

## Letters

### Intracranial aneurysm and HLA-DR2

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

A recent study by Østergaard *et al*<sup>3</sup> 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.<sup>3</sup> 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%).<sup>3</sup> 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 ( $\chi^2$  [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,<sup>1</sup> 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.<sup>4</sup> De la Monte *et al*<sup>5</sup> 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*.<sup>6</sup>

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*.<sup>3</sup> 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.<sup>1</sup> They can present as acute subarachnoid haemorrhage<sup>1,2</sup>; alternatively, cranial nerve palsies, cerebellar or pyramidal dysfunction may be their first manifestation.<sup>2-4</sup> 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

on the left side of her body, with signs of mild left sided cerebellar incoordination and an ataxic gait. Reflexes were more sluggish on the left side and the left plantar response extensor.

Computed tomography (CT) showed a lesion in the right posterolateral aspect of the brain stem (fig. a). Angiography showed a large aneurysm arising from the origin of the right posterior inferior cerebellar artery (fig. b). It was thought that this was the aneurysm which bled 16 years previously.

A posterior fossa craniectomy was performed and the aneurysm was found to have invaginated the right lateral aspect of the pons. The vertebral artery was clipped proximal to the aneurysm as the aneurysm itself could not be clipped. Despite a short post-operative period of difficulty in swallowing and dysarthria the patient made a good recovery. On review 6 months later the only abnormality was a fine horizontal nystagmus on left lateral gaze.

Giant aneurysms most frequently occur in the 6th decade. The majority of giant aneurysms arise from the left vertebral artery. Only one other case has been reported where the aneurysm has arisen from the posterior inferior cerebellar artery.<sup>2</sup> The type and position of such an aneurysm is usually associated with a poor surgical outcome.<sup>6</sup> However, we report a case where surgery was successful. Giant aneurysms of the posterior fossa normally

present as subarachnoid haemorrhages or space occupying lesions. Other associated signs are cranial nerve palsies (most commonly the fifth, sixth, eighth and ninth nerve<sup>1</sup>), ipsilateral cerebellar symptoms,<sup>6</sup> contralateral pyramidal signs and sensory dysfunction.<sup>1,2</sup>

The case presented is interesting in that the lateral gaze palsy was the main clinical sign. Lateral gaze palsies are normally associated with intrinsic brain stem abnormalities. Causative lesions extrinsic to the pons are rare, although it has been ascribed to platybasia<sup>3</sup> and to expansive lesions confined to the cerebellum, especially abscesses.<sup>7</sup> The lateral gaze palsy is thought to be due to the aneurysm compressing the paramedian pontine reticular formation which is responsible for lateral gaze<sup>8</sup> and lies in the region of the sixth nerve nucleus. The sensation of falling to the opposite side may be due to involvement of the anterior spinocerebellar tract which passes between the olive and the inferior cerebellar peduncle and then crosses over lower down in the spinal cord. The dysaesthesia on the opposite side of the body is due to involvement of the lateral spino-thalamic tract which also crosses over at the appropriate level of the spinal segment. Of interest is the contralateral facial pain which may be due to interruption of the dorsal trigemino-thalamic tract which consists of both crossed and uncrossed fibres. Interruption of the crossed

fibres would thus explain the contralateral facial pain.<sup>9</sup>

The operative findings in our case support the concept of Coppeto and Lessell, that the aneurysm burrows into the pons owing to its pulsations, with the result that the aneurysm insinuates into the tissue.<sup>4</sup>

Giant aneurysms of the posterior fossa have a poor prognosis and surgery for such aneurysms has previously been disappointing<sup>5</sup>; however, clipping of the aneurysms may result in partial, if not complete, resolution of the unusual symptoms here reported.

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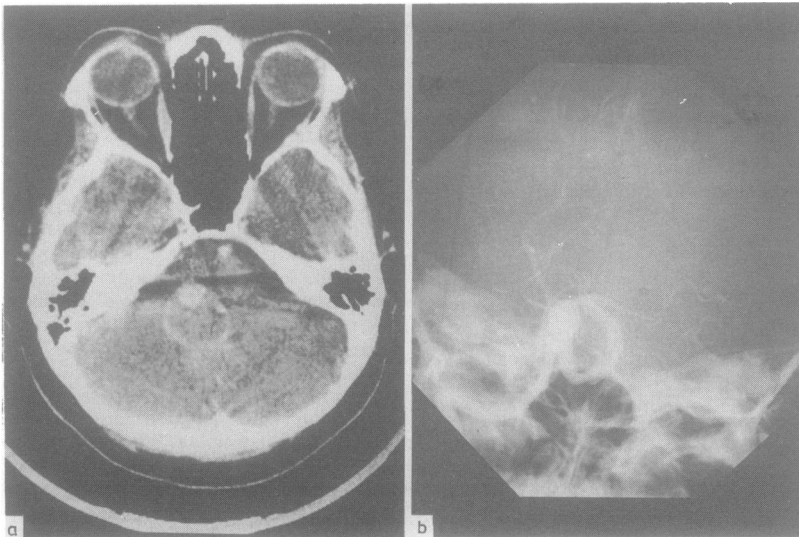


Fig a CT scan showing aneurysm indenting and distorting the fourth ventricle.

Fig b Angiogram showing the large aneurysm arising from the origin of the right posterior inferior cerebellar artery.

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