Ischaemic papillopathy

Clinical and fluorescein angiographic review of forty cases

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The clinical features resulting from acute infarction of the optic nerve head are characterized by sudden visual impairment, nerve fibre bundle field defects and optic disc oedema. These features were fully discussed 50 years ago by Uhthoff (1924); an earlier description of visual loss after severe haemorrhage had been given by Gowers (1879). An association with temporal arteritis was reported by Jennings (1938) although many other causes have since been recognized. Systemic causes include arteriosclerotic disease (François, Verriest, and DeLaey, 1957), diabetes and hypertension (Cullen, 1967), migraine and syphilis (Sanders, 1971), polyarteritis nodosa (King, 1935; Kimbrell and Wheliss, 1967), and polycythaemia (Friedenwald, 1919). Recent reviews of large numbers of patients (Cullen, 1967; Ellenberger, Keltner, and Burde, 1973) have contributed to our understanding of the natural history, although pathological reports have been restricted to cases of temporal arteritis which have recently been reviewed by Henkind, Charles, and Pearson (1970). An arbitrary division into two groups, as suggested by Cullen (1967), is of clinical value, because patients with giant cell (temporal) arteritis generally have a worse visual prognosis than those in whom the condition is due to other causes.

Premonitory obscurations in a few cases precede an acute episode of visual impairment, and pain is not usually a feature. Impairment of visual acuity was seen in two-thirds of their patients by Ellenberger and others (1973) and of these half subsequently improved. In all their cases and in most of those in Cullen's series, an arcuate field defect was present. The optic disc was swollen, either totally or segmentally, with a few superficial linear haemorrhages. Resolution to an atrophic disc occurs over the ensuing months, and cupping may be seen if infarction is total (Miller, 1972). Fluorescein studies (Foulds, 1969; Sanders, 1971; Miller, 1972) in the early stages show impaired choroidal perfusion of the disc, with dilatation of the retinal peripapillary capillaries in segmental infarction. Marked hyperfluorescence is seen in the late stages and this also may be segmental. Irregularity of the retinal arterioles may signify arteriosclerotic disease. Involvement was bilateral in 25 per cent. of Cullen's cases and in 48 per cent. of those of Ellenberger and others (1973); the involvement of the two eyes was often separated by an interval of several months up to one year. The condition has been attributed for many years to acute impairment of blood flow to the distal optic nerve involving either the posterior ciliary arteries (Meadows, 1954; Hayreh, 1969) or the artery of the optic nerve (François, Verriest, and Baron, 1957).

Treatment with systemic corticosteroids in patients with ischaemic papillopathy due to temporal arteritis is in general use for the control, not only of the ocular involvement but also of the systemic disease (Parsons-Smith, 1959). Adequate evidence for the therapeutic

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efficacy of steroids in ischaemia due to other causes is lacking; their use is advocated by some (Foulds, 1969; Sanders, 1971) and rejected by others (Ellenberg and others, 1973).

Terminology

Confused terminology has bedevilled this condition, misled authors, and probably been responsible for the clinical neglect from which it has suffered. Anatomical, aetiological, and clinical terms have been introduced and of these "ischaemic optic neuropathy" encompasses all subgroups. However, it is crucial for accurate diagnosis to document ophthalmoscopically, or preferably by fluorescein angiography, the presence of disc oedema. We have seen a series of patients with recent visual loss, arcuate defects, and segmental pallor of the optic disc, who were subsequently found to have optic nerve compression. Many of these patients with acute visual impairment without disc swelling and in whom investigations were negative, presumably had infarction of the optic nerve behind the lamina cribrosa. With the facilities currently available, the diagnosis of ischaemic optic neuropathy in the posterior optic nerve remains a matter of exclusion. The clinical classification that we find satisfactory is the term "ischaemic papillopathy" for infarction of the optic disc (Walsh and Hoyt, 1969; Sanders, 1971; Lindenberg, Walsh, and Sacks, 1973) and "ischaemic optic neuropathy" for posterior lesions without disc oedema and in which a compressive lesion has been excluded. We recognize that these terms are not fully satisfactory, but they are euphonic, clinically prudent, and analogous to the terms "papillitis" and "optic neuritis" which are used universally for inflammatory conditions of the optic nerve.

Present investigations

This report describes forty patients (56 eyes), most of whom were studied at The National Hospital, Queen Square, and St. Thomas' Hospital, London, who presented with acute visual impairment and disc oedema.

