

LETTERS TO THE EDITOR

Pulsed intravenous methylprednisolone combined with oral steroids as the initial treatment of inflammatory myopathies

Pulsed intravenous methylprednisolone (IVMP) was given to 11 patients with polymyositis and dermatomyositis (group A) whom we studied prospectively. The outcome was compared with that of 14 patients who had been treated with oral steroids alone (group B). Group B comprised all cases of polymyositis and dermatomyositis with sufficient information in our past medical records studied retrospectively. Definite diagnoses of polymyositis and dermatomyositis were made in all cases.¹ Cases of myositis associated with cancer and inclusion body myositis were excluded.

For group A, methylprednisolone sodium succinate (500 mg diluted in 200 ml of 5% dextrose in water) was infused for two hours. A course of treatment consisted of three consecutive daily infusions, and was repeated three to nine times at intervals of a week, except in one patient who had only one course of IVMP. Oral steroids were given as in group B except on the days of IVMP.

For group B, treatment with oral prednisolone (1 mg/kg body weight per day) was started, maintained for two months, and then tapered down gradually over two years. When recovery was inadequate, the cases were kept either on the initial dose for up to four months, or the dose was increased up to 100 mg daily, or immunosuppressive agents were added. After two years, steroids were tapered off in some patients, and a small dose was maintained in others.

Muscle power was assessed both by neurologists and physiotherapists. The physiotherapists were not informed of how the steroids were given. The handicap was rated according to the disability grade.² The patients were followed up for one to five years.

Remission was defined as recovery of the strength of the weakest muscle or muscles by one grade or more on the British Medical Research Council (MRC) scale, in association with normalisation of the serum creatine kinase activity (falling to an activity lower than 200 IU/l). Partial remission was defined as recovery in either muscle strength or creatine kinase alone. Recovery of strength was judged in the same way as in the remission group. When neither muscle strength nor creatine kinase satisfied the standard of recovery, the case was included in the no improvement group. When recurrence occurred after remission, the patients were classified as remission and recurrence. Here recurrence was defined as worsening of muscle strength by one grade or more.

Groups A and B were not exactly comparable because of the difference in method of sampling, but to estimate characteristics of IVMP treatment, the two groups were compared statistically with Fisher's exact probability or Wilcoxon rank sum tests. The *p* values <0.05 were regarded as statistically

Comparison of cases of groups A and B and their outcome

Groups	A (IVMP + oral steroids)	B (oral steroids)
Number of cases	11	14
Age (y)*	54 (19)	43 (12)
Sex (female/male)	10/1	11/3
Diagnoses (PM/DM)	8/3	10/4
Duration (months)*	12.6 (15.8)	9.8 (6.6)
Oral prednisolone (mg)*	54.6 (9.3)	61.1 (13.9)
Disability grade**:		
Before steroids	6 (1)	4 (1)
On steroids	1 (1)	2 (1)
sCK*:		
Before steroids	3241 (2991)	4732 (3368)
On steroids	73 (62)	457 (614)
Weeks needed to normalise sCK*	6.6 (3.6) (n = 10)	11.7 (5.1) (n = 7)
Outcome:		
Remission	10	6
Remission/recurrence	1	4
Partial remission	0	2
No improvement	0	2

* Mean (standard deviation); **median (semi-interquartile range).

significant. Null hypotheses were tested two sided.

The table summarises the results. For group A, on average, 4.3 courses of IVMP was given to a case. Ten cases had persistent remission (remission group). Another, who had only one course of IVMP, had a recurrence after two years of remission (remission and recurrence group), requiring three more courses of IVMP to induce remission again. None needed immunosuppressive agents. One case required treatment for diabetes mellitus and candida stomatitis, but no change in the steroid treatment was needed.

For group B, six cases out of 14 had persistent remission (remission group). Four had a recurrence after a period of remission (remission and recurrence group). Two were classified as having partial remission, as they did not have recovery of muscle strength as defined, despite normal creatine kinase. Two belonged to the no-improvement group. Three had immunosuppressive agents six to 24 months after the initial treatment.

There was no significant difference between the groups for age, duration of the illness, or the maximum dose of oral prednisolone. The disability grade before treatment was higher in group A than in group B (*p* = 0.002).

Six months after initiation of steroids, half of the cases of group B and all the cases of group A were in remission. The difference was significant (*p* = 0.014). Persistent remission was seen in 10 out of 11 cases of group A and six out of 14 of group B (*p* = 0.034). There was no difference in the outcome between the cases of polymyositis and dermatomyositis.

