SHORT REPORTS

Successful plasmapheresis in the Miller-Fisher syndrome

The Miller-Fisher variant of acute idiopathic polyneuropathy (Landry-Guillain-Barré syndrome) is characterised by external ophthalmoplegia, ataxia, and areflexia.¹ Though the syndrome is usually benign, progressive motor and respiratory impairment necessitating ventilatory support has been reported.² The anatomical basis of this condition and its relation to the Landry-Guillain-Barré syndrome is contentious.³ We report a case with clinical and radiological evidence of a cerebellar parenchymal lesion and progressive respiratory impairment that responded appreciably within six hours of plasmapheresis on day 8 of the illness.

Case report

A previously well 14-year-old boy presented two weeks after a mild respiratory illness with a two-day history of diplopia and ataxia. Examination showed minimal external ophthalmoplegia, bilateral mydriasis, prominent horizontal phasic nystagmus on abduction, vertical nystagmus on supraduction, and truncal ataxia. All deep tendon reflexes were absent despite Jendrassik reinforcement, and there was minimal weakness in the limbs. Sensory modalities were intact apart from vibration sense, which was lost to the level of the sternum. By day 8 he had developed complete iridoplegia and ophthalmoplegia, including ptosis, and respiratory vital capacity had fallen to 1.4 l. He could not walk unaided owing to severe ataxia. Autonomic instability, including arterial hypertension, was present.

Cerebrospinal fluid protein on day 4 was 1.45 g/l and the IgG:protein ratio normal. Cerebrospinal fluid contained no significant cells, and the venereal disease research laboratory test was negative. Routine haematological and biochemical variables were normal. A computerised brain scan with contrast injection on day 3 showed a small low-density area in the left cerebellar hemisphere, which was absent on repeat scanning at seven weeks. Electromyography and nerve conduction studies including upper limb sensory and motor M- and F-wave latencies were performed on days 10 and 17 and were normal.

Treatment consisted of four sessions of plasmapheresis totalling 6.4 l on days 8, 9, 10, and 11. Vital capacity increased to 2.5 l after the first session, fell to 2.2 l the following morning, and rose to 2.9 l after the second session (figure). Pupillary response to light and minimal horizontal eye movements were detected after the second session. Six days after the start of plasmapheresis abduction was 45° and infraduction complete. Pupillary responses were normal, and he walked unaided with a wide-based gait. Biceps reflexes were detectable on day 20. He was fully recovered at eight weeks.

Comment

Plasmapheresis has been increasingly reported to be of value in acute idiopathic polyneuropathy and chronic progressive demyelinating polyneuropathy since it was first suggested in 1978.⁴ The immunopathology of these conditions is not completely understood and the beneficial action of plasmapheresis not clear.

On day 8 of our patient's illness respiratory vital capacity fell to 1.4 l and was accompanied by complete ophthalmoplegia and iridoplegia. Four sessions of plasmapheresis totalling 6.4 l were conducted on four successive days. A dramatic improvement in vital capacity (figure) followed the first session and was subsequently maintained. The ocular disorder recovered within days but truncal ataxia persisted for six weeks. A recent report of a contrast-enhancing lesion in the midbrain tegmentum seen on computerised brain scanning in a patient with the Miller-Fisher syndrome is of interest.⁵ The initial scan in our patient showed a low-density area in the left cerebellar hemisphere, but interpretation in this region is notoriously difficult. Prominent vertical and horizontal nystagmus early in the illness suggests a central parenchymal lesion.

The clinical course of acute idiopathic polyneuropathy and the Miller-Fisher variant is extremely varied. We are unaware of reports of plasmapheresis in the Miller-Fisher syndrome. The progressive deterioration in ventilatory and oculomotor function in our patient, followed by dramatic respiratory improvement within hours of plasmapheresis, suggests a role for this treatment in complicated Miller-Fisher syndrome. Future confirmation of a parenchymal demyelinating component in this condition may have implications for plasmapheresis in other demyelinating disorders of the nervous system.

