Case report

Acute autonomic neuropathy in association with systemic lupus erythematosus

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SUMMARY   A patient is described with acute autonomic neuropathy, developing post partum in association with systemic lupus erythematosus, and showing a rapid clinical response to steroids. The pattern of tissue damage is suggestive of an immunologically mediated mechanism.

Key words: cerebral lupus, post partum, ileus.

Acute autonomic neuropathy is a rare but well described clinical entity, there being 15 cases[1-12] reported to date. One[10] was associated with mixed connective tissue disease (MCTD), and we now report a case occurring in a patient with systemic lupus erythematosus (SLE). This case is unusual because the autonomic neuropathy appeared post partum and a rapid clinical recovery occurred when corticosteroids were prescribed.

Case report

A 21-year-old female presented in November 1977 with a normochromic anaemia. She complained of tiredness and weight loss of 6 kg over six months, but there were no abnormal physical signs. A diagnosis of an 'autoimmune disease' was made on the basis of the abnormal results shown in Table 1. Early in 1981 she developed anosmia attributed to a viral infection. In November 1981 she had acute parotitis, but sialograms were normal and symptoms resolved within five days. At this time she also complained of dry eyes; no tear secretion could be shown, and a provisional diagnosis of Sjögren's syndrome was made. In August 1982 she developed joint pains which responded to piroxicam (Feldene) and a transient erythematous rash over her body and limbs. She became pregnant in October 1982 and during her pregnancy remained clinically well. In June 1983 she delivered a full-term baby boy who

had 2:1 heart block at birth which later progressed to complete heart block.

After the birth of her baby she felt unwell, dizzy, anorexic, intermittently nauseated, and had difficulty swallowing. By September 1983 she had developed persistent vomiting, mucus diarrhoea, and had lost 10 kg in weight over the preceding two to three months. She had previously been very constipated and was taking Dorbanex and the contraceptive pill, Norimin, which had been re-started one month previously. On admission to hospital she was thin and pale but had no rash, joint swelling, or lymphadenopathy. She had a resting tachycardia of 110 beats/minute. There was tenderness in the left iliac fossa, scanty bowel sounds, and impacted hard faeces in the rectum. Neurological examination showed anosmia and an irregular left pupil. Both pupils reacted sluggishly to light and accommodation. Ten days after admission she developed complete bowel obstruction and increasingly severe dysphagia, being barely able to swallow liquids.

Relevant initial investigations are summarised in Table 1. Metabolic causes of ileus were excluded since her urea and electrolytes, calcium, and blood sugar were normal. Barium enema and sigmoidoscopy were normal. Rectal biopsy showed no amyloid tissue and normal ganglion cells. Barium meal and follow through showed a very slow intestinal transit. Attempts to measure bowel transit time were abandoned as the capsules did not leave the stomach. Oesophageal manometry showed grossly impaired oesophageal transit with absent peristaltic contractions. Bladder cystometrography showed no

Table 1 *Initial investigations in 1977, and during admission in 1983*

	1977	1983	Normal range
Haemoglobin (g/dl)	10·1	12·1	11·5–16·5
ESR (mm/h)	47	77	1–15
Immunoglobulin IgG (g/l)	39·5	35·4	2·5–17·98
Antinuclear factor	++ pos.	Positive 1 in 384	Negative
DNA* binding (U/ml)	16·5	22	0–25
LE cells	Not done	Positive	Negative

*DNA = deoxyribonucleic acid.

initiation of micturition and no rise in detrusor pressure, but despite these findings she only had slight hesitancy of micturition. Cardiovascular autonomic function tests[13] were grossly abnormal (Table 2), and a 24-hour electrocardiograph (ECG) tape recording showed a persistent heart rate of 100–110 beats/minute with little heart rate variation (Fig. 1). Where the heart rate tests are abnormal, this is indicative of parasympathetic damage, while blood pressure abnormalities indicate more widespread sympathetic damage. Taken together, therefore, the clinical features and abnormal tests suggested that she had widespread autonomic abnormalities involving both parasympathetic and sympathetic pathways.

In view of her deteriorating clinical condition she was started on intravenous hydrocortisone and parenteral feeding via a Hickman catheter. Ten days after insertion of the central line (day 42 from admission) she developed superior vena cava obstruction confirmed by venogram. The partial thromboplastin time with kaolin was short (patient 24 seconds, control 29 seconds) and there was no evidence of a lupus anticoagulant. Streptokinase therapy (BRL 26921 5 mg twice daily for two days) was instituted, followed by heparin, with complete resolution of the clot. It was also discovered that she was still taking the contraceptive pill on her own initiative and this was stopped!

