CASE REPORT: MULTIPLE SCLEROSIS AND SLE REVISITED

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SUMMARY: The distinction between Multiple Sclerosis (MS) and neurological Systemic Lupus Erythematosus (SLE) can sometimes be difficult especially in the early stages. The occasional patient may have both diseases. MS, SLE and other auto-immune disorders may run in the same family. We describe a young Asian woman who had clinical and serological features of both diseases and whose mother has scleroderma.

Key Words: Multiple sclerosis, Systemic lupus erythematosus, Familial auto-immune diseases.

INTRODUCTION

Both MS and SLE are diseases resulting from states of disordered immunity. In both diseases there appears to be a genetic predisposition to the disorder triggered by exogenous factors. There is a higher prevalence of MS and SLE within families and both disorders may occasionally occur in the same individual. Not surprisingly, it may be difficult to differentiate between the two disorders especially in the early stages and when neurological complaints are the sole presenting features in SLE. We describe a woman who presented with isolated optic neuropathy and had a high titre of antinuclear antibodies (ANA). Subsequent course suggested that she has both MS and SLE. Her mother has scleroderma.

CASE HISTORY

A 23 year-old Asian woman was referred to the Neurology clinic at Wentworth Hospital in August 1996 because of a ten day history of pain over the left eyebrow followed a few days later by poor vision in the left eye. She had no other complaints. There was no family history of neurological disease, but her mother had longstanding scleroderma. A left relative afferent pupil defect was present. The visual acuity in the left eye was 6/36 whilst, on the right it was 6/9. Mild pallor of the left optic disc was present. MRI of the brain showed high intensity signals in the posterior commusure of the corpus callosum and centrum semiovale (Figure 1). No abnormality was detected in the optic nerves. The blood investigations are summarized in Table 1. The antinuclear factor (ANF) was positive in a titre of 1:3200 (Table 1). Antibodies to extractable nuclear antigen (ENA) to ribonucleo protein (RNP) were present. Anticardiolipin antibodies (ACA) were not detected and the C3 component of the complement cascade was normal. The ESR was 10 mm/hr. Urine examination was also normal. The CSF examination revealed a mild pleocytosis and oligoclonal bands (Table 2). The visual evoked response (VER) test in the abnormal left eye showed a prolonged P 100 of 138 msec, but normal amplitude. The VER on the right was normal. A repeat ANF in October 1996 was 1:800. After consultation with an immunologist the patient was started on a course of prednisone and azathioprine. Apart

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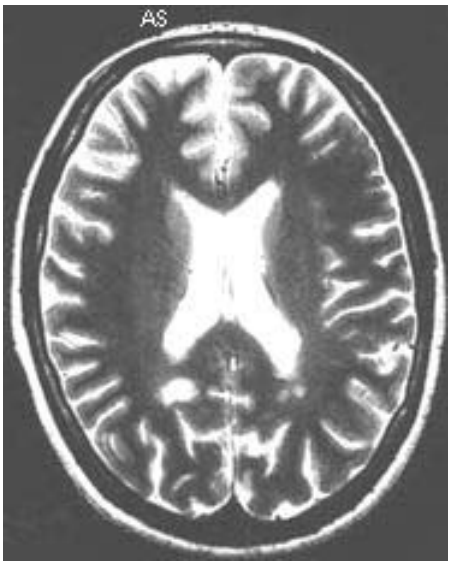


Figure 1: MRI performed at initial presentation shows corpus collosal lesions.

from persistent poor vision in th left eye she remained well. The ANF titre had declined to 1:200. (Table 1).

In October 1997, whilst on a decreased dose of prednisone (20 mg/day) and azathioprine (50 mg/day), the patient presented with a five day history of numbness of the hands and from the waist downwards. The visual acuity remained unchanged. Tone was normal. She had mild weakness (4+/5) of ankle dorsiflexion bilaterally. The tendon reflexes were brisk and symmetrical, the abdominal reflexes were absent and both plantar responses were equivocal. Pin prick and light touch were impaired up to the T1 dermatome whilst vibration sense was impaired up to T4. Joint position was intact. Livedo reticularis was present on the thighs. The ANF was positive 1:200, ESR 15 mm/hr and the ACA was negative. Spinal MRI showed extensive hyperintensities, but there was no enhancement after gadolinium administration (Figure 2). A repeat CSF examination gave results similar to the first examination. A five day course of IV methylprednisone 500 mg daily was given. The patient improved. The oral prednisone was increased to 60 mg/day and azathioprine to 100 mg/day. Over the ensuing months she remained stable. An attempt was made once more to decrease her therapy. However, at a prednisone dose of 10 mg/day and azathioprine dose of 50 mg/day, she developed recurrence of the myelopathic symptoms in March 1998. She was treated as for a MS relapse and improved again. The patient remained stable until July 1999 when for the first time she complained of joint pains in the hands and shoulders. There was no objective evidence of arthritis. A repeat ANF was 1:800, anti DNA and ACA were negative. The serum complement and urine examination were normal. MRI of the brain (Figures 3a and 3b) showed extensive lesions resembling those seen typically in MS. Apart from pain relief, her immunosuppressive therapy of prednisone 40 mg/day and azathioprine 100 mg/day remains unchanged.

