Matters arising

Histocompatibility antigens and postencephalitic Parkinsonism

Sir: We have read with interest the article on histocompatibility antigens and postencephalitic Parkinsonism by Lees et al recently published in your journal. The authors compared the phenotypic frequencies of selected histocompatibility antigens in 21 patients with postencephalitic Parkinsonism and controls, and did not find any differences between the groups. Missing, however, were the ethnic composition of both the patient and control populations, and the antigenic frequency data with resultant p values corrected statistically for total number of antigens tested in each HLA locus.

We had previously reported a highly significantly increased frequency of HLA-B14 antigen (corrected p = 0.001) in 18 unrelated American-Jewish patients of Eastern European extraction who had classical postencephalitic (von Economo's) Parkinson's disease, compared with 147 ethnically-matched controls; the 17 patients with idiopathic Parkinson's disease concurrently studied did not show any evident differences in HLA frequencies compared to the same matched controls. In our paper, we emphasised that we were dealing with a specific, relatively homogeneous, ethnically-defined and matched study population, and that we were well aware of the known wide variations in prevalence of specific HLA antigens in various ethnic groups. The disease association we reported, while not necessarily reflecting genetic susceptibility to the disease, certainly suggests the possibility that a genetic factor may play a role in the pathogenesis of this particular variant of Parkinsonism in certain ethnic groups. The negative study of Lees et al, while of interest, is not comparable to ours, nor does it negate our contentions.

References


Lees et al reply:

Dr Elizan and Professor Yahr are correct in drawing attention to the lack of precision in detailing the ethnic composition of our patients and control populations in our report. All the patients with postencephalitic Parkinsonism were of North European Caucasian stock, had been born in the United Kingdom and their families have been settled here for at least two generations and matched controls were chosen.

We in fact typed all 78 presently recognised HLA-A, B, C and Dr antigens, but as no statistically significant results appeared we chose for brevity to tabulate only those antigens in which an increased frequency has been reported in either idiopathic Parkinson's disease or Von Economo disease. We acknowledge in our discussion that the fact that the two studies deal with different ethnic groups and are therefore not strictly comparable.

Stroke as an early manifestation of systemic lupus erythematosus

Sir: We have read with interest the article by Dr Haas entitled Stroke as an early manifestation of systemic lupus erythematosus. We entirely agree that stroke can occur as an early manifestation of systemic lupus erythematosus. Unless the diagnosis is actively considered the true nature of the underlying disease may not be established. However, he did not stress that one of the difficulties in making a diagnosis is because of the lack of a specific diagnostic test for cerebral systemic lupus erythematosus. We would like to report a further case of systemic lupus erythematosus to illustrate the difficulties in arriving at the diagnosis and the particular use of skin biopsy in this case.

A 25-year-old aboriginal man was admitted four days after the sudden onset of right hemiplegia, mixed dysphasia and one grand mal seizure. Physical examination revealed no peripheral stigmata of vasculitis or infective endocarditis. Numerous purplish lesions were present over the buttocks and lower abdomen. His blood pressure was normal with regular pulses. No cardiac murmur or carotid bruit was detected. He had receptive and expressive aphasia, right homonymous hemianopia, right facial weakness and right hemiplegia. The right deep tendon reflexes were brisker than the left, with right plantar response being extensor. Sensory testing was not possible because of dysphasia. Shortly after admission he developed transient episodes of pleuritic chest pain with radiologically proven bilateral basal pulmonary infiltrates and small pleural effusions. There was no evidence of infection to account for the pulmonary lesions.

The initial investigations showed a persistently elevated ESR, up to 122 mm/h with otherwise normal haematological and biochemical tests. CT head scan showed a large left cerebral infarction in the distribution of the middle cerebral artery territory. Antinuclear factor was strongly positive, with titre of 1/125 and a mixed staining. However, anti-DNA by membrane assay was not raised and serum C3 and C4 were normal. Although a vasculitic process like systemic lupus erythematosus was strongly suspected, normal anti-DNA activity and complement levels did not allow the diagnosis to be confirmed. However, antibodies to extractable nuclear antigen were positive @ 1/125 (positive RNP and Sm antibodies). Muscle biopsy revealed only non-specific myositis with no arteritis. A skin biopsy showed granular IgM, IgA, IgG and C3q deposits at dermoepidermal junction and appendages. There was also in vivo speckled ANA. These findings helped to confirm the diagnosis of systemic lupus erythematosus. Prednisolone was then commenced about two months after the stroke. There was gradual fall in his ESR and some improvement in his neurological state. Before being discharged, he had a moderate degree of right hemiparesis, but was able to ambulate with a stick.

