The natural history of non-arteritic anterior ischaemic optic neuropathy

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Abstract

Seventy one patients with non-arteritic anterior ischaemic optic neuropathy were studied retrospectively. Sixty three (89%) were followed to the end of the study or death, mean follow up time was 5.3 years. Whilst twenty (28%) had diabetes or hypertension, in thirty nine (55%) no predisposing condition was identified. In those who had monocular disease at presentation (68), subsequent involvement of the second eye occurred in seventeen (25%), seven within the first year. Nineteen patients died within the study period. Of these, nine died from myocardial infarction and four from cerebrovascular disease. This is a significant increase above figures calculated from the Office of Population Census and Surveys ($p < 0.001$ for all causes, $p < 0.002$ for myocardial infarction and cerebrovascular disease). Such an increase in mortality has not been previously reported, and implies that this condition carries a more sinister systemic prognosis than is frequently supposed.

Anterior ischaemic optic neuropathy is characterised by a sudden painless loss of visual acuity or field and a characteristic appearance of the optic disc. Initially there is swelling of the disc with or without peripapillary nerve fibre layer haemorrhages. These changes are followed by disc pallor.¹⁻³

An association with temporal arteritis has been shown, with histological changes in the ciliary arteries. In non-arteritic anterior ischaemic optic neuropathy (na-AION) the presumed aetiology is ischaemia of the optic nerve after it passes through the scleral canal, caused by insufficiency of the ciliary circulation.⁴ Rare cases of embolic occlusion of these vessels have been reported.⁵ Mechanical factors such as constriction of axons or blood vessels as they pass through this region might be a contributing or independent cause⁶⁻⁸ and might explain the frequent bilateral occurrence of na-AION. Bilateral disease might also reflect generalised atheroma which would in turn be associated with an increased morbidity and mortality from other diseases. To assess the prognosis of patients with na-AION, we have studied the natural history of patients presenting to the Medical Eye Unit at St Thomas' hospital.

Methods

The case records of patients diagnosed with na-AION from 1973-87 were reviewed. The diagnosis had been made on the basis of a clinical history of sudden loss of acuity or visual field with an acutely swollen disc or subsequent pallor. Arteritis was excluded as a cause for visual loss by measurement of the erythrocyte sedimentation rate and (where clinical uncertainty remained) by temporal artery biopsy. All patients had been fully investigated for predisposing conditions and to exclude other causes of visual loss. Information was extracted from case notes on concurrent medical conditions at the time of diagnosis, including hypertension (diastolic blood pressure > 110 mm Hg or already on anti-hypertensive therapy), ischaemic heart disease, peripheral vascular disease, diabetes mellitus, migraine, transient ischaemic attack, stroke, or carotid bruit. Those with previous stroke, ischaemic heart disease, peripheral vascular disease or carotid bruit were presumed (for the purpose of comparison with other studies) to have "atherosclerosis."

We also recorded visual acuity and field, pupillary reaction, second eye involvement, intraocular pressure, a description of disc appearance and the peripapillary retina. We wrote to all patients at their last known address and those able to attend were seen for review in early 1988. In other cases we contacted patients' relatives, general practitioners or other hospital specialists. Where patients had died, death certificates were obtained from the Office of Population Censuses and Surveys (OPCS).

The expected number of deaths for each study year after diagnosis were calculated using the 1979 mortality figures for England and Wales published by the OPCS. For fatal ischaemic heart disease, ICD codes 410-414 were used and for fatal cerebrovascular disease, ICD codes 430-438.⁹ From the observed and expected mortality data, survival graphs were drawn. In this analysis each year's observed mortality was compared with the expected mortality, including only those patients known to have been alive at the beginning of the year. The observed death rates were compared with the calculated expected figures using the Poisson distribution.

Results

Seventy one patients and ninety one eyes with na-AION were identified from hospital

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Received 6 October 1989 and
in revised form
31 January 1990.

Accepted 14 February 1990

Table 1 Age and sex at presentation

Age	Male	Female
25-34	1	0
35-44	2	0
45-54	13	3
55-64	18	7
65-74	11	11
75-84	1	4

Table 2 Duration of follow up

Years	Patients
<1	6
1-5	29
6-9	27
>10	9

records. The age and sex distribution of these is shown in table 1. The age range was 26-83. All but three patients were over the age of 44. Median age range for the men was 55-64 and for the women 65-74. There were forty six men and twenty five women in the study (1:0.54). Sixty three (89%) of these patients were followed to the end of the study or death. The mean follow up period was 5.3 years (table 2).

