

recently been detected in the serum of patients with acquired immuno-deficiency syndrome,¹¹ systemic lupus erythematosus,¹² rheumatoid arthritis¹² and asbestosis¹³ and it has been suggested that persistent lymphocyte stimulation due to an immune disorder may lead to high levels of interferon in the serum. Our study, using a reliable immunological assay, suggests that elevated CSF interferon- α concentrations are not present in multiple sclerosis. However, further studies using IRMAs for interferon- γ will allow further insight into the possible role of interferons in the aetiology of multiple sclerosis.

RJ ABBOTT
PD GILES

I BOLDESON

Departments of Neurology and Immunology,
St James's University Hospital,
Beckett St, Leeds, LS9 7TF, UK

References

- Behan PO, Currie S. *Clinical Immunology*. London, WB Saunders 1978.
- Jacobs L, O'Malley J, Freeman A, Murawski J, Ekes R. Intrathecal interferon in multiple sclerosis. *Arch Neurol* 1982;39:609-15.
- Neighbour PA, Bloom. Absence of virus induced lymphocyte suppression and interferon production in multiple sclerosis patients. *Proc Nat Acad Sci (USA)* 1979;76:476-81.
- Salonen R, Ilonen J, Reunanen M, Salmi A. Detective production of interferon- α associated with HLA-DW2 antigen. *J Neurol Sci* 1982;55:197-206.
- Santoli D, Hall W, Kastrukoff L, et al. Cytotoxic activity and interferon production by lymphocytes from patients with multiple sclerosis. *J Immunol* 1981;126:1274-8.
- Tovell DR, McRobbie IA, Warren KG, Tyrell DLT. Interferon production by lymphocytes from multiple sclerosis and non-multiple sclerosis patients. *Neurology (NY)* 1983;33:640-3.
- Degre M, Dahl H, Vandvik B. Interferon in the serum and cerebrospinal fluid in patients with multiple sclerosis and other neurological disorders. *Acta Neurol Scand* 1976;53:152-60.
- Haahr S. Virus inhibiting activity in the cerebrospinal fluid from patients with acute and chronic neurological diseases. *Acta Pathol Microbiol Immunol Scand (B)* 1971;79:606-8.
- Salonen R. CSF and serum interferon in multiple sclerosis. Longitudinal study. *Neurology (NY)* 1983;33:1604-6.
- Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis. Guidelines for research protocols. *Ann Neurol* 1983;13:227-31.
- Abbott SR, Bulmovici-Klein E, Cooper LZ, Lange M, Briggs M, Weller IVD. Rapid detection of immunoreactive interferon- α in AIDS. *Lancet* 1984;1:564.
- Hooks JJ, Moutsopoulos HM, Geis SA, Stahl NI, Decker JL, Notkins AL. Immune interferon in the circulation of patients with auto-immune disease. *N Engl J Med* 1979;301:5-8.
- Kagamimori S, Watanabe M, Kubota M, Okada A, Yokoyama K, Nobutomo K. Serum interferon levels and natural killer cell activity in patients with asbestosis. *Thorax* 1984;39:65-66.

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Treatment of acute myelopathy in systemic lupus erythematosus with plasma exchange and immunosuppression

Sir: Central nervous system involvement occurs in up to 50% of patients with systemic lupus erythematosus (SLE). Happening early or late in the disease, alone or in combination with such manifestations as arthritis, nephritis and cutaneous lesions, it may include generalised epilepsy, disorders of mental function, central disturbances of extra-ocular and pupillary innervation, tinnitus and vertigo. Hemiparesis affects about 5% of patients, and transverse myelopathy in SLE has only been reported in thirty cases in the world literature.²⁻⁶ Clinical improvement in the published cases could not be reliably attributed to high dose corticosteroid therapy.^{2,9} A slow recovery occurred in only three paraplegic and in one quadriplegic patient from a total of twenty six.²