Investigations included a medical and ophthalmic examination with fundus and fluorescein photography. Visual field analysis was performed with either the Bjerrum screen or the Goldmann perimeter. Routine blood investigations included a full blood count, erythrocyte sedimentation rate, sugar, cholesterol, plasma proteins, and serological tests for syphilis. An electrocardiogram was performed and a biopsy taken of the temporal artery when indicated. The skull and optic foramina were x-rayed.

Assessment of the efficacy of treatment is hampered by inadequate knowledge of the aetiology and natural history of the condition, but a retrospective study was made of the value of corticosteroids.

Although Foulds (1968, 1969) found an incidence of raised intraocular pressure in 28 per cent. of his cases of ischaemic optic neuropathy, this has not been substantiated by other authors (Cullen, 1967; Ellenberger and others, 1973). The use of the term ischaemic optic neuropathy to describe the association of disc haemorrhages and field loss (Begg, Drance, and Sweeney 1971) in chronic simple glaucoma further complicates the terminology and such patients have not been included in this series. Similarly, patients with accelerated hypertension in whom disc oedema coincided with the typical retinopathy were excluded although the fundamental pathogenesis is admittedly ischaemic (Ashton, 1972).

AETIOLOGICAL GROUPS

The patients were divided into four aetiological groups:

- (1) Giant cell arteritis (7 cases, 9 eyes, average age 75 yrs)
- (2) Vascular disorders (17 cases, 24 eyes, average age 59 yrs)
- (3) Related disease (not included in Group 2) (10 cases, 17 eyes, average age 54 yrs)
- (4) No specific cause detected (6 cases, 6 eyes, average age 55 yrs)

Although this subdivision is arbitrary, it facilitates our understanding of the possible differences in the natural history of the different groups. The average age of patients with giant cell arteritis is much higher (75 yrs) than that of all other groups (57 yrs); this factor may be contributory to the poor visual prognosis in these patients.

BILATERAL INVOLVEMENT

In sixteen patients (40 per cent.) both eyes were involved. In two of those with giant cell arteritis, the second eye had a central retinal artery occlusion in addition to marked disc swelling. Bilateral involvement was seen in almost half the cases with vascular disease (41 per cent.) and in two-thirds (70 per cent.) of those with associated systemic disease. In Group 4, in which no objective signs of systemic or vascular disease were found, only one was affected bilaterally.

SYMPTOMS

(a) Premonitory obscurations of vision

These occurred in one patient in Group 1; after the loss of vision in one eye due to giant cell arteritis, she noted obscurations in the second eye before severe visual impairment set in. One patient with carotid occlusion (Group 2) experienced numbness in the supraorbital region.

(b) Ocular pain

Headaches were experienced by four patients with giant cell arteritis, one with vascular disease and two with migraine. Ocular pain immediately preceding the visual loss was noted by two patients and a further patient complained of supraorbital pain. None complained of pain on ocular movements.

GROUP 1. GIANT CELL ARTERITIS (Table I)

The diagnosis was confirmed in six of the seven cases by temporal artery biopsy, and this was particularly important in two cases with the classical symptoms and signs but normal erythrocyte sedimentation rate readings. Biopsy was not performed in one patient with the classical picture (bilateral blindness and an erythrocyte sedimentation rate of 131 mm/1st hr).

Table I Giant cell arteritis (7 cases; average age 75yrs)

Erythrocyte sedimentation rate (mm/1st hr)	Biopsy	No. of eyes		Visual acuity	Visual field
Above 50 - 5/7	Positive 6/7	Bilateral	2/7	> 6/60	8
13 - 1/7		Unilateral	5/7	6/12 - 6/60	nil
30 - 1/7		Total	9	6/6 - 6/12	1

Visual acuity and fields

The visual loss was almost complete, being vague perception of light in seven eyes, counting fingers in one, and 6/9 in one. Deterioration occurred in one eye after the initial episode. One patient developed an inferior arcuate defect with central involvement while on systemic steroid therapy with visual reduction to 3/60; improvement to 6/9 followed the retrobulbar injection of 40 mg. triamcinolone. This was the only patient in this group to show arcuate field loss, and the only patient to show any visual recovery. All patients received high-dosage steroid therapy.

