is ascribed to lacunar stroke in both supratentorial and brainstem locations.¹ Several reports²⁻⁶ have established that accompanying hemihypoesthesia indicates a thalamocapsular rather than a pontine location for lesions causing the AH syndrome. We describe a variant of

AH with sensory impairment restricted to a cheiro-oral topography, in association with contralateral small posterior capsular infarction.

A 73 year old woman, known to have been hypertensive and diabetic for 10 years, suddenly developed slurred speech and a tingling sensation around the left corner of the mouth and in her left thumb, index and middle fingers. Soon after she noticed weakness in her left arm and leg. On admission the next day, general physical examination was normal. Blood pressure was 220/110 mmHg. She was alert and had normal mental status. Her speech was dysarthric. There was slight left central facial weakness and a grade 3/5 left hemiparesis. Reflexes were increased on the left, with Babinski's sign present. Pinprick and light touch sensation were diminished in the left tongue, buccal mucosa, lips and cheek, and in the thumb, index and middle fingers of the left hand. Proprioceptive sensation was unimpaired. The patient was unable to walk alone and fell to the left. ECG and routine laboratory tests were normal except for a blood glucose level of 207 mg/dl.

By the sixth day, her power improved to grade 4/5. It was at this time that she appeared to have moderate dysmetria and intention tremor of the cerebellar type in performing the heel-shin and finger-nose tests on the left. The ataxia was more apparent in the leg than in the arm. CT scan obtained at that time revealed a small hypodense area in the right posterior limb of the internal capsule with possible involvement of the adjacent lateral thalamus (see below). Parietal-recorded somatosensory potentials following contralateral median nerve stimulation were studied two weeks after clinical onset. The short-latency components from the left side showed decrease in amplitude of N20 to 35% of the normal side and slight attenuation of the subsequent peaks. Latencies were normal.

Eight months after onset, there was no weakness but minimal ataxia of the left extremities persisted. Paresthesiae remained in the tips of the left first to third fingers and hypoesthesia for pain and light touch continued in the left perioral region. CT scan again revealed the capsular hypodense lesion (figure). Somatosensory evoked potentials did not show any asymmetry or abnormal responses.

Originally, persistent sensory disturbances were not considered as part of the AH syndrome.¹ In subsequent reports,²⁻⁶ the clinical spectrum of AH was widened to include cases with persistent hemisensory deficit ipsilateral to the cerebellar-like ataxia and pyramidal tract weakness. This has been termed "hypesthetic ataxic hemiparesis". The sensory loss involves several sensory modalities, more often of the spinothalamic than the dorsal column type. Huang and Lui² indicated that patients with capsular AH are likely to have sensory loss, while those with a pontine lesion do not. Hypesthetic AH was attributed to anterior choroidal artery territory infarction by Helgason *et al*,³ with lacunar infarcts localised by CT or MRI to the posterior limb of the internal capsule. This anatomical distribution is the same as that found in our case. A small haemorrhage of the posterior limb of the internal capsule is thought to produce an AH with hemisensory loss.⁴ Hypesthetic AH has also been correlated to infarction⁵ or haemorrhage⁶ of the thalamus.

AH with cheiro-oral sensory deficit, as

Figure CT scan taken at 8 months of onset showing lacunar infarct in the right posterior limb of the internal capsule.

seen in our patient, has not been previously reported. The cheiro-oral syndrome is a sensory disturbance affecting both the hand and the corner of the mouth on the same side, but without motor impairment. It usually occurs as a result of a vascular lesion in the region of the ventroposterior nucleus of the thalamus and in the brainstem sensory pathways projecting to this nucleus.⁷ Selective involvement of some, rather than all, fingers (as described in our case), may also occur as a result of parietal cortical infarction.^{8,9} In cheiro-oral syndrome due to a thalamic infarct, the sensory deficit exactly conforms to the representation of body surface in the ventroposterior nucleus, the fingers being represented adjacent to the tongue in the most medial pole of the nucleus.¹⁰ In our case, involvement of the ventroposterior nucleus might be responsible for the sensory deficit, because CT revealed infarction in the posterior limb of the internal capsule bordering the adjacent thalamus. However, the foot could have sensory change rather than the face and fingers, in view of the fact that the foot is represented laterally in the ventroposterior nucleus and most adjacent to the internal capsule. This suggests that the patient's symptoms are most probably due to involvement of sensory thalamocortical radiation, which occupies the posterior part of the posterior limb of the internal capsule.¹¹ Abnormalities in short-latency components of somatosensory evoked potentials, as those observed in our patient, have been reported as being the same in lesions of the thalamus and thalamo-cortical radiations.¹²

In summary, ataxic hemiparesis associated with ipsilateral cheiro-oral syndrome is a previously undescribed symptom complex following capsular infarction. This association should be included in the spectrum of clinical syndromes presumably related to anterior choroidal artery territory infarction.

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