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Continuous subcutaneous insulin infusion corrects exercise-induced albuminuria in juvenile diabetes

Juvenile-onset diabetes treated with insulin is characterised by either a normal¹ or slightly raised² urinary albumin concentration as measured at rest. Viberti *et al* reported a reduced increase in urinary albumin excretion when insulin treatment was changed from conventional injections to continuous subcutaneous infusion.³ Patients with normal urinary albumin excretion at rest, however, may excrete increased amounts of albumin during exercise.³ Hence values obtained after exercise may be a more sensitive measure of abnormal renal handling of albumin than values obtained at rest.³ We report correction of exercise-induced albuminuria after two weeks of continuous subcutaneous insulin infusion in patients with juvenile-onset diabetes.

Patients, methods, and results

We studied 10 insulin-dependent diabetic men aged 19 to 40 years (mean age 27 ± SEM 2 years, mean weight 70 ± 2 kg, mean height 179 ± 2 cm). They were known to have had diabetes for two to 19 years (mean 10 ± 2 years) and were taking 28 to 74 units (mean 53 ± 4 U) of intermediate-acting or short-acting and intermediate-acting insulin daily. There was no clinical

evidence of diabetic retinopathy, neuropathy, or nephropathy (Albustix —) in any of the patients. Eight healthy men matched for age (mean 25 ± 1 years) and body size (weight 76 ± 3 kg, height 182 ± 2 cm) served as controls.

All patients were admitted to Helsinki University Hospital and during the first four days received their usual dose of insulin. On the third day diurnal blood glucose values were determined and urine collected for measurement of glucose, albumin, and β_2 -microglobulin excretion.² In the urinary albumin measurement the sensitivity of the method was $25 \mu\text{g/l}$ and the coefficients of interassay and intra-assay variation were 6.8% and 3.1% respectively. On the fourth day the patients performed a 40-min cycle ergometer exercise test, starting at 9 am.

On the fifth day a constant subcutaneous insulin infusion was started with a portable, battery-driven infusion pump (Model AS2C, Auto-Syringe Inc, Hooksett, New Hampshire, USA). We used an initial basal infusion rate of 0.2 mU insulin/kg/min. The remainder we gave as bolus injections before meals to provide 30–35% before breakfast, 25% before lunch, 30–35% before dinner, and 5–10% before evening snack, as described.⁴ After initial stabilisation on the regimen for four days the infusion was continued for 14 days, during which the patients remained in hospital. The postinfusion studies were carried out on the last two days of infusion.

Mean diurnal blood glucose concentrations, measured at two-hour to four-hour intervals, fell after two weeks of insulin infusion from 9.3 ± 0.7 mmol/l (168.0 ± 12.6 mg/100 ml) to 5.7 ± 0.4 mmol/l (103.0 ± 7.2 mg/100 ml) ($p < 0.005$); the control value, however, was 4.1 ± 0.1 mmol/l (74.0 ± 1.8 mg/100 ml); ($p < 0.005$). Urinary glucose excretion fell from 233 ± 67 mmol/24 h (42 ± 12 g/24 h) to 11 ± 5.5 mmol/24 h (2 ± 1 g/24 h) after two weeks of infusion treatment ($p < 0.01$). With the improvement in metabolic control insulin requirements declined by 28% ($p < 0.02$).

Albuminuria in the resting state fell by 39% from $5.2 \pm 0.4 \mu\text{g/min}$ to $3.5 \pm 0.6 \mu\text{g/min}$ ($p < 0.05$) after two weeks of pump infusion treatment (figure). Nevertheless, there was definite overlap between diabetic and

restored to normal. The decrease in albuminuria was associated with near-normal diurnal blood glucose concentrations and virtual elimination of glucosuria.

Enhanced albumin excretion may be due either to augmented glomerular filtration or to decreased tubular absorption of albumin, or to both. In this study no change in urinary β_2 -microglobulin excretion (which reflects tubular reabsorption) was observed after pump infusion treatment. These data thus suggest that the correction of exercise-induced albuminuria was achieved primarily by a reduction in the glomerular permeability to albumin.