Plasma exchange has been used in diseases where auto-antibodies and/or circulating immune complexes have a demonstrated role in pathogenesis.¹⁰ Examples include myasthenia gravis (anti-acetyl choline receptor antibody),¹¹ type 1 diabetes mellitus (anti-islet cell antibody),¹² and SLE (anti-double stranded DNA antibody).¹³ A good response has been observed in fulminating, steroid-unresponsive SLE, or where cytotoxic drugs were contra-indicated by haematological considerations. Numerous reports of the use of plasma exchange in neurological disorders have been unable to supply firm evidence of efficacy except in certain forms of myasthenia,^{14,15} frequently because of the small numbers of patients with rare conditions, as in the case reported below.

A 49-year-old woman was referred in July 1982. She had experienced one week's progressive gait disturbance and impaired manual dexterity, culminating in a 24 hour onset of quadriplegia and acute urinary

retention. Five years earlier she had been investigated for polyarthritis affecting the knees and interphalangeal joints. The latex test for rheumatoid disease was negative. Serum anti-nuclear factor titre was 1/1000 and SLE was diagnosed. A year later, a photosensitive skin rash settled spontaneously in a few weeks. She remained well until early 1982 when she again noticed hand and knee stiffness: this responded quickly to phenylbutazone. Soon after, transient attacks of vertical diplopia were reported. Early in July she developed unsteadiness, trembling, tingling sensations in both hands and legs, and difficulty in initiating micturition with normal bladder sensation.

Systemic examination revealed facial erythema and telangiectasia with a scaly rash on the arms. The bladder was enlarged. She was well oriented and alert; speech was normal, although the content revealed a high degree of anxiety and repetition, not in keeping with her previous character. No abnormalities were found in the cranial nerves or upper limbs. Walking was impossible owing to an asymmetrical spastic paraparesis, denser on the right. The tendon reflexes were pathologically brisk, with extensor plantar responses. She was initially treated with prednisolone at 60 mg/day, increased after 24 hours to 120 mg/day. After continued deterioration over the next day, she was transferred to Guy's Hospital.

Examination again revealed a high degree of anxiety. She had a spastic tetraparesis greater on the right side. Sensation was impaired up to the C5 level, affecting both light touch and pain; two point discrimination in all fingers was absent, and vibration sense was lost below the tibial tuberosities. A myelogram was normal and CSF examination showed a white cell count of 165/mm³, mainly polymorphs; the CSF protein concentration was 0.33 g/l. A diagnosis of transverse cervical myelopathy was made.

The first plasma exchange was performed on the night of admission, and in total, eight exchanges were made on alternate days; five litres initially and subsequently four litres of plasma were exchanged using a Haemonetics model 30 machine. Circulatory access was by a 'Vygon' 3.3 mm catheter placed in the left femoral vein; return was via a 14 gauge 'Abbocath' placed in an anticubital vein.

Replacement fluid was physiological saline and a 5% solution of human serum albumin (Armour), in equal proportions. Intravenous methyl prednisolone (Upjohn) 1 g was given for the first six days, changing to oral prednisolone 45 mg/day, subsequently. Azathioprine (Wellcome) 25 mg/kg/day was used throughout and the blood count was monitored. Cimetidine 400 mg bd was given prophylactically against peptic ulceration.

A striking improvement in the condition of the patient was noted within 24 hours of the first exchange, although anxiety resulting in hyperventilation was a recurring problem, possibly a psychiatric manifestation of the disease. Power in the arms returned symmetrically to MRC 4 or better although the intrinsic hand muscles remained at MRC 3 for a considerable time. She was able to feed herself using thick-handled cutlery after four days.

Blood samples before and during treatment revealed an initially high level of circulating immune complexes, C3 and C4, which quickly returned to normal after initiation of plasmapheresis. (Fig). With intensive physiotherapy, the patient was able to stand after two weeks. Discontinua-

tion of urinary catheterisation was followed by normal bladder function. She was discharged to the care of the referring hospital by mid-August 1982, and was walking slowly, unaided, by December 1982. Almost normal power and fine movement of the hands were reported. Improvement continued and examination in April 1983 demonstrated normal processes and a stable gait. Tone was normal and power was MRC 5 in all muscle groups.

