up a double-blind crossover controlled trial, the results of which we hope to publish during 1977.

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CONDENSED REPORTS

Amaurosis fugax and carotid artery disease: indications for angiography

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Summary

A prospective study of 80 patients presenting with amaurosis fugax was performed in an attempt to relate clinical features to angiographic findings in the internal carotid artery. Carotid bruit, transient cerebral ischaemic attacks, hypertension, and claudication were associated with a high prevalence of angiographic abnormality. Every patient who showed all these features had an operable lesion, as did 88% of those who had three features. In patients over 50 years of age carotid stenosis and atheromatous ulceration were occasionally found in the absence of bruit and transient cerebral ischaemia, but only one patient aged under 50 had an operable lesion and no associated features. Clinical features were therefore valuable in predicting the outcome of angiography, but it seems prudent to restrict angiography to patients aged over 50, who are most likely to benefit from surgery on the carotid artery.

Introduction

A brief episode of visual loss in one eye (amaurosis fugax) is usually caused by a transient reduction in the ocular blood supply. Fisher¹ first drew attention to the occurrence of this symptom in some patients who also had transient or permanent hemiparesis on the contralateral side. He showed that the underlying abnormality in these patients was in the internal carotid artery, which was either occluded by thrombus or narrowed by atheroma. Subsequent reports have indicated two possible mechanisms. The carotid artery may be the site of origin of

emboli to the ocular or cerebral circulation,² or the low perfusion pressure distal to an occlusion may render the eye vulnerable to ischaemia should there be a temporary reduction in systemic blood pressure.³

Since amaurosis fugax may precede a permanent cerebral deficit, and since stenosis of the carotid artery is amenable to surgery, Fisher's observations have stimulated a policy of active clinical investigation in the hope of preventing cerebral infarction. In many centres carotid angiography is routinely advised in all such patients in the search for a carotid lesion which can be treated surgically.⁴⁻⁶ But such a policy has several disadvantages. Firstly, many patients with amaurosis fugax do not subsequently develop a permanent deficit, either cerebral or ocular, and the proportion of such "benign" cases has been variously estimated at 40% to 84% of the total.⁶⁻⁷ Secondly, some patients with amaurosis fugax show no radiological abnormality in the carotid artery.⁸ Presumably the disturbance in ocular circulation in these patients is due to emboli from the heart or proximal great vessels, transient reductions in cardiac output, or other factors such as vasospasm or abnormal platelet or coagulant activity. Thirdly, even when a carotid lesion is found, surgical treatment is not always effective, although most controlled trials have shown fewer transient cerebral ischaemic attacks and completed strokes in patients who have undergone operation.⁹

We performed a prospective study to clarify the second question—the frequency with which angiography shows an abnormality amenable to surgical treatment in patients with amaurosis fugax—and so to provide simple clinical guidelines about investigating this common and alarming symptom.

Patients and methods

Eighty consecutive patients who presented for the first time with uniocular amaurosis fugax to a general hospital, an eye hospital, or a neurological hospital were studied. The study was prospective and continued over three years. Amaurosis fugax was defined as an episode of uniocular visual loss of less than four hours' duration which left no residual impairment either of visual field or visual acuity.

Angiography was performed in 67 patients. One patient refused the investigation, and 12 were excluded: in seven angiography was judged to be hazardous on grounds of age, severe hypertension, or severe coronary artery disease in older patients; and five patients had an alternative basis for these attacks, such as polycythaemia or cardiac valvular disease. All patients underwent electrocardiography and

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had their packed cell volume, sedimentation rate, serological reactions, and serum lipid concentrations measured as part of a general vascular assessment. Angiography was then performed by direct puncture of the appropriate common carotid artery low in the neck; views were taken of the region of the carotid bifurcation in at least two planes and the carotid system was visualised throughout its extent.

A kink was defined as angulation of the vessel more acute than 90° or where the vessel formed a complete loop. A stenosis was defined as a narrowing of the vessel lumen by 30% or more, since we found it difficult to be confident of the presence of a stenosis of lesser degree. The vessel was described as irregular when the lumen, though not significantly narrowed, had lost its normal smooth contour and showed either small elevations or depressions (fig a).

An "operable lesion" was defined as stenosis or an irregularity restricted to the proximal 5 cm of the internal carotid artery. Patients with kinks or loops of the internal carotid artery were not operated on.

Results

Of the 67 patients undergoing angiography, 38 described a curtain coming from above or below to obscure vision in the affected eye. Sometimes only half the field of vision was lost; on other occasions there was progression to complete blindness. Less often the obscuration was likened to a cloud, shadow, or shutter. Eight patients described a curtain drawn across the vision in the vertical plane. Four suffered headache concurrent with some attacks; another complained of itching about the affected eye. Six patients also experienced bright moving spots of light occurring in attacks with or without loss of vision and confined to the affected eye. Otherwise the loss of vision was not attended by local pain, headache, or systemic upset.