Systemic findings

Medical conditions identified at the time of initial diagnosis are shown in table 3. Most common were hypertension and atherosclerosis. Previous stroke had occurred in five patients, one of whom had a carotid bruit and ischaemic heart disease and one who had peripheral vascular disease. One patient in the study had a history of migraine and one had intraocular pressures of 25 mmHg and 28 mmHg in the right and left eyes respectively at night, although intraocular pressure was less than 20 in each eye during the day.

Ocular findings

Thirty six (40%) eyes had a visual acuity of 6/12 or better and eleven (12%) had a visual acuity of hand movements or worse at initial presentation (table 4). Forty eight (53%) eyes presented with an inferior defect (table 5). Three patients were referred to the Medical

Table 5 Field defect at presentation

Field Defect	Number of eyes (n = 91)
Normal	0
Inferior Altitudinal	27
Superior Altitudinal	9
Central Scotoma	17
Inferior Quadrantic	10
Inferior Arcuate	11
Constricted	3
Other	8
Blind	6

Table 6 Time between first and second eye involvement

Interval between 1st and 2nd eyes (years)	Number of patients (n = 17)
0-1	10
2-3	3
4-5	2
6-10	1
>10	1

Eye Unit at the time of second eye involvement. Of the remaining 68 patients, subsequent involvement of the second eye occurred in seventeen (table 5), of whom ten patients suffered second eye involvement within the first year. The longest delay before second eye involvement was 10.5 years.

Ophthalmological follow up data was available for fifty three eyes. In this group only four patients experienced further reduction in visual acuity of more than one line which was not attributable to ocular disease. In one eye acuity fell from 6/6 to 6/36. The patient complained of multiple episodes of visual loss with variable recovery. Seven patients had an improvement in visual acuity of more than one line. One of these patients improved from hand movements to 6/6 following treatment with systemic steroids.

Forty eight patients had a relative afferent pupillary defect (RAPD). Fifteen patients with monocular disease had no RAPD.

Mortality

Nineteen (27%) patients died during the course of the study (expected 8.44), nine from myocardial infarction (expected 2.67) and four

Table 3 Concurrent conditions at time of diagnosis

Diabetes mellitus	4 (5.6%)
Hypertension	15 (21%)
Hypertension and diabetes	1 (1.4%)
Atherosclerosis	6 (9%)
Atherosclerosis and hypertension	4 (6%)
Migraine	1 (1.4%)
Raised intraocular pressure	1 (1.4%)
Idiopathic	39 (55%)

Table 4 Visual acuity at presentation

Visual Acuity	Number of eyes
6/6-6/5	20
6/12-6/9	16
6/36-6/18	23
CF-6/60	21
PL-HM	5
NPL	6

Figure 1 Survival curve for males and females combined after presentation with non-arteritic anterior ischaemic optic neuropathy, compared with the expected survival for the equivalent age and sex in England and Wales, 1979.

Figure 2 Survival free from fatal cardiac disease for males and females combined after presentation with non-arteritic anterior ischaemic optic neuropathy, compared with the expected survival for the equivalent age and sex in England and Wales, 1979.

from cerebrovascular disease (expected 0.93). Four died from neoplasia (expected 2.27), one from mitral valve disease and one from chronic renal failure. Figure 1 shows the survival curve for the study group. Mortality from all causes significantly exceeds that predicted by the figures taken from the OPCS ($p < 0.001$). Figure 2 shows survival free from fatal cardiac disease. The increase in mortality from both cardiac and cerebrovascular disease is significant ($p < 0.002$ for each). Four patients with bilateral disease died, all from cardiac causes. Only four patients dying from cardiac or cerebrovascular disease had no past medical history of cardiovascular disease or diabetes.

Discussion

AION is caused by vascular insufficiency of the posterior ciliary arteries.^{4 10 11} The frequency of arteritis varies widely in different reports.^{12 13} Non-arteritic AION may be associated with diabetes or hypertension, but there has been no evidence that it has any implications for mortality. There have been two previous studies of the natural history of na-AION. Guyer *et al*¹² reported 200 patients from the Johns Hopkins Medical Institute Baltimore, and Repka *et al*¹⁴ reported 169 patients from the Wills Eye Hospital Philadelphia. Neither of these studies identified a significant increase in mortality following na-AION, though Guyer reported an increase in non-fatal stroke and myocardial infarction and Repka reported a slight but statistically insignificant increase in non-fatal myocardial infarction. Our finding of a significant increase in fatal myocardial infarction, fatal stroke and death from all causes therefore contradicts previous studies. It is thus of importance to compare the study populations.