The rare quadriplegia of acute cervical myelopathy in SLE has been reported at levels C2 and C6,³ C6¹⁷ and C5¹⁸; transverse myelopathy at a lower level causing paraparesis is slightly more common. Rapid evolution of the paresis with sensory impairment below the affected level is typical.³ Sphincter function is affected in the majority of cases. A range of pathological lesions has been demonstrated post-mortem, from widespread infarction of the cord to much smaller areas of necrosis.² In a few cases, gross cord damage occurred in the absence of vascular abnormalities; however, thrombosed arteries and veins have been observed in relation to microscopic haemorrhages.⁸ Some small arteries showed inflammatory cell infiltrates and fibrinoid necrosis within their walls. In contrast, other vessels had much less florid stigmata of an immune complex vasculitis: changes included peri-vascular inflammatory cell aggregation and peri-capillary microglial proliferation.⁷ The severity of an attack of SLE is not strictly paralleled by the level of circulating immune complexes, nor is recovery always commensurate with a reduction in that level. In the described case, the fall in concentration of immune complexes, and the observed deranged levels of C3 and C4 were, as reported elsewhere,¹⁶ compatible with a vasculitic process.

In cases where a typical vasculitis is not a feature, an alternative mechanism of pathogenesis by antibody mediated cytotoxicity might be operating. Neurocytotoxic antibodies have been found in the serum of SLE patients.¹⁹ These may form following the release of neurological tissue antigens from already disrupted CNS tissues. Alternatively, crossreactive antibodies may be formed elsewhere and subsequently penetrate the CNS to instigate damage. The latter hypothesis is supported by animal experiments where antibodies to nervous tissue, when injected into a normal recipient, resulted in CNS lesions.²⁰ Access of protein molecules to the CNS involving passage across the blood-brain barrier has also been demonstrated experimentally, by

vesicular transport.^{21, 22} Relevant autoantibody specificities so far identified in SLE include those of neuroglia,²³ glycolipids and an antigen shared by brain tissue and the lymphocyte surface.^{25, 26} More recently anti-cardiolipin and anti-sphingomyelin specificities have been reported in a patient suffering from a lupus-like syndrome.²⁷

Poor response to plasma exchange rebound after therapy may be explained by re-equilibration and release into the circulation of neurocytotoxic antibodies from sequestered complexes. Also, renewed autoantibody synthesis could be expected to prolong the disease process without adequate immune suppression.

Whatever the precise mechanism, the use of sequential plasma exchange and continual immune suppression now appears to have a place in steroid-unresponsive SLE. If it is to be used it should be started early, particularly in the presence of neurological complications such as those described here, previously associated with permanent paralysis or death.

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DR DI SLOAN,
National Hospital for Nervous Diseases,
Queen Square,
London WC1N 3BG, UK

References

- Estes D, Christiaan CL. The natural history of systemic lupus erythematosus by prospective analysis. *Medicine (Baltimore)* 1971;50:85-95.
- Andrianakos AA, Duffy J, Suzuki M, Shapiro JT. Transverse myelopathy in systemic lupus erythematosus. Report of three cases and review of the literature. *Ann Intern Med* 1975;83:616-24.
- Johnson RT, Richardson EP. The neurological manifestations of systemic lupus erythematosus. A clinical pathological study of 24 cases and review of the literature. *Medicine (Baltimore)* 1968;47:337-69.
- Grainger DP. Transverse myelitis with recovery: the only manifestation of systemic lupus erythematosus. *Neurology (Minneapolis)* 1960;10:325-9.
- Penn AS, Rowan JA. Myelopathy in systemic lupus erythematosus. *Arch Neurol* 1968;18:337-49.
- Johnson RT. Systemic lupus erythematosus. In: Vinken PJ, Bruyn GW, eds. *Handbook of Clinical Neurology*. Amsterdam: North-Holland 1980;39:273-93.
- Piper PG. Disseminated lupus erythematosus with involvement of the spinal cord. *JAMA* 1952;153:215-7.

