

Short report

Cerebral systemic lupus erythematosus: a case report and evaluation of diagnostic tests

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SUMMARY We describe a 34 year old woman who presented initially with a progressive pseudobulbar palsy. A delay of five months occurred before a diagnosis of cerebral systemic lupus erythematosus was made. Currently available investigations for cerebral systemic lupus erythematosus are evaluated and the need for an easily performed specific diagnostic test is discussed.

Central nervous system (CNS) involvement in systemic lupus erythematosus (SLE) may be pleomorphic in its presentation and, if other systemic features of the disease are not present, diagnosis may be delayed. As a result SLE should be considered in any patient with obscure neurological problems.

Extensive neurological investigations carried out in the following patient failed to reveal any other significant pathology to account for her presentation with a pseudobulbar palsy. There was, however, sufficient clinical and laboratory evidence to make a confident diagnosis of SLE, although her particular neurological presentation was a most unusual one. It might be anticipated that brainstem syndromes would be more common in CNS lupus considering the frequency with which lesions are reported at this site at necropsy.¹ Diagnosis was only thought of relatively late after onset of the neurological problem when there was development of arthralgia, photosensitivity and Raynaud's phenomenon associated with leucopenia and thrombocytopenia.

Case report

A 34 year old caucasian woman presented in November 1978 with a nine month history of dysarthria, difficulty opening her mouth and pro-

truding her tongue. These symptoms had come on over seven days and had been progressive up to the time of presentation. There was no history of diplopia, visual loss or ataxia.

Examination of the pupils, fundi and anterior segments of both eyes with a slit lamp was normal. The patient had great difficulty opening her mouth due to spasm of the masseters, and her tongue which could not be fully protruded, was small, pointed and spastic. The gag reflex was diminished with poor palatal movement. The remainder of the neurological and physical examination was normal.

Full blood count, ESR and serum biochemistry were all normal. CSF protein, sugar, immunoglobulins and cell count also were normal. Special investigations including edrophonium test, electromyography, technetium-99 pertechnetate brain scan using the gamma camera, metrizamide cisternography, and computerised axial tomography with posterior fossa cuts were normal.

When the patient was reviewed in March 1979 further progression of her neurological disability was observed with development of hyperreflexia in the limbs and ankle clonus. At this time a history of photosensitivity, arthralgia of the hands and wrists and Raynaud's phenomenon affecting the fingers was elicited. The patient complained of a new symptom of persisting throbbing headache. She was taking no medications or the contraceptive pill.

Further investigations revealed a haemoglobin of 11 g/dl with normal indices, but the white

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cell count was $1700/\text{mm}^3$ of which $986/\text{mm}^3$ were neutrophils and $629/\text{mm}^3$ were lymphocytes. Platelet count was $120\,000/\text{mm}^3$. Bone marrow examination was consistent with increased peripheral destruction as the mechanism of the neutropenia and thrombocytopenia. The ESR was normal. Antinuclear factor was positive at a titre of 1:1000 with homogeneous staining, and DNA binding was 35.6% (upper limit of normal being 30%). LE cells were plentiful in the peripheral blood. Complement screen revealed reduced CH_{50} (C_3 and C_4 normal).

A diagnosis of SLE with CNS involvement was made. The patient was treated with steroids initially, and later with plasmapheresis and azathioprine without improvement. The steroid therapy, however, did return the white cell and platelet count to normal.

Discussion

Neurological involvement, frequently transient, occurs sometime during the clinical course of SLE in 25 to 75% of patients.^{2,3} Particular problems arise, as in the case described, when a patient initially presents with an unusual complication of SLE in the absence of the other common manifestations of the disease.