If one applies the newly revised systemic lupus erythematosus criteria of the American Rheumatic Association the patient meets the criteria for systemic lupus erythematosus having four of the eleven criteria. He had seizure, pleurisy, fluorescent antinuclear antibody and anti Sm antibody. The new revision contains reference to anti Sm for the first time, and thus allows this case to meet the criteria. However, it is interesting to note that "stroke" is not included in the diagnostic criteria.

Hughes has commented that currently available routine laboratory tests are still not reliable enough for accurate assessment and management of cerebral systemic lupus erythematosus patients. DNA binding levels occasionally may be normal. In the most floridly psychotic systemic lupus...
erythematous patients, CSF analysis is only abnormal in about 50% of patients with slight protein and IgG elevation. The initial reports of the value of low CSF C4 levels have not been substantiated. The same is true for SCF cyclic GMP levels, CSF immune complexes, lymphocytotoxic antibodies and DNA antibodies. EEG, CT scan, angiographic changes are not diagnostic. The use of 15-oxygen and C15O2 scan is promising, but too sophisticated for routine use. Recently, Morrow and others have commented that existing individual immunological tests are generally poor indices of disease activity (notably so with cerebral manifestations and thrombocytopenia). Monitoring the activity of systemic lupus erythematosus remains a difficult task.

In conclusion, early diagnosis of cerebral systemic lupus erythematosus still relies on high clinical suspicion. In difficult cases a combination of various immunological tests including immunofluorescence study of skin biopsy, may be useful in making a definite diagnosis so that steroid therapy can be commenced early.

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Anticonvulsant peripheral neuropathy

Sir: The article by Shorvon SD, and Reynolds EH, entitled Anticonvulsant peripheral neuropathy: a clinical and electrophysiological study of patients on single drug treatment with phenytoin, carbamazepine or barbiturates, represents progress in the attempt to determine neurotoxic side effects occurring from anticonvulsive medication. However, a few statements regarding earlier clinical studies need to be corrected.

(1) Shorvon and Reynolds write: "Hopf reported a reversible slowing in nerve conduction in human volunteers ...". The study by Hopf does not allow this conclusion as only two patients were electrophysiologically examined after the medication was discontinued. A closer look at Shorvon's and Reynolds' study 1 p621—Previous clinical and electrophysiological studies of phenytoin-induced peripheral neuropathy—reveals a number of mistakes, or at least undue simplifications.

(2) The study by Lovelace and Horwitz is said not to have used a control group. Table 4 p74 in Lovelace's and Horwitz's study shows that controls were used, although the reader might be left with some doubt about how the controls were obtained.

(3) The patients reported in the study by Eisen et al were all treated for more than ten years. It should therefore read correctly in Shorvon's and Reynolds' table 1 >10. In contrast to the information Shorvon and Reynolds give in table 1, Eisen et al stated in their abstract that their patients had normal serum folate concentrations. Furthermore Eisen et al 4 did compare the electrophysiological measurements with the results derived from 70 controls, which again is not mentioned in Shorvon and Reynolds table 1.

(4) Some of the information which Shorvon's and Reynolds' table 1 gives about a Polish study is incorrect. Zebrowska-Szymusik 5 described on p429 that one patient had a serum diphenylhydantoin concentration in the toxic range. However, table IV p430 in Zebrowska-Szymusik's paper contains probably a typographical error, as the reader may get the impression that a diphenylhydantoin serum concentration of 10 mg/ml is considered to be in the toxic range. Zebrowska-Szymusik's Table III p429 shows that five patients (11-9%) has absent or weak reflexes. In my view it cannot be concluded from the information given by Zebrowska-Szymusik that the patients in her study received other drugs besides phenytoin. R DANNER
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References
1 Shorvon SD, Reynolds EH. Anticonvulsant peripheral neuropathy: a clinical and electrophysiological study of patients on single drug treatment with phenytoin, carbamazepine or barbiturates. J Neurol Neurosurg Psychiatry 1982;45:620-626.

Shorvon and Reynolds reply:

Table 1 in our paper is no more than a summary of previous papers as an introduction to our own work. It was not our purpose nor did we discuss these previous publications in any detail. Professor Danner's comments and interpretation of the papers by Hopf, Lovelace and Horwitz, and Eisen et al are, to say the least, debatable. However, we are grateful to him for pointing out two errors in our table.

(1) The length of phenytoin treatment in the paper by Eisen et al should have read "more than 10 years" and not "10 years". This was an error overlooked at the proof stage. (2) The incidence of clinical neuropathy in the paper by Zebrowska-Szymusik should have read 8-9% and not 0%. This was due to a mistranslation from the original Polish.

None of Professor Danner's comments have any bearing on our own findings and conclusions.

Treatment of acquired aphasia: speech therapists and volunteers compared

Sir: In a recent issue of J Neurol Neurosurg Psychiatry, David, Enderby and Bainton 1 reported the results of a multicentre study comparing the effects of speech therapists and untrained volunteers on aphasia out-