Men outnumbered women three to one, and most of the patients were in their 50s or 60s (table A*). Twelve patients gave a history of transient cerebral ischaemic episodes and 15 a history of intermittent claudication. There was a bruit over the ipsilateral carotid artery in 21 and over the contralateral carotid artery in six. In 22 the blood pressure was greater than 150 mm Hg systolic or 90 mm Hg diastolic. Emboli were seen on inspection of the retina in only five patients; an area of retinal artery sheathing was seen in one.

Of the findings in the ipsilateral internal carotid arteries at angiography in these 67 patients (table B*), 26 patients had no abnormality throughout the length of the vessel, and six had only a kink. The origin of the internal carotid artery was abnormal in 31: eight had an irregular vessel wall, 16 had stenosis, and seven had total occlusion of the lumen. Four with abnormalities at the origin of the vessel also had irregularity or stenosis of the siphon (cavernous region) of the internal carotid artery. Abnormalities limited to the siphon were seen in four patients—as an irregularity of the vessel wall in two and stenosis in two. There was no relation between the angiographic appearance and either the number of attacks the patients experienced or the length of time that these had been occurring. The prevalence of potentially operable abnormalities (localised stenosis or irregularity)

*Copies of tables A and B and fig a may be obtained from the authors.

increased with age, such lesions being found in only three of the 15 patients aged under 50 years (table I).

A bruit was heard over the carotid bifurcation in 21 patients, and angiography showed a stenosis at the origin of the vessel in 14 of these patients, an irregularity of the origin in one, and total occlusion in four. One showed only a kink, and another only a stenosis of the external carotid artery. In five of the 21 patients a separate bruit was heard over the region of the contralateral carotid bifurcation.

No patient with a history of transient cerebral ischaemia had a normal vessel. Twelve patients had experienced such episodes, and four had a totally occluded vessel, seven had stenosis at the origin, and one had stenosis in the siphon alone.

Raised blood pressure was also associated with a high prevalence of abnormalities. Thirteen of the 22 with blood pressure greater than 150 mm Hg systolic or 90 mm Hg diastolic or both showed stenosis of the origin, two irregularity of the origin, two total occlusion of the vessel, and two abnormality only in the siphon. Eleven of the 15 with a history of intermittent claudication had potentially operable lesions, as did six of the nine with a history of angina.

Discussion

As Fisher¹ showed, there is a significant association between amaurosis fugax, transient cerebral ischaemia, and a lesion of the internal carotid artery. Nevertheless, our findings confirm that in many cases amaurosis fugax occurs without cerebral symptoms and with a normal angiogram.⁸ The proportion of patients with kinks was no greater than in a control population.¹⁰ Ten per cent of abnormalities consist of total occlusions, which are not amenable to surgery, and in other cases abnormalities may be restricted to the siphon. This series shows that although amaurosis fugax usually occurs at an age when degenerative vascular disease is common, the overall yield of potentially operable carotid lesions is small. In only one patient in three did the angiogram show a lesion suitable for endarterectomy. Given that surgery is then the best management for patients with transient ocular ischaemia, is there any way of selecting patients for angiography so that the radiological findings are likely to lead to surgical treatment?

By restricting angiography to include only patients aged over 50 with a history of transient cerebral ischaemic attacks, intermittent claudication, blood pressure over 150/90 mm Hg, or a carotid bruit, the percentage of operable lesions shown by angiography can be increased.¹¹ Every patient in our series who showed all of these features had an operable carotid lesion. If three of these factors were present the chances of finding an operable lesion were greater than 85% (table II).

The numbers of treatable lesions that will be missed by restricting angiography to these clinical groups must also be considered (tables I-III). One-fifth of patients who have no

TABLE I—Predictive value of single features (67 patients)

Clinical features	Features present		Features absent	
	No of patients	No with operable abnormality	No of patients	No with operable abnormality
Age ≥50 ..	42	21	15	3
Hypertension ≥150/90 mm Hg ..	22	15	45	9
Carotid bruit ..	21	15	46	9
Transient cerebral ischaemic episodes ..	12	7	55	17
Claudication ..	15	11	52	13

TABLE II—Predictive value of multiple associated features (67 patients)