Headache, both migraine and other types,⁴ is a common symptom in lupus. Involvement varies greatly, the most common objective neurological syndrome is psychiatric,⁵ in the form of a psychosis or mild neurosis. An organic brain syndrome with hallucinations and dementia also occurs. The next most frequent manifestation is seizures, usually grand mal in type.⁶ Other neurological problems recognised occasionally as being due to lupus include visual loss, visual hallucinations and optic neuritis which may be indistinguishable from that of multiple sclerosis.⁸ Tremor, chorea and cerebellar dysfunction,⁹ transverse myelopathy which may be associated acutely with a low CSF sugar,¹⁰ and peripheral neuropathy¹¹ also may occur. Bizarre and unusual CNS symptoms may appear in SLE and the diagnosis must be considered in any patient with obscure neurological problems. It is important to remember that the diagnosis of SLE may be difficult, unless the patient has clear-cut evidence of multisystem disease sufficient to fulfil the ARA diagnostic criteria.¹² Otherwise it may not be possible to attribute the neurologic syndrome to this aetiology with any confidence.¹³

Patients with SLE also are prone to neurological disorders unrelated to the pathology of the primary disease. Opportunistic infection of

the CNS with common and unusual pathogens is frequent,¹⁴ especially when these patients are treated with immunosuppressive agents. Similarly, psychosis and obtundation may be encountered during treatment with steroidal and non-steroidal anti-inflammatory agents and with anti-hypertensive drugs.¹⁵

Difficulties in diagnosing neurological involvement in SLE and its separation from neurological syndromes due to the primary pathology or to unrelated disease, emphasise the need for a diagnostic test for CNS lupus. Attempts to develop a peripheral blood test using antibodies which react with lymphocytes, foetal red cells and cortical neurons, is in progress,^{16,17} but the value of such tests has not yet been proven. CSF complement levels may be reduced in CNS lupus, but the technique is difficult and the abnormality insufficiently reliable to make this a useful diagnostic test.^{18,19} Variations in the titre of antibody to double-stranded DNA do not relate reliably to exacerbations and may therefore not be of diagnostic value. When CNS involvement is the predominant clinical manifestation it is usually normal.^{20,21} Other neurological investigations such as the electroencephalogram often are abnormal, but are not diagnostic.^{19,22}

Isotope brain scanning using standard techniques has not been reliable in neuropsychiatric lupus. Some studies,^{9,18,19} have failed to demonstrate abnormalities in a large percentage of patients with CNS lupus. Others^{23,24} however, show close correlation between the results of isotope scanning and neurological disorders, and discrepancies may be accounted for by differences in technique. Oxygen-15 brain scanning has been reported to detect cerebral abnormality, but the technology involved in this technique precludes its use as a routine diagnostic test.²⁵ Cranial computerised axial tomography also frequently is abnormal, the most common but non-specific finding being sulcal widening and ventricular enlargement.²⁶

There does not appear to be a characteristic pathological lesion in the CNS analogous to that found in the spleen. Most common in CNS lupus are microinfarcts involving capillaries and arterioles, although macroscopic infarcts and haemorrhage also are encountered. True vasculitis, that is inflammatory cells within the vessel wall, is uncommon; though perivascular infiltrates are often found.^{1,18} Immune complexes are strongly implicated in lupus nephritis, but immunofluorescent studies of cerebral cortex, cerebellum and brainstem have shown no difference from non-lupus controls. On the other hand, immunofluor-

escence of the choroid plexus in lupus does show diffuse deposits of gamma globulin.²⁷ The relationship of these choroid plexus lesions, and of vascular changes, to temporary or permanent neuronal dysfunction has not been defined.

At the present time there is no specific test for cerebral SLE, although peripheral blood antinuclear factor is a useful adjunct. Cerebral scanning using oxygen-15 is promising, but only available in some centres, and its specificity has to be established. An easily performed blood test to diagnose cerebral lupus so as to separate it from other CNS pathology is needed.