Fundus changes

There was pallid swelling of the optic disc in all cases and often a solitary linear haemorrhage. Retinal infarcts were also visible in the peripapillary region in two cases (Fig. 1a) and central retinal artery occlusions in a further two. Fluorescein studies showed deficient choroidal filling (Fig. 1b) with retinal arterioles of normal calibre. Hyperaemia of the disc due to compensatory retinal capillary dilatation at the disc was not seen. In the later stages, optic atrophy with loss of tissue at the disc head producing cupping was seen ophthalmoscopically and fluorescein studies showed reduced or absent disc capillaries with peripapillary pigment epithelial damage.

FIG. 1 *Giant cell arteritis*
(a) Copy of a colour photograph to show ischaemic papillopathy with associated peripapillary retinal infarcts

GROUP 2. VASCULAR DISEASE (Table II)

Objective evidence of vascular disease was found in seventeen cases (42 per cent.). In three patients angiographic evidence of carotid disease was obtained, in two cases cholesterol emboli were seen, and in two more temporal artery biopsy showed intimal thickening. The remaining patients showed objective evidence of arteriolar irregularity or focal attenuation of arterioles on fluorescein angiography; the associated vascular conditions are listed in Table II. Hypertension occurred in six cases: mild in five and 190/120 in one. Associated cerebrovascular disease in three cases included two with hemiplegia and one with drop attacks. High cholesterol blood levels were detected in three patients, one of whom had myxoedema, and one rheumatoid arthritis. One normotensive patient with bilateral

(b) *Fluorescein angiography in arterio-venous phase, showing delayed choroidal filling of the disc and peripapillary region, although the retinal arteries are of good calibre*

Table II Vascular disease (17 cases; average age 59 yrs)

Aetiology		No. of eyes		Visual acuity		Visual field	
Hypertension	6	Bilateral	7	> 6/60	3	- 5	
Cerebrovascular	3	Unilateral	10	6/12 - 6/60	9		
Cholesterolaemia	3	Total	24	6/6 - 6/12	12		
Myxoedema	1					- 3	
Immunoglobulin abnormality	1						
Rheumatoid arthritis	1						
Retinal arterio-sclerosis only	2					- 16	

involvement showed minor immunological abnormalities which included a positive antinuclear factor and raised levels of IgM (188) and IgA (402). The significance of these abnormalities is as yet obscure, but further study may indicate pathogenetic factors not currently under consideration. Ischaemic papillopathy was the initial sign of proximal carotid disease in three patients.

In one patient a right-sided ischaemic papillopathy (Fig. 2a) with left hemiplegia was diagnosed. Ophthalmodynamometry readings were within normal limits (R 100/45; L 120/50) and a carotid bruit was present on the right. Angiography revealed an internal carotid occlusion (Fig. 2b).

In two further patients cholesterol emboli were visible (Fig. 3, overleaf) in conjunction with visual loss due to ischaemic papillopathy.

Visual acuity and fields

In contrast to Group 1, 50 per cent. of the eyes in Group 2 had visual acuity which was 6/12 or better, 37 per cent. between 6/12 and 6/60, and only three (12 per cent.) worse than 6/60. Visual field involvement was also correspondingly less severe and solitary arcuate or altitudinal defects occurred in 66 per cent.; of these sixteen eyes only two had altitudinal defects in the upper half, the remainder being inferior. Typical defects are shown in Fig. 4g (overleaf). Superior and inferior defects without central involvement occurred in 12 per cent., and with central involvement in 22 per cent.

FIG. 2 *Carotid occlusion*
 (a) *Pallid swelling of nasal portion of disc showing hyperfluorescence in venous phase of fluorescein angiogram*

(b) *Carotid angiography, showing complete occlusion of internal carotid*

Of twelve eyes that received no treatment three improved; of the remaining twelve, five improved on steroid administration. In one patient the second eye became involved while on systemic steroids and in another further deterioration occurred in the same eye while on steroids. In patients with bilateral involvement the second eye became involved between 1 and 14 months after the first in five cases. Bilateral visual loss was noted in one man who had smoked forty cigarettes whilst deeply involved in a television thriller the previous evening.

FIG. 3 Embolization

(a) Pallid oedema of optic disc associated with visual loss; preliminary examination failed to reveal any emboli

(b) Altering the angle of incident light showed multiple cholesterol emboli; an atheromatous plaque was demonstrated on carotid angiography

Fundus changes

In all cases the optic disc was swollen in the acute phase. In some instances the disc was pale (Fig. 4a) but at other times the disc appeared hyperaemic (Fig. 4d).