Guyer studied patients aged 17 to 90 (median 61:65, M:F) with a follow up of one month to nine years (mean 3.49). Repka studied patients aged 42 to 88 (mean 64) with follow up three to 13 years (mean 5). The age structure of our population was similar to these studies, though less extreme than the Guyer population. Our follow up period was at least as long as that of Repka and exceeded that of Guyer. We found a slightly higher male:female ratio than the other studies (1:0.54 vs 1:1.12 for Guyer and 1:0.83 for Repka). Thus the structure of our study population does not provide an obvious explanation for our finding of an increased mortality.

ation for our finding of an increased mortality.

An alternative explanation might be that our patients had more pre-existing cardiac or other disease. On the contrary, we found less pre-existing cardiac disease (4.22% versus 30% in Guyer) or diabetes (7% versus Repka 15%). Our idiopathic group was larger than previously reported, although all patients were examined and investigated by both physicians and ophthalmologists in a specialist medical eye unit. Criteria for admission to both diabetic and hypertensive groups were, however, a little different from the Guyer study; exact admission criteria for these groups were not given in the other papers. Guyer reported no category for hypertensive or diabetic patients with atherosclerosis, whereas we and others identified such combinations. Guyer and Repka found an increased prevalence of hypertension and diabetes mellitus in those patients developing AION in the under 65 age group (compared with public health service data). Guyer also found a significant increase in pre-existing cerebrovascular and cardiovascular disease in patients over 45.

Although our patients did not have an increased prevalence of pre-existing cardiac or other disease, it might nevertheless be assumed that they were drawn from an atypical and disseminated population, following tertiary specialist referral. This was not so, however. The Medical Eye Unit is situated within a general hospital and most of the patients included in the study were from its local population. Furthermore, the studies of Guyer and Repka were also conducted within specialist eye units.

There is thus no obvious explanation for our finding of increased mortality in terms either of the age structure of the population studied, the profile of pre-existing illness, or the means of referral. This finding remains unexplained therefore and whilst awaiting confirmation from other studies must question the belief that na-AION carries no increased mortality risk.

Although follow up was incomplete in some cases, this does not influence our conclusions on mortality. The analysis by survival includes only those patients known to be alive at the beginning of a year when calculating the expected mortality. Patients lost to follow up during a year are excluded from further analysis.

Non-arteritic AION may occur bilaterally and this is thought to relate to anomalies of either vascular supply or anatomical configuration of the disc. Thus the cup/disc ratio in the normal fellow eye may be reduced (Beck *et al* and Feit *et al*^{6 7 8}). The overall reported incidence of bilateral eye involvement has varied between 10.5%¹² and 73%.¹⁵ A prospective study by Beri¹⁶ found a cumulative incidence of bilateral involvement in na-AION at five years of 35%, increasing at ten years to 57%. Of those who ultimately developed bilateral disease, 32% did so within one year. The overall incidence in this study was 25% over 5.3 years, 42% of these experiencing bilateral eye involvement within the first year. It may be that atherosclerotic changes, which may reasonably be expected to be bilateral, act as the

final insult to an anatomically compromised blood supply in these crowded discs.

The ophthalmological prognosis for affected eyes is bleak. Visual field analysis and presenting visual acuity were in broad agreement with previous findings,^{13 17 18} and overall visual acuity at follow up was little changed from that at presentation. A single patient with intermittent visual loss and variable recovery is of interest in the light of occasional reports of embolic posterior ciliary artery disease^{5 19} and progressive and recurrent visual loss.²⁰

AION is regarded as a serious condition because of the poor visual prognosis for the affected eye, the risk of involvement of the second eye, and the association with giant cell arteritis. Whilst giant cell arteritis carries a significant non-ocular morbidity and mortality, non-arteritic AION has been thought less serious from the systemic point of view. This is questioned by our study, which suggests that the natural history of this condition is far from benign.

We thank Richard Morris, Department of Community Medicine, St Thomas' Hospital for statistical advice.

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