In late October 1983 (day 48) she developed a severe frontal headache but with no focal signs. A few hours later she had three generalised grand mal convulsions and became deeply comatosed with a decerebrate posture. A computerised tomographic (CT) brain scan was normal, an electroencephalogram (EEG) was grossly abnormal with no organised background rhythm, and a lumbar puncture showed a raised cerebrospinal fluid protein of 430 mg/dl (4·3 g/l). Intravenous phenytoin and dexamethasone were given, and after careful consideration heparin was restarted. She regained con-

Table 2 *Cardiovascular autonomic function test results*

	Valsalva ratio	30:15 ratio	Heart rate variation (beats/min)	Systolic BP fall on standing (mmHg)	Diastolic BP rise during sustained hand grip (mmHg)
13 Oct 1983	1·00	1·00	0	32	5
17 Nov 1983	1·02	1·00	0	30	10
8 Dec 1983	1·16	1·00	9	24	12
12 Jan 1984	1·02	1·00	11	10	10
9 Feb 1984	1·11	0·97	19	6	16
22 Mar 1984	1·02	1·06	18	10	10
3 May 1984	1·09	0·98	21	+2	15
12 July 1984	1·12	1·00	22	10	13
Normal values	>1·21	>1·04	>15	<10	>16

October 1983
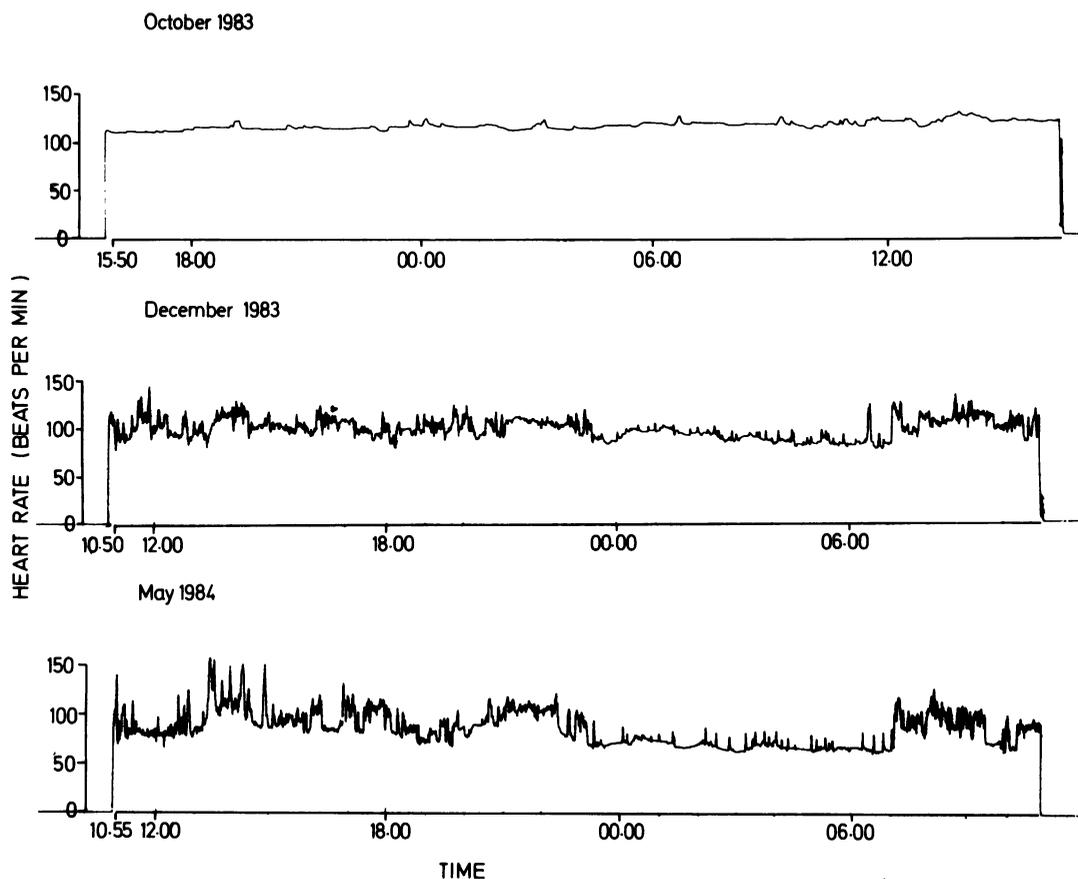
December 1983

May 1984

TIME

Fig. 1   *Twenty-four hour ambulatory heart rate record during the acute episode (October 1983) and during recovery (December 1983 and May 1984).*

sciousness over the next 24 hours. Formal testing showed a left parietal lobe lesion with poor memory, inability to calculate, astereognosis, and apraxia; all of which gradually recovered over the next three-week period. A repeat CT scan three days later was normal and an EEG 5 days later showed considerable improvement. Electrophysiology studies showed no evidence of peripheral somatic nerve involvement.