With infarction of the upper portion of the disc and an inferior field defect, the greatest capillary dilatation was visible at the lower pole. In two instances a macular star was present, and in three instances focal peripapillary pigment epithelial defects were visible. Disc swelling lasted for between 3 weeks and 3 months, and was followed by segmental or diffuse atrophy. Cupping was not seen in this group.

Fluorescein angiography showed late filling of the choroidal disc vessels and this may be segmental in nature (Figs 4 b,e and 5).

Compensatory dilatation with marked leakage from the retinal capillaries may be seen

FIG. 4 Arteriosclerosis

(a) A 47-year-old normotensive man presented with an inferior field defect and pallid disc oedema in the right eye
 (b) Fluorescein angiography showed irregularity of the arterioles and delayed filling of the papillary capillaries of the upper pole

(c) Residual picture (10 min. later) showed marked leakage

(d) 7 months later an inferior defect developed in the left eye, and the disc was hyperaemic

(4 *b,e*). Irregularity or focal attenuation indicates arteriosclerotic disease of the retinal vessels. The late pictures show extensive leakage from the dilated retinal peripapillary capillaries (Fig. 4 *c,f*).

(e) Arteries were irregular in calibre with ostial stenosis; delayed filling of the superior capillaries was seen, with marked dilatation of the inferior capillaries

(f) Leakage in the late phase (after 10 min.)

(g) Visual fields showing arcuate defects; there has been no deterioration during 3 years of continued observation and visual acuity is 6/6 in both eyes

Pigment epithelial defects may indicate associated short ciliary involvement in the peripapillary area (Fig. 6, overleaf).

GROUP 3. RELATED DISEASE (Table III, overleaf)

In ten patients associated systemic or ocular disease was considered to be of aetiological significance.

FIG. 5 Arteriosclerosis. Superior segmental filling defect on fluorescein angiography associated with inferior capillary dilatation and an inferior field defect

FIG. 6 Peripapillary pigment epithelial defects in association with ischaemic papillopathy, with marked attenuation of inferior retinal arterioles

Table III Related disease (10 cases; average age 54 yrs)

Aetiology		No. of eyes		Visual acuity		Visual field	
Diabetes	3	Bilateral	7	> 6/60	5		5
Migraine	2	Unilateral	3	6/12 - 6/60	4		7
Syphilis	2	Total	17	6/6 - 6/12	8		5
Blood disorder	2						
Glaucoma	1						

In three patients bilateral involvement was associated with diabetes; one patient also had associated arteriosclerosis, and another had aortic valve and myocardial disease. Two patients developed ischaemic papillopathy in relation to migraine, one in relation

solely to the migraine and the other in conjunction with taking four Migril tablets in 4 hrs during an attack. In both patients involvement was uniocular with inferior arcuate field defects. The loss of retinal neurones after ischaemic papillopathy is well demonstrated (Fig. 7).

FIG. 7 *Migraine*

(a) *Pallid disc oedema, peripapillary haemorrhages, and mild distension of the retinal veins in the acute phase*

(b) *One year later there is extensive loss of neurones. The disc is pale with sheathing of the arterioles in the peripapillary region*

In two patients (three eyes involved) syphilis was diagnosed. The bilateral case presented with inferior field loss in one eye, and the other eye showed disc oedema and fluorescein leakage although no field defect was detected at that time (the Kahn, Reiter, VDRL, Wassermann, and FTA-ABS tests were all positive in the blood but negative in the CSF). Steroid treatment was started and the visual acuity progressively deteriorated in both eyes to 1/60 with pale, flat, atrophic discs.

Haematological disturbances were seen in two cases. One was an 89-year-old man with an

erythrocyte sedimentation rate of 89 mm./1st hr who was previously diagnosed as a case of giant cell arteritis without biopsy confirmation. Steroid therapy failed to prevent visual loss in the second eye and a blood count showed abnormal monocytes. Bone marrow examination suggested a form of monoblastic leukaemia. The second patient, aged 43 years, had bilateral involvement with associated polycythaemia (Hb 18.3 g. per cent.) and hypertension. The second eye became involved 10 months after the first eye, but the visual acuity has remained at 6/6 in each eye with inferior arcuate defects for 3 years; he has been treated with venesection and Aldomet.

One patient in this series had unilateral papillopathy with raised intraocular pressure (28 mm. Hg, R and L); vision has been maintained by treatment of the chronic simple glaucoma.

Bilateral involvement (70 per cent.) in this group was higher than in the other groups in this series and the incidence of severe visual loss was higher in the patients with systemic disorders.