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References

- 1 Johnson RT, Richardson EP. The neurological manifestations of systemic lupus erythematosus. *Medicine (Baltimore)* 1968; **47**:337-69.
- 2 Lee PR, Urowitz MB, Bookman AA *et al*. Systemic lupus erythematosus. *Q J Med*, New Series, XLVI 1977; **181**:1-32.
- 3 Fulford KW, Catterall RD, Delhanty JJ, Doniach D, Kremer M. A collagen disorder of the nervous system presenting as multiple sclerosis. *Brain* 1972; **95**:373-86.
- 4 Hughes GRV. Systemic lupus erythematosus: treatment and prognosis. *Br Med J* 1979; **ii**:1019-22.
- 5 Appenzeller O, Williams RC. Cerebral lupus erythematosus. *Ann Int Med* 1979; **90**:430-1.
- 6 Estes D, Christian CL. The natural history of systemic lupus erythematosus by prospective analysis. *Medicine (Baltimore)* 1971; **50**:85-95.
- 7 Brandt KD, Lessell S, Cohen AS. Cerebral disorders of vision in systemic lupus erythematosus. *Ann Intern Med* 1975; **83**:163-9.
- 8 Hackett ER, Mackinez RD, Larson RF. Optic neuritis in systemic lupus erythematosus. *Arch Neurol* 1974; **31**:9-11.
- 9 Feinglass EJ, Arnett FC, Dorsch CA, Zizic TM, Stevens MB. Neuropsychiatric manifestations of systemic lupus erythematosus: diagnosis, clinical spectrum and relationship to other features of the disease. *Medicine (Baltimore)* 1976; **55**:323-39.
- 10 Andrianakos AA, Duffy J, Suzuki M, Sharp JT. Transverse myelopathy in systemic lupus erythematosus. *Ann Intern Med* 1975; **83**:616-24.
- 11 Dubios EL, Tuffanelli DL. Clinical manifestations of systemic lupus erythematosus. *JAMA* 1964; **190**:112-9.
- 12 Cohen AS, Reynolds WE, Franklin EC *et al*. Preliminary criteria for the classification of systemic lupus erythematosus. *Bull Rheum Dis* 1971; **21**:643-8.
- 13 Allen IV, Millar JH, Kirk J, Shillington RK. Systemic lupus erythematosus clinically resembling multiple sclerosis and with unusual pathological and ultrastructural features. *J Neurol Neurosurg Psychiatry* 1979; **42**:392-401.
- 14 Sieving RR, Kauffman CA, Watanakunakorn C. Deep fungal infection in systemic lupus erythematosus: three cases reported, literature reviewed. *J Rheumatol* 1975; **2**:61-72.
- 15 Goodman LS, Gilman A. *Pharmacological basis of therapeutics*. Fourth edition. New York: Macmillan, 1970.
- 16 Bresnihan B, Oliver M, Williams B, Hughes GRV. An antineuronal antibody cross-reacting with erythrocytes and lymphocytes in systemic lupus erythematosus. *Arthritis Rheum* 1979; **22**:313-20.
- 17 Bluestein HG, Zvaifler NJ. Brain-reactive lymphocytotoxic antibodies in the serum of patients with SLE. *J Clin Invest* 1976; **57**:509-16.
- 18 Gibson T, Meyers AR. Nervous system involvement in systemic lupus erythematosus. *Ann Rheum Dis* 1976; **35**:398-406.
- 19 Small P, Mass MF, Kohler PF, Harbeck RJ. Central nervous system involvement in SLE. *Arthritis Rheum* 1977; **20**:869-78.
- 20 Winfield JB, Brunner CM, Koffler D. Serologic studies in patients with systemic lupus erythematosus and central nervous system dysfunction. *Arthritis Rheum* 1978; **21**:289-94.
- 21 Minitzer MF, Stollar BD, Agnello VD. Reassessment of the clinical significance of native DNA antibodies in systemic lupus erythematosus. *Arthritis Rheum* 1979; **22**:959-68.
- 22 Kiloh LG, McComas AJ, Osselton JW. *Clinical electroencephalography*. Third edition. London: Butterworth, 1972: 151.
- 23 Tan RF, Gladman DD, Urowitz MB, Milne N. Brain scan diagnosis of central nervous system involvement in systemic lupus erythematosus. *Ann Rheum Dis* 1978; **37**:357-62.
- 24 Bennahum DA, Messner RP, Shoop JD. Brain scan findings in central nervous system involvement by lupus erythematosus. *Ann Intern Med* 1974; **81**:763-5.
- 25 Pinching AJ, Travers RL, Hughes GRV, Jones T, Moss S. Oxygen-15 brain scanning for detection of cerebral involvement in systemic lupus erythematosus. *Lancet* 1978; **1**:898-900.
- 26 Gonzalez-Scarano F, Lisak RP, Bilaniuk LT, Zimmerman RA, Atkins PC, Zweiman B. Cranial computed tomography in the diagnosis of systemic lupus erythematosus. *Ann Neurol* 1979; **5**:158-65.
- 27 Atkins CJ, Kondon JJ, Quismorio FP, Friou GJ. The choroid plexus in systemic lupus erythematosus. *Ann Intern Med* 1972; **76**:65-72.