The time needed for serum creatine kinase activity to return to normal was examined in cases in which the creatine kinase activity exceeded 500 IU/l before treatment and returned to normal later. The time was shorter in group A (*n* = 10) than in group B (*n* = 7; *p* = 0.014).

Studies of the effect of IVMP on adult dermatomyositis and polymyositis have been few.³⁻⁵ The effectiveness of IVMP at the initial stage of treatment of polymyositis and dermatomyositis has been mentioned.^{6,7}

In this study IVMP led to remission more often and serum creatine kinase returned to normal more rapidly than oral steroids alone. Among our cases, whereas none of those with a duration of illness longer than 24 months had remission with oral steroids alone, two cases with a duration of 30 and

54 months had a remission with IVMP.

Recurrence in a case of group A hinted that only one course of IVMP was not sufficient to induce sustained remission. Although immunosuppressive agents were not used in group A, they might enable us to decrease the number of courses of IVMP.

IVMP can help to decrease the complications of long term high dose oral steroids by shortening the time needed to induce remission and by increasing the rate of remission. Although this trial was open and small, the results suggest a beneficial effect of IVMP and warrant further studies.

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Familial inflammatory demyelinating polyneuropathy: a Guillain-Barré syndrome variant without autoimmune predilection

The putative pathogenesis of acute inflammatory demyelinating polyneuropathy (AIDP) is immune mediated.¹ Unlike other autoimmune diseases, such as systemic lupus erythematosus, rheumatoid arthritis, juvenile diabetes mellitus, and multiple

sclerosis, however, familial association is not an epidemiological feature of AIDP. In fact, familial cases have rarely been reported.²⁻⁴ We recently encountered a father and his daughter who developed an unusual but clinically similar course of AIDP after triggering factors associated with occurrence of AIDP.

The father, a 50 year old, previously healthy Kurdic Jew, complained of right hand weakness a few days after haemorrhoidectomy under general anaesthesia. Within a few more days, lower limb weakness and paresthesias ensued and slowly progressed. He did not consult a physician at that time as his condition had stabilised. A year later, he was first referred for consultation. On examination there was global areflexia, minimal distal weakness, atrophy of the right hand, and pronounced distal weakness in both legs, greatest on the left. Vibration and superficial sensation were impaired in a glove and stocking distribution in both legs and in the right hand. Cerebrospinal fluid (CSF) was acellular, with a protein concentration of 0.94 g/l and a normal glucose concentration. Nerve conduction velocities were 38, 37.5, and 39 m/s in the median, ulnar, and lateral popliteal nerves respectively; F wave latencies were prolonged in all extremities. Sensory potentials were reduced or could not be elicited and sensory conduction velocities were slowed (left sural nerve 22 m/s). Sural nerve biopsy showed massive loss of myelinated fibres with remyelination and some onion bulb formation, without an inflammatory reaction. During the next few years, his clinical condition improved slightly. Motor conduction velocities four years later were 53 and 46 m/s in the median and ulnar nerves respectively.

Four years later, at the age of 24, the first patient's daughter had serologically established Epstein-Barr virus infection. Two weeks later, she progressively developed lower limb weakness. On examination she had bilateral foot dorsiflexion weakness, more pronounced on the right with diminished deep tendon reflexes in the legs. Pinprick sensation was decreased in the right leg and the left hand in a glove and stocking distribution. During the next three days, her weakness progressed to involve also the plantar flexion of the feet and the iliopsoas on the right. Global areflexia appeared but sphincter functions were preserved. The CSF was acellular with normal protein (0.3 g/l) and glucose concentrations and no oligoclonal bands. Motor nerve conduction velocities were reduced (median nerve 45 m/s; tibial nerve 32 m/s; common peroneal nerve 28 m/s) and distal latencies were prolonged (right tibial nerve 17.5 ms; left tibial nerve 18.4 ms; right common peroneal nerve 20.8 ms; left common peroneal nerve 17.1 ms), as were F wave latencies in the legs (>60 ms). Right sural nerve conduction was 34 m/s. Electromyography was normal. Treatment with prednisone was initiated. Her condition gradually improved, but residual left dorsiflexion weakness was still evident after a year. Motor conduction velocities six months later were improved (38 and 37 m/s in the common peroneal and tibial nerve respectively).

Erythrocyte sedimentation rate, haemogram, serum electrolytes, liver and kidney function tests, latex, Rose Waler, antinuclear factor, VDRL, AST, creatine phosphate protein electrophoresis, HIV and hepatitis B surface antigen serology, and

chest radiographs were within normal limits or negative in both patients.