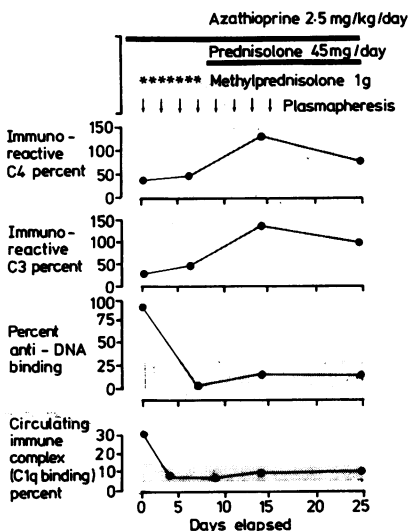


Fig The variation of serum immune complexes, anti-DNA titre, C3 and C4 levels in relation to the indicated treatment by plasma exchange and immunosuppression. Normal ranges for the laboratory are shown in stipple.

- ⁸ Sinkovics JG, Gyorkey F, Thoma GW. A rapidly fatal case of systemic lupus erythematosus: structures resembling viral nucleoprotein strands in the kidney and activities of lymphocytes in culture. *Texas Rep Biol Med* 1969;27:887-908.
- ⁹ Michael AF, Vernier RL, Drummond KN, Levitt JJ, Herdman RG, Fih AJ, Cood RA. Immunosuppressive therapy for chronic renal disease. *N Engl J Med* 1967;276:817-28.
- ¹⁰ Berkman EM, Umlas J, eds. *Therapeutic Haemapheresis. A Technical Workshop*. Washington DC: American Association of Blood Banks, 1980.
- ¹¹ Newsom-Davis J, Wilson SG, Vincent A, Ward CD. Long term effects of repeated plasma exchange in myasthenia gravis. *Lancet* 1979;i:464-8.
- ¹² Ludvigsson J, Heding L, Lieden G, Marner B, Lernmark A. Plasmapheresis in the initial treatment of insulin-dependent diabetes mellitus in children. *Br Med J* 1983;286:176-8.
- ¹³ Verrier Jones J, Bucknall RC, Cumming RH, et al. Plasmapheresis in the management of acute systemic lupus erythematosus. *Lancet* 1976;i:709-11.
- ¹⁴ Dau PC. Plasmapheresis: therapeutic or experimental procedure? *Arch Neurol* 1984;41:647-53.
- ¹⁵ Lisak RP. Plasma exchange in neurologic diseases. *Arch Neurol* 1984;41:654-7.
- ¹⁶ Petz LD, Sharp GS, Cooper NR, Irvin WS. Serum and cerebral spinal fluid complement and serum antibodies in systemic lupus erythematosus. *Medicine (Baltimore)* 1971;50:259-75.
- ¹⁷ Vitale C, Cardinaud JP. Ramollissement medullaire au cours d'un lupus erythematosus dissemine. *Bordeaux Med* 1970;3:707-18.
- ¹⁸ Vitale C, Kahn MF, de Seze M, de Seze S. Neurite optique, myelite maladie lupique. A propos de deux observations. *Ann Med Interne (Paris)* 1973;124:211-16.
- ¹⁹ Bluestein HG. Neurocytotoxic antibodies in serum of patients with systemic lupus erythematosus. *Proc Natl Acad Sci USA* 1978;75:3965-9.
- ²⁰ Simon J, Simon O. Effect of passive transfer of anti-brain antibody to a normal recipient. *Exp Neurol* 1975;47:523-34.
- ²¹ Westergaard E. The blood-brain barrier to horseradish peroxidase under normal and experimental conditions. *Acta Neuropathol (Berl)* 1977;39:181-7.
- ²² Zvaifler NJ, Bluestein HG. The pathogenesis of CNS manifestations of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:862-6.
- ²³ Bluestein HG, Woods VL Jr. Antineuronal antibody in systemic lupus erythematosus. *Arthritis Rheum* 1982;25:773-8.
- ²⁴ Hirano T, Hashimoto H, Shiokawa Y, et al. Anti-glycolipid autoantibody detected in sera of systemic lupus erythematosus patients. *J Clin Invest* 1980;66:1437-40.
- ²⁵ Bresnihan B, Oliver M, Grigor G, Hughes