GROUP 4. NO RELATED DISEASE (Table IV)

In this group there was no objective evidence of systemic or retinal vascular disease, and the patients are under continued observation for vascular disorders. In all cases involvement was unilateral and in 75 per cent. the visual acuity has remained better than 6/12.

One patient of particular interest had a second episode in the involved eye. In December, 1972, an inferior arcuate field defect developed in one eye, to be followed 4 months later by a superior arcuate defect in the same eye. This is the only example in this series of a second episode at a later date in the involved eye. The significance of an elevated IgA level in this patient is not understood.

Table IV No related disease (6 cases; average age 55 yrs)

Erythrocyte sedimentation rate (mm/1st hr)	Blood pressure	No. of eyes	Visual acuity	Visual field
Less than 20 in all cases	Less than 130/80 in all cases	Unilateral 6	> 6/60 1 6/12 - 6/60 1 6/6 - 6/12 4	- 3 - 3

Results of treatment

Steroids are the main therapeutic agent for ischaemic papillopathy and can be administered either systemically or by retrobulbar injection or both. The visual acuity in treated (36) and untreated (20) eyes is set out in Table V; the nine eyes in cases of giant cell arteritis have been identified.

It is apparent that those with the worst visual outcome were more likely to have received steroids than those with a final result better than 6/12. Some patients also received a short course of Diamox, or Rheumacrodex, but the behaviour of this group did not differ significantly and the information has not been included.

Improvement was obtained in nine eyes out of 36 (25 per cent.) with steroids and in four eyes out of twenty (20 per cent.) without steroids.

These results do not provide a conclusive case for the efficacy of steroids, and although their value in protecting the second eye in cases of giant cell arteritis is unequivocal, their

use in restoring vision in an affected eye is open to doubt. There are, however, spectacular instances of steroids improving vision, and occasional cases in which steroids probably had a deleterious effect. The route of administration does not appear to provide any guide lines for the future.

Discussion

Pathophysiology of ischaemic papillopathy

The distal optic nerve is vulnerable to hypoxic and ischaemic changes as a result of the special anatomical and physiological features of this region. Anatomical studies in monkeys (Hayreh, 1970) have demonstrated that the prelaminar, laminar, and retrolaminar portions of the optic nerve are supplied by the short ciliary arteries, and though potential anastomoses with retinal vessels may occur in the prelaminar region, these vessels alone appear to supply the retro-laminar region. A border zone between the retinal and ciliary arterial supply therefore exists and, as in the cerebral circulation, watershed zones are vulnerable to impaired perfusion states. Furthermore, the laminar and prelaminar vessels are subjected to a high extramural pressure due to the normal intraocular pressure, and elevation of the intraocular pressure has been shown experimentally to impair perfusion of the disc and peripapillary region (Blumenthal, Gitter, Best, and Galin, 1970). The short ciliary vessels as they enter the nerve are small, of the order of 30–50 μm ., and may not possess the facility of autoregulation attributed to the retinal vessels (Alm and Bill, 1972). The laminar vessels are unique in being contained within a connective tissue septum (Anderson and Hoyt, 1969), which may make them more vulnerable to senile fibrotic changes.

Pathological studies have been undertaken mainly in cases of giant cell arteritis and show infarction primarily in the retrolaminar portion (Henkind and others, 1970). There are no well-documented cases in which the histological changes in arteriosclerotic ischaemic papillopathy are described and in this more benign group it is possible that the primary infarction may be in the laminar or prelaminar region.

Fundus and fluorescein angiographic appearances

The present report emphasizes the varied pattern of disc changes seen with infarction of the

optic nerve. Disc oedema usually appears concomitantly with the visual loss, though disc swelling may precede visual loss (Foulds, 1969). The disc may be pale or hyperaemic depending on the extent of infarction, the facility to develop compensatory vascular channels, and the time sequence. The development of dilated vessels on the disc surface as a compensatory mechanism suggests a favourable prognosis and is rarely seen in giant cell arteritis. Resolution of disc swelling occurs over a period of 2 weeks to several months leaving a variable degree of optic atrophy. After severe infarction, cupping of the optic disc may occur (Greenfield, 1951; Miller, 1972), and this is most often seen with giant cell arteritis. The occurrence of peripapillary infarcts in either the retina or the pigment epithelium lends credence to the hypothesis that short ciliary artery occlusive disease is the primary factor. A macular star may also be seen, and when extensive may resemble the appearance described as the stellate retinopathy of Leber (François and others, 1968), the aetiology of which is unknown. Retinal vascular changes are often inconspicuous, but in the early stage venous dilatation may appear and in the late stages peripapillary sheathing of the retinal vessels. This sheathing may be related to vascular damage incurred as the vessels traverse hypoxic tissue.

