Short report

Histocompatibility antigens and post-encephalitic Parkinsonism

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SUMMARY Twenty-one patients with Parkinsonism secondary to von Economo's encephalitis were typed for HLA-A, B, C and DR antigens. No differences were found in the phenotype frequencies of these antigens compared with controls. This finding fails to support the hypothesis of genetic susceptibility to post-encephalitic Parkinsonism.

The subsequent development of Parkinson's disease in some patients who apparently recovered from von Economo's encephalitis (epidemic encephalitis lethargica) is well known but has not been adequately explained. Among the suggested aetiological possibilities is the reactivation of a persistent virus. The recent finding of oligoclonal immunoglobulin G bands in the cerebrospinal fluid of two patients with sporadic post-encephalitic Parkinsonism indicates the presence of a continuing immune response in the CNS and would be compatible with the presence of a slow latent putative virus.¹ The finding of an increased frequency of HLA B14 in 18 post-encephalitic patients resident at the Beth Abraham Hospital in New York has been interpreted to mean that genetic factors may also be involved in the development of the chronic complications of von Economo's disease.² We have therefore HLA-typed 21 patients who contracted von Economo's encephalitis between 1916 and 1926 and who subsequently developed Parkinsonism.

Patients and methods

Seventeen of the surviving patients with post-encephalitic Parkinson's disease at the Highlands Hospital, Winchmore Hill and four adequately documented patients with Parkinsonism following von Economo's disease were included. HLA typing was carried out as previously described³ using validated anti-sera in a complement-mediated cytotoxicity

test on unfractionated lymphocytes for the assignment of HLA-A, B and C antigens and an enriched population of B lymphocytes for the DR antigens. Phenotype frequencies were compared with 153 controls for the HLA-A, B and C antigens and 113 matched controls for the DR antigens. HLA antigen frequencies were compared by the Chi-squared method.

Results

No difference in phenotype frequencies was found between patients and controls. The results of typing for each of the HLA DR antigens and other HLA antigens which have been claimed to show an association with either idiopathic or post-encephalitic Parkinsonism are shown in the table.

Discussion

We were unable to confirm the findings of Elizan and her colleagues of an increased frequency of HLA-B14 (44%) in post-encephalitic Parkinsonism compared with matched controls (8%).² The fact that the American patients in the above study were all of East European Jewish stock may be one explanation for these discrepant findings. There has been no previous study of DR typing in this disease, but we have found no significant associations.

Three studies of HLA antigens in idiopathic Parkinson's disease have provided no conclusive results and it seems likely that no strong HLA association exists. In a study from Finland no HLA antigen associations were found in patients⁴ whereas there was a slightly increased frequency of the cross-reacting antigens HLA-

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Table Selected HLA frequencies in patients with post encephalitic Parkinsonism

HLA antigen	Controls		Patients		Chi squared	p value
	Number	Percentage	Number	Percentage		
A2	82/153	54%	11/21	52%	0.01	< 0.90
A28	18/153	12%	0/21	—	0.93	< 0.40
B14	14/153	9%	1/21	5%	0.90	< 0.40
B17	10/153	7%	3/21	14%	1.60	< 0.20
B18	13/153	9%	3/21	14%	0.74	< 0.40
Bw35	19/153	12%	2/21	10%	0.14	< 0.70
DR1	12/113	11%	4/20	20%	1.41	< 0.30
DR2	22/113	19%	4/20	20%	0.003	< 0.95
DR3	34/113	30%	7/20	35%	0.19	< 0.70
DR4	37/113	33%	9/20	45%	1.12	< 0.30
DR5	20/113	18%	3/20	15%	0.08	< 0.80
DR6	27/113	24%	1/20	5%	3.64	< 0.10
DR7	30/113	27%	7/20	35%	0.60	< 0.50
DR8	—	—	—	—	—	—
DRw9	2/113	1%	1/20	5%	0.80	< 0.40
DRw10	—	—	—	—	—	—

A2 (46% cf 30% of controls) and HLA-A28 (20% cf 10% controls) in an Israeli investigation⁵ and a higher prevalence of HLA-B17 and B18 was found in a French study.⁶

More than 300 patients with post-encephalitic Parkinsonism were originally admitted to the Highlands Hospital. Few were discharged and the remaining 20 patients represent the survivors of the pandemic, most of whom contracted the infection in their early childhood. A study of this sort cannot totally exclude the possibility of genetic susceptibility to post-encephalitic Parkinsonism, but makes it very unlikely that the presence of any HLA antigen influences survival in the disease.

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