Though albumin leakage has been thought to contribute to the thickening of glomerular basement membrane,⁵ the exercise-induced increase in albuminuria has no known structural implications. It will be interesting to see if long-term correction of albuminuria by strict metabolic control with continuous insulin infusion prevents or delays the onset of irreversible structural nephropathy in juvenile-onset diabetes.

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Urinary albumin excretion at rest and after exercise in healthy subjects and diabetic patients during conventional treatment and after two weeks of continuous subcutaneous insulin infusion. Chart shows individual values and means $\pm$ SEM. * $p < 0.05$ v resting value during conventional treatment. † $p < 0.02$ v exercise value after pump infusion or in control subjects.

control values, and neither preinfusion nor postinfusion levels in diabetic patients differed significantly from those in controls ($4.9 \pm 0.4 \mu\text{g/min}$). The exercise-induced rise in albuminuria in the diabetic group during conventional treatment ($3.0 \pm 0.7 \mu\text{g/min}$) was 3.8-fold greater than in the healthy controls ($0.8 \pm 0.7 \mu\text{g/min}$) ($p < 0.05$). Thus the mean postexercise value in diabetics ($8.1 \pm 0.8 \mu\text{g/min}$) was 42% higher than in controls ($5.7 \pm 0.6 \mu\text{g/min}$; $p < 0.02$). After two weeks of pump infusion treatment the exercise-induced rise in albuminuria in diabetic subjects ($0.8 \pm 0.5 \mu\text{g/min}$) was indistinguishable from that in controls, and the postexercise values were comparable in the two groups. Urinary β_2 -microglobulin secretion in diabetic patients remained unchanged during pump infusion treatment, both at rest (60 ± 9 ng/min before v 73 ± 12 ng/min after treatment) and during exercise (77 ± 9 ng/min v 87 ± 13 ng/min). The relative exercise intensity employed was similar in patients and controls, as reflected by a comparable rise in heart rate (to 136 ± 3 v 138 ± 1 beats/min) and blood lactate concentrations (to 3.2 ± 0.6 mmol/l (29.0 ± 5.4 mg/100 ml) v 2.6 ± 0.4 mmol/l (23.4 ± 3.6 mg/100 ml)) respectively in diabetic and control subjects.

Comment

Before starting pump infusion treatment the patients had albumin excretion in the high-normal range at rest, whereas in response to exercise it was significantly raised. After two weeks of insulin infusion treatment, however, the exercise-induced rise in albuminuria was

Intravascular haemolysis with acute renal failure after angiocardiology

Complications of coronary angiography are uncommon and usually cardiovascular.¹ We report a case of intravascular haemolysis with acute renal failure after angiocardiology.

Case report

A 58-year-old blacksmith presented with a three-year history of retrosternal pain on exertion. Electrocardiograms were normal at rest and on exercise. He had mild hypertension controlled with methyldopa and a thiazide diuretic but no history of renal disease and was not diabetic. His pain, which initially responded to conventional medical treatment, progressed to limit his exercise tolerance to 30 yards (27 m). On admission his haemoglobin concentration, white cell and platelet counts, reticulocyte index, urea and electrolyte values, serum creatinine concentration, and chest x-ray picture were within normal limits. Routine urine analysis showed no abnormality.

Left ventricular angiography was performed with 50 ml (0.75 ml/kg) Urografin 370 (an aqueous solution of sodium diatrizoate 66% w/v and meglumine diatrizoate 10%) injected at 12 ml/s. Selective coronary angiography was then carried out using a further 80 ml of the same contrast medium. The patient was nauseated for 12 hours after the procedure but slept normally that night. Next morning he was clinically jaundiced, though there were no new findings on physical examination. He voided 10 ml of black urine and became severely oliguric. No erythrocytes were seen on urine microscopy but the sample contained protein ++, blood +++, urobilinogen +++, and bilirubin + on stick testing. The blood urea concentration had risen from 4 mmol/l (24 mg/100 ml) to 23.8 mmol/l (143 mg/100 ml), and the plasma concentration of unconjugated bilirubin had risen from 14 mmol/l (0.81 mg/100 ml) to 138 mmol/l (8 mg/100 ml). There was no appreciable change