GRV. Brain reactivity of lymphocytotoxic antibody in systemic lupus erythematosus with and without cerebral involvement. *Clin Exp Immunol* 1977;30:333-7.

- ²⁶ Bluestein HG, Zvaifler NJ. Brain reactive lymphocytotoxic antibodies in the serum of patients with systemic lupus erythematosus. *J Clin Invest* 1976;57:509-16.
- ²⁷ Harris EN, Boey ML, Gharavi AE, Patel BM, Mackworth Young CG, Loizu S, Hughes GRV. Anticardiolipin antibodies: Detection by radioimmunoassay and association with thrombosis in systemic lupus erythematosus. *Lancet* 1983;ii:1211-14.

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Familial hypoplasia of the thenar eminence: a report of three cases

Sir: Some individuals are born without certain muscles.¹ These variations of the musculature are most often sporadic but hereditary absence of muscles has been reported.²⁻⁵ The pattern of inheritance in these families has been described as autosomal dominant. Congenital hypoplasia or absence of the thenar muscles is rare and only four sporadic cases have been

reported.⁶⁻⁹ The purpose of this letter is to report three cases from two generations of a family presenting congenital hypoplasia of the thenar eminence. In addition two of the cases had no extensor pollicis longus muscles.

Case 1 was a 28-year-old man, referred to the department of neurology because of a left common peroneal nerve palsy which recovered during the following months. Since childhood bilateral hypoplasia of the thenar eminences had been noticed but apart from this there had never been any symptoms or signs of neuromuscular disease until the peroneal nerve palsy. A pronounced bilateral hypoplasia of the thenar eminence was found, with almost complete absence of the abductor pollicis brevis muscles (fig). In addition the extensor pollicis longus muscles were absent on both sides. Sensation, vibration and position sense of the hands was normal as was the rest of the neurological examination. Hand radiographs showed moderately hypoplastic scaphoid bones.

Case 2 was a 27-year-old woman, the sister of case 1, who since childhood had noticed hypoplasia of the thenar eminences. There had been no other symptoms or signs of

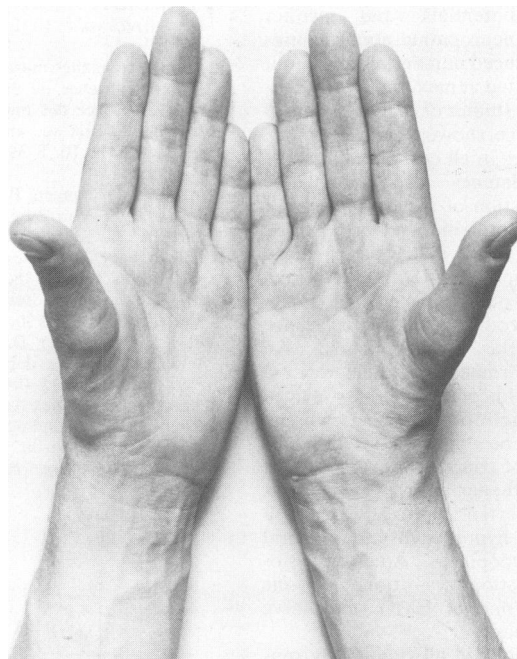


Fig Case 1, showing hypoplasia of both thenar eminences.