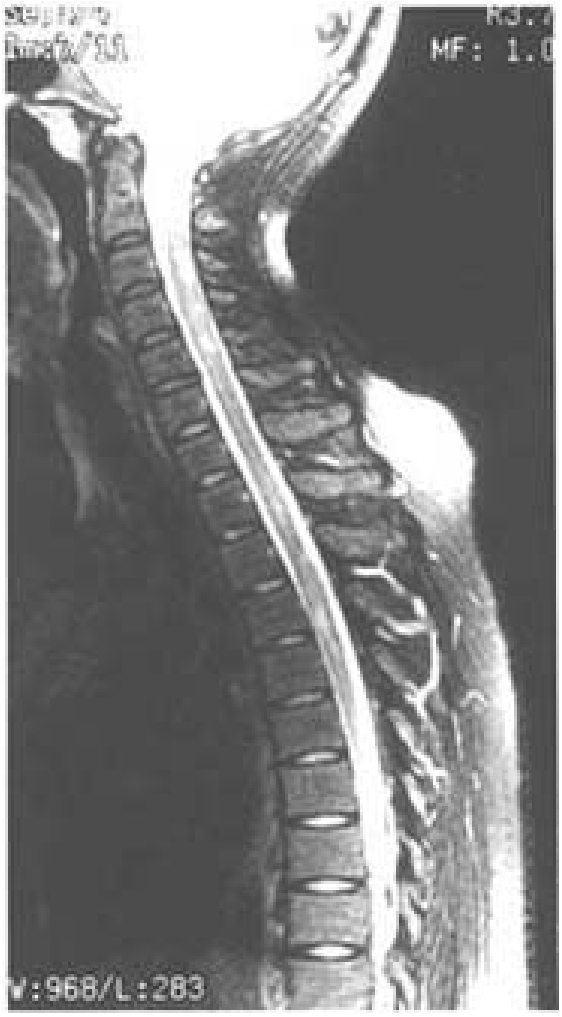
HLA studies and a more detailed auto-immune profile were performed on the patient and her mother who has scleroderma, in November 1999. The results are summarized in Tables 3 and 4 respectively.

Table 1 : Results of ANA tests, ACA and Complement components.

	1996		1997			1998	1999
	AUG	NOV	JAN	JUN	OCT	AUG	AUG
ANA	3200	800	800	200	200	800	800
ACA	0.5	-	-	-	0.7	-	-
C3	1.56	-	-	-	-	-	1.20
C4	0.26	-	-	-	-	-	0.19
FACTOR B	0.45	-	-	-	-	-	0.46

ANA = Antinuclear antibodies ACA = Anticardiolipin antibodies

Figure 2: Spinal MRI showing numerous hyper-intense lesions.



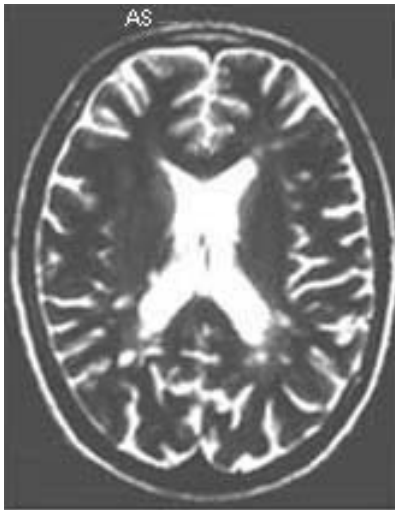
DISCUSSION

The differential diagnosis of MS is wide and ranges from acute disseminated encephalomyelitis, sarcoidosis, vasculitis, other auto-immune diseases, through to compressive lesions. While neurological involvement in SLE is common, there is seldom diagnostic confusion with MS as evidence of systemic disease is usually present. Problems arise when the initial presentation of SLE is neurological. Earlier studies (1,2) allude to the diagnostic difficulties, but these studies were done before the era of modern neuroimaging.