Multiple features	Features present		Features absent	
	No of patients	No with operable abnormality	No of patients	No with operable abnormality
Hypertension, bruit, and claudication ..	8	7	36	5
Hypertension, bruit, and transient cerebral ischaemic episodes ..	6	6	33	5
Bruit, transient cerebral ischaemic episodes, and claudication ..	4	4	41	7
Claudication, transient cerebral ischaemic episodes, and hypertension ..	4	4	33	5

TABLE III—Predictive value of paired features (67 patients)

Paired features	Features present		Features absent	
	No of patients	No with operable abnormality	No of patients	No with operable abnormality
Bruit and transient cerebral ischaemic episodes	9	7	43	9
Bruit and hypertension	13	12	37	6
Transient cerebral ischaemic episodes and hypertension	6	6	39	8
Bruit and claudication	12	9	43	7
Hypertension and claudication	10	8	37	9
Claudication and transient cerebral ischaemic episodes	4	4	44	

bruit may yet have an operable lesion, as may some without transient cerebral ischaemic attacks or claudication (table II). The number of lesions missed is not insignificant even if combinations of these four factors are used. This is because atheromatous ulceration shown angiographically as an irregularity of the lumen may be a source of mural thrombus and platelet embolism without giving rise to a bruit or to transient cerebral ischaemia.¹² The age of the patient is of practical importance since it is unusual for a surgical lesion to be discovered before the age of 50. We found a lesion in only one patient aged under 50 who had no other associated features.

When screening patients for potentially treatable carotid lesions, it therefore seems prudent, especially where resources are limited, to restrict angiography to those aged over 50 unless they have a carotid bruit, a history of transient cerebral ischaemia, hypertension, or claudication. The presence of hypertension, a bruit, a history of transient cerebral ischaemic episodes, or claudication increases the yield of positive angiograms, but the investigation is still advisable over the age of 50 in the absence of these features to detect localised atheromatous ulceration.

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Copies of the unpublished tables and figure may be obtained from Dr L A Wilson, Department of Neurological Studies, Middlesex Hospital Medical School, London W1.

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SHORT REPORTS

Relationships between ascorbic acid and serum proteins of the immune system

There have been numerous clinical surveys investigating the possible prophylactic effect of ascorbic acid (AA) in common colds, though there is considerable doubt whether it is beneficial.¹ No beneficial effect of AA has been shown on viral replication in tissue culture^{2,3} or on antibody production in rabbits.³ There have been no recent reports of investigations into relationships between AA and immunoglobulins. This paper presents the results of such an investigation on subjects isolated from new sources of infection for almost a year.

Subjects, methods, and results

Throughout a year on a British Antarctic base (February 1972 to February 1973), during the course of a survey investigating AA nutrition,⁴ blood was collected on eight occasions from the eight subjects wintering on the base and on several occasions from visitors from other bases. From these samples plasma (PAA) and leucocyte ascorbic acid (LAA), serum IgG, IgM, and complement C3 titres were measured. All subjects were healthy young men aged 21-38 years. None contracted upper respiratory tract infections during the survey.

Blood AA levels were estimated by the method of Denson and Bowers,⁵ analysis beginning within 15 minutes of sample collection. Serum IgG, IgM, and complement C3 titres were measured by radial immunodiffusion on Hyland plates.

Direct relationships were found between increasing blood AA levels and serum IgG and IgM titres. Those between IgG and LAA ($P < 0.05$) (figure) and PAA ($P < 0.01$) and IgM and LAA ($P < 0.01$) were statistically significant,

Plasma IgG titre in relation to leucocyte ascorbic acid content ($P < 0.05$).

Conversion: SI to traditional units—LAA: 1 nmol/ 10^8 leucocytes $\approx$ 0.18 μ g/ 10^8 leucocytes.

while that between IgM and PAA ($0.1 > P > 0.05$) was not. IgG (but not IgM) significantly ($P < 0.02$) increased in four subjects who received a dietary supplement of 1 g AA daily for one week. Over the next month IgG significantly ($P < 0.025$) decreased. During this period the mean PAA titre of these subjects rose from 12.5 ± 1.7 μ mol/l (0.22 ± 0.03 mg/100 ml) to 86.5 ± 8.6 μ mol/l (1.70 ± 0.15 mg/100 ml) then fell to 20.4 ± 6.8 μ mol/l (0.36 ± 0.12 mg/100 ml), while LAA levels rose from 78.9 ± 3.3 nmol/ 10^8 leucocytes (Ls) (13.9 ± 0.58 μ g/ 10^8 Ls) to 141 ± 33.5 nmol/ 10^8 Ls (24.9 ± 5.9 μ g/ 10^8 Ls) then fell to 110 ± 40.9 nmol/ 10^8 Ls (19.3 ± 7.2 μ g/ 10^8 Ls). No relationships were evident between blood AA levels and complement C3 titres.