

Letters

Intracranial aneurysm and HLA-DR2

Sir: The annual incidence of aneurysmal subarachnoid haemorrhage is approximately 12 per 100,000,¹ while intracranial aneurysms (ICAs) may be found in at least 5% of the population, ruptured and unruptured.² In spite of their common occurrence, the pathogenesis of ICAs is poorly understood.

A recent study by Østergaard *et al*³ has provided tentative evidence of the existence of a genetic predisposition to ICA. In a group of 116 consecutive ICA patients no significant association could be found between any of the HLA-A, B, and C antigens, but for HLA-B7 a significant deviation from the Hardy-Weimberg equilibrium with an increase of homozygotes was found.³ Owing to linkage disequilibria this could indicate an association with HLA-DR2. Fifteen Danish ICA patients used as cadaver kidney donors were therefore examined and the HLA-DR2 frequency was found to be significantly increased (66.7% vs 29.7%).³ To confirm or refute this association we have examined the HLA-DR2 frequency in a similar group of Dutch patients with proven ICA.

The medical records of all patients with subarachnoid haemorrhage, admitted to the three neurosurgical centres in Amsterdam between January 1981 and January 1987 and used as cadaver kidney or multi-organ donors, were reviewed. The diagnosis of subarachnoid haemorrhage was confirmed by lumbar puncture or computed tomography. Thirty-one Caucasian patients with an angiographically or necropsy proven ICA were included in this study. There were 21 women and 10 men, aged 16 to 64 years (mean 37.9 years). In 11 patients the ruptured aneurysm arose from the internal carotid artery, in nine from the anterior communicating artery, in seven from the middle cerebral artery and in four from the basilar artery. Multiple aneurysms were found in six patients. The control group consisted of 1269 healthy blood donors. Tissue typing was performed by means of standard lymphocytotoxic assays.

HLA-DR2 was present in 10 of the 31 patients (32.3%) and in 338 of the 1269 controls (26.6%). This difference is not significant (χ^2 [with Yates correction] = 0.24; $p = 0.62$).

It remains a matter of some debate whether ICAs are an inherited disorder, whether the initial lesion is acquired, or whether a combination of hereditary and en-

vironmental factors is required. The incidence rate of aneurysmal subarachnoid haemorrhage has been shown to increase with age,¹ which would suggest that most ICAs are acquired during life. Cigarette smoking and arterial hypertension have been reported to be associated with an increased risk of subarachnoid haemorrhage.⁴ De la Monte *et al*⁵ have investigated a variety of risk factors and implicated a decreased synthesis of prostaglandin E as the common factor leading to the development and rupture of ICAs. A proposed viral aetiology of subarachnoid haemorrhage could recently not be confirmed by Timmons *et al*.⁶

An important aspect of the hypothetical genetic substrate of patients with ICAs would be their HLA constitution. In the present study we were not able to confirm the association between ruptured ICA and HLA-DR2 noted by Østergaard *et al*.³ However, the patients studied by Østergaard *et al* and the patients in our study represent a selected group, since they died from aneurysmal rupture and were used as organ donors. This latter fact probably accounted for the lower average age of these patients compared with that of all patients with ruptured ICAs admitted to our institution during the same period (37.9 vs. 48.4 years). An association between ICA and HLA D/DR products needs to be tested in large, unselected groups of patients with ruptured and unruptured aneurysms. The HLA profile of familial versus isolated cases of ICAs may be of special interest, since ICAs occurring among blood relatives are considered a distinct population of aneurysms.

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Lateral gaze palsy due to giant aneurysm of the posterior fossa

Sir: Giant aneurysms of the posterior fossa are rare.¹ They can present as acute subarachnoid haemorrhage^{1,2}; alternatively, cranial nerve palsies, cerebellar or pyramidal dysfunction may be their first manifestation.²⁻⁴ We report a case where the aneurysm presented as a progressive intrinsic brain stem lesion with a lateral gaze palsy as the predominant neurological abnormality and surgery resulted in a successful outcome.

A 45 year old, right handed housewife presented with a 1 year history of difficulty in turning her eyes to the right and this was associated with unsteadiness, tendency to fall to the left side and painful sensation down the whole of the left side of her body. Sixteen years previously, she had suffered a subarachnoid haemorrhage without any localising signs. At that time, three vessel angiography of the right and left internal carotid and the left vertebral arteries revealed no abnormality. She was noted to be hypertensive and had subsequently been on antihypertensive medication. Neuro-ophthalmological examination revealed normal funduscopy, visual acuity and visual fields. She had loss of conjugate gaze to the right side and nystagmus was present on left lateral gaze. Vertical eye movements were normal. There was, in addition, dysaesthesia