After this catastrophic set back the patient continued to improve and by day 53 after admission was eating without vomiting and was opening her bowels normally. Postural hypotension became symptomatic as she was mobilised. She was eventually discharged home on Warfarin, phenytoin, and prednisolone. Subsequently she has remained well with resolution of all symptoms and a gradual improvement in her autonomic function tests (Table

2) and 24-hour ECG tape recording (Fig. 1). Her anosmia and dry eyes have also improved, though she is still unable to cry, and her pupillary light reflexes are normal. Her Warfarin was stopped after three months, and the dose of prednisolone was reduced as azathioprine was added to the drug regimen. She is now asymptomatic 12 months after discharge but still maintained on prednisolone, azathioprine, and sodium valproate.

Stored sera dating back to April 1981 were analysed and showed positive antibodies to the two components of extractable nuclear antigen: ribonuclease sensitive antigen (RNP) and ribonuclease-resistant antigen (Sm), as well as Ro and La antibodies. Rheumatoid factor (Rose-Waaler) was greater than 1 in 1280, complement components C4 and CH50 were low normal, and circulating immune complexes were positive.

Discussion

Acute autonomic neuropathy is characterised by severe sympathetic and parasympathetic impairment with preservation of somatic motor and sensory function. In previously described cases, approximately half have been associated with other neurological defects.[2 6 7 8 9 10 12] Cases have occurred in association with infectious mononucleosis,[9] herpes simplex,[12] and mixed connective tissue disease (MCTD).[10] All described cases have had gastrointestinal, cardiovascular, and pupillary abnormalities, with the majority having genitourinary and sweating abnormalities as well. Our patient showed all these features, except that sweating was not formally tested.

The onset of symptoms in this patient was acute after the birth of her baby. However, retrospectively, it is possible that the development of Sjögren's syndrome two years previously may have been an early feature of autonomic neuropathy; particularly as some tear formation has recurred with steroids.

Most of the previous cases have either not been treated at all or treated symptomatically with fludrocortisone or carbachol. Only one patient[1] was treated with corticosteroids and made a complete clinical recovery within six months of starting steroid therapy; his symptoms had progressed over the previous 12 months when only supportive measures were used. Our patient also showed a rapid clinical response to steroids, which we feel is unlikely to be coincidental. In the other reported cases, only two[6 9] showed a complete clinical recovery. There are still residual abnormalities of autonomic function in this lady on formal testing but whether these are commonplace in SLE remains speculative. As yet autonomic function has not been assessed in any series of patients with SLE.

The target organ of damage in acute autonomic neuropathy is unknown. As there were widespread abnormalities of autonomic function with no electrophysiological evidence of peripheral somatic nerve involvement, we would postulate that the central pathways of the autonomic nervous system were probably involved. The grand mal fits suggestive of a cortical lesion might support this view, though it is also possible that this might have been a result of a cortical venous thrombosis after the superior vena caval obstruction.

The response to steroids combined with azathioprine and the presence of SLE suggest that an immunological mechanism is responsible for the autonomic neuropathy. Although this patient does not strictly fulfil the criteria of the American Rheumatism Association[14] for the diagnosis of SLE, we feel that this is the most appropriate diagnosis in view of the mild arthropathy, presumed cerebral vasculitis, the birth of a baby with congenital heart block,[15] exacerbation of disease post partum, positive LE cells, and positive autoantibodies. In a review by Sharp[16] anti-RNP antibodies alone were strongly associated with MCTD; in contrast anti-Sm and anti-RNP antibodies together were almost exclusively associated with SLE.

Evans *et al.*[17] reported a case of cerebral lupus associated with high levels of antineuronal antibodies and circulating immune complexes, that showed no response to steroids but responded clinically to plasmapheresis, which reduced the circulating immune complexes to zero for 60 days. Atkins *et al.*[18] first suggested that the central nervous system manifestations of cerebral lupus may be explained by alterations in choroidal function and permeability caused by immune complexes. Zvaifler and Bluestein[19] postulate that these changes may allow antineuronal antibodies access to the brain, with consequent tissue damage. A similar mechanism may operate in acute autonomic neuropathy with a specific but as yet undefined autoantibody acting on central autonomic pathways.

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