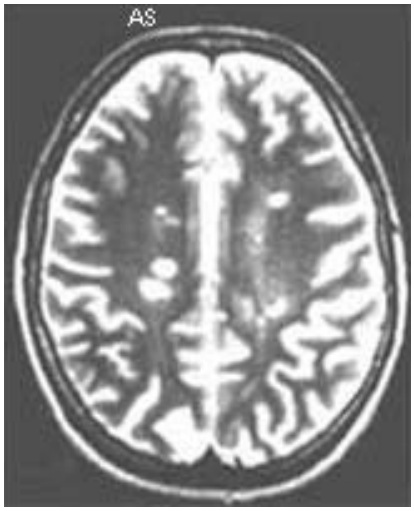
Our patient fulfils both the Schumacher (3) and the Poser (4) criteria for clinically definite MS. Furthermore, at the presentation of isolated optic neuropathy, there was already paraclinical evidence of dissemination of lesions (MRI – Figure 1) and oligoclonal bands were detected in the CSF. She subsequently developed a partial myelopathy. During both the presentations there were no other systemic or constitutional symptoms and ESR remained normal. The serial MRI studies (Figures 1, 2, 3) demonstrate some large lesions, some ovoid, periventricular, infratentorial and corpus callosal lesions. These features satisfy the MR imaging criteria of Paty *et. al.* (5) and Fazekas *et. al.* (6) for MS.

There is little doubt that this patient has MS. More difficult is to determine whether she has SLE as well. The

Figures 3: More extensive lesions in the brain in 1999.



(a)



(b)

most frequent neurological manifestations of SLE are neuropsychiatric signs and seizures. Optic neuropathy is uncommon and thought to be primarily ischaemic nature (8). Clinically it is usually indistinguishable from the optic neuritis of MS. Visual evoked responses may be delayed, of decreased amplitude or totally absent.

Myelopathy in SLE is rare eg. Dubois found a lupus myelopathy in only 2 of his 464 SLE patients. The myelopathy tends to be severe often leaving the patient wheelchair bound. This has been our experience as well (4 cases – unpublished data). This is not surprising as pathological examination more often shows necrosis. ACA and anti DNA antibodies are usually present.

Our patient had a partial myelopathy and had neither of these antibodies. Her ESR, serum complement and urine examinations have been persistently normal. However, two episodes of livido reticularis were noted and on one occasion she complained of arthralia. These findings together with high ANA titres (discussed later) suggest that the patient has SLE as well. Co-existing MS and SLE is rare (9, 10). The best documented series are that of Kinnuen *et. al.* (10). In all of their three patients, systemic involvement was more obvious than in our patient. Of interest, while patient 1 had a high ANA titre, the anti DNA antibodies were negative.

Serological and immunological aberrations are common in both diseases. ANA are commonly present in MS patients (11, 12), but the titres were low – usually between 1:80 – 1:160. The staining pattern was variable. Our patient had a peak titre of 1:3200, but the anti DNA

Table 2: CSF findings over the course of the disease.

Date	Polys	Lymphs	RBCs	Protein	Globulin	Sugar	Oligo-Clonal Bands
9/96	2	18	2000	0.42	Trace	2.7	+
10/97	2	22	440	0.41	No increase	3.1	+
8/99	4	14	-	0.41	Trace	2.8	+

Table 3: HLA profiles in patient and mother.

Locus	Patient	Mother
A	1.24	3.24
C	3.6	3.27
B	57.62	44.62
DRB 1	02.07	02.07
DQB 1	02.0601	02.0601

antibody was persistently negative. CSF oligoclonal bands may be present in up to 90% of patients with MS (13), but 42% of SLE (14) patients also have oligoclonal bands. So this test is of little help.There is a genetic and familial predisposition to development of MS, SLE and other autoimmune disease. There have been instances where one identical twin developed MS and the other SLE (15), familial cases of SLE (16), and MS occurring in one generation and SLE in another (17). The mother of our patient has longstanding scleroderma. Both show remarkably similar HLA typing. However, neither showed profiles commonly seen in MS (18) or SLE (19).

CONCLUSION

This patient illustrated some of the diagnostic dilemma in differentiating MS from SLE.

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Table 4: Comparative serological markers in patient and mother (September 1999).

TEST	PATIENT	MOTHER
ANF Screen	Positive	Positive
ANF Titre	1:800	-
ANF Hep 2 Cells	Positive	Positive
Hep 2 Patterns	Speckled and Cytoplasmic Dot staining resembling Lysosomal pattern	Centromere pattern
Anti-DNA	Negative	Negative
ACA	Negative	Negative
SM AB	Negative	Negative
SSA AB	Negative	Negative
SSB AB	Negative	Negative
LKM AB	Negative	Negative
SCL - 70 AB	Negative	Negative
ANCA	Negative	Negative
Lupus Anticoagulant	Negative	Negative
Smooth Muscle AB	Negative	Negative
Parietal Cell AB	Negative	Negative
Mitochondrial AB	Negative	Negative

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