GM1 gangliosides, galactocerebroside (GalC), and myelin basic protein (MBP) autoantibodies were determined as previously described.⁵ The daughter had increased GM1 and MBP antibodies whereas levels in the father were normal. GalC antibodies were raised in both.

The disorder in these two patients fulfils the criteria required for the diagnosis of AIDP.¹ In both it occurred after an antecedent event associated with occurrence of AIDP, was diffuse, affecting all four limbs with widespread slowing of nerve conduction, and was followed by gradual improvement on follow up studies. Their disease course differed, however, from typical AIDP by several features: the disorder was clearly asymmetrical, did not involve respiratory and cranial nerves, and was associated with residual deficit for several years of follow up.

The fact that familial cases have not been described more often in AIDP, a relatively common condition of putative immune mediated pathogenesis, is intriguing. The clinical history and the laboratory work-up in these patients did not support a possible common basic autoimmune predisposition. There was no evidence for an immunological abnormality on auxiliary and serological studies or for an associated autoimmune condition. GM1 antibodies, present in about a quarter of patients with AIDP were significantly raised only in the affected daughter's serum; her serum also contained detectable MBP antibodies. Human leucocyte antigen (HLA) analysis of the affected father and daughter did not show any of the previously reported HLA alleles associated with systemic or neurological autoimmune conditions. The presence of serum GalC antibodies in patients with AIDP might be an indicator of peripheral nerve injury, but whereas they may induce experimental peripheral nerve demyelination, there is no evidence to link them with AIDP pathogenesis.

Thus the unusual course, the lack of serological abnormalities, and the absence of immunological features associated with AIDP suggest that the familial predisposition in these two patients may be coincidental or belong to a different pathogenetic mechanism. The paucity of reported familial cases and a lack of any immunological disturbances in our patients seems to indicate that AIDP is different from other general and neurological autoimmune disorders.

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Peripheral neuropathy in association with insulinoma: clinical features and neuropathology of a new case

Peripheral neuropathy associated with hypoglycaemia secondary to insulinoma is unusual and just 30 patients have been described.¹

Three years before admission this 60 year old woman started episodes of confusion, self abuse, and irrational behaviour. Six months before entry, she noted progressive loss of sensation and weakness below the knees and hands. Neurological examination disclosed a mild paresis with mild impairment of all sensations in a glove and stocking distribution. The deep tendon reflexes were decreased. Laboratory investigations showed a fasting plasma glucose concentration below 50 mg/dl and a serum insulin concentration of 18.1 μ U/ml. A fasting test showed hypoglycaemia associated with inappropriately raised insulin levels. Coeliac angiography, abdominal echography, and abdominal CT showed a vascular tumour in the head of the pancreas. The motor nerve velocities were slightly decreased and there was an important reduction in muscle action potential amplitude. Sensory nerve action potentials were absent with the exception of the right median nerve; F wave velocities were decreased except for the left tibial nerve. Electromyography showed evidence of denervation in the right first dorsal interosseous, tibialis anterior, and both extensor digitorum brevis muscles. No denervation was found in the left vastus medialis. These abnormalities were compatible with an axonal sensorimotor neuropathy. Sural nerve biopsy showed axonal degeneration. Other causes of acquired polyneuropathy such as carcinomatous polyneuropathy, paraproteinaemias, uraemia, alcohol, diabetes mellitus, connective tissue diseases, amyloidosis, and hypothyroidism were excluded but a 4 cm insulinoma was identified and surgically removed. Hypoglycaemic attacks have not recurred and there has been motor improvement but paresthesiae have persisted during the next three years. Electrophysiological studies demonstrated no significant change.

Peripheral neurological symptoms in the course of hypoglycaemic attacks are unusual and are probably due to maintained hypoglycaemia rather than secondary to hyperinsulinaemia. After excision of a pancreatic tumour, sensory symptoms tend to regress but definite improvement in muscle power is uncommon. After three years of follow up, no objective sensory impairment was evident in our patient. Motor improvement was also found. Electrophysiological studies were carried out in only 10 of the 30 cases previously reported.¹ In one case, there was an analysis of nerve histology and there are two necropsy studies.¹⁻³ The neuropathology of this syndrome, however, remains controversial. Muscle histology has been described in three cases, showing different degrees of fibre atrophy indicative of denervation.^{1,4,5} Pathological studies disclosed degeneration of pyramidal tracts, myelin