Fluorescein angiographic changes are not diagnostic, and similar segmental choroidal filling defects may be seen in papilloedema and papillitis (Fig. 8). The early stages show absent or deficient choroidal filling of the whole disc in severe cases or of a segment in mild cases. Compensatory dilatation of the retinal capillaries can be assessed and late leakage of fluorescein detected. Repeated studies show re-establishment of peripapillary choroidal filling with reduction of capillaries in the atrophic area and absence of leakage. Irregularity of the calibre of retinal arterioles with focal attenuation may indicate early arteriosclerotic disease. Visual field defects usually correspond with the fluorescein angiographic changes in both total and segmental infarction. Inferior arcuate defects occurred as the only visual field abnormality in 42 per cent. of cases and in none was an isolated superior arcuate defect detected. Some constant anatomical feature may explain this finding—possibly the improved vascular supply to the inferior nerve due to the presence of pial or neural branches to the optic nerve from the retrolaminar course of the central retinal artery.

FIG. 8 *Papillitis*

Acute visual loss, with a central scotoma and impaired filling of the retinal and deep disc capillaries in the superior temporal quadrant on fluorescein angiography. The patient subsequently developed other signs of demyelination

Aetiological considerations

Virchow is usually credited with having related thrombosis of a vessel to abnormalities in the vascular intima, in the constituents of the blood, and in the blood flow. Analysis of Virchow's triad provides an adequate platform for this discussion.

(I) ABNORMALITIES OF THE VASCULAR WALL

(a) Giant cell arteritis

The pathological features of giant cell arteritis include fragmentation or absence of the elastic lamina, and acellular thickening of the intima, with replacement of the media by lymphocytes, plasma cells, and giant cells to cause virtually complete obliteration of the lumen.

The extensive involvement of orbital vessels (Crompton, 1959) and the age of the patients accounts for the severe visual loss and the absence of compensatory changes. The importance of arterial biopsy in all suspected cases is stressed, because not only may the ESR be normal in a minority of cases, but in others a high ESR may be produced by other conditions.

(b) Vascular disease

The importance of arteriosclerotic disease in ischaemic optic neuropathy has been recognized for the past two decades (François, Verriest, and Baron, 1957), and histological examination has shown extensive thickening of the walls of arterioles supplying the optic nerve, with increased perivascular fibrosis (Ellenberger and Netsky, 1968). Though often associated with hypertension or accelerated hypertension, many cases are normotensive (70 per cent. in this series). Recent clinicopathological correlations of retinal vessels in patients with accelerated hypertension have shown particular involvement of arterioles (Harnish and Pearce, 1973). In severe retinal arterial changes (sheathing and silver wiring), intimal changes consist of florid hyperplasia, matrix deposits, intimal cell swelling, and atheroma. Haemodynamic studies also indicate the vulnerability of ostial or branch lesions (Texon, 1974) and these correlate with the fluorescein angiographic studies.

All cases included in the arteriosclerotic group in our series had objective signs of retinal vascular disease, or associated cardiac or aortic arch disease capable of producing ophthalmic artery flow disturbances.

(c) Diabetes, Syphilis, Migraine, Collagenoses

Involvement of small arterioles occurs in this group, either in conjunction with or because of associated large vessel involvement.

In diabetes pathological changes have been recorded in capillaries, but also particularly in the precapillary arterioles with occlusion of the lumen (Ashton, 1953, 1974) and lipid thrombi have also been demonstrated (Chester and Banker, 1967). A generalized micro-circulatory disturbance occurs in diabetes, though ciliary involvement has been infrequently reported.

Syphilitic arteritis, though infrequent, must be excluded in a young patient with unilateral or bilateral disease. Arteritis of the small vessels (Nissl Alzheimer endarteritis) is described and is often associated with other signs of neurosyphilis (Merritt, Adams, and Solomon, 1946). One of the patients in this series suffered progressive visual deterioration with high steroid dosage before penicillin therapy was started, and there is some evidence that steroids may activate or potentiate the arteritis (Nicol, 1973).

Migraine has also been shown to be due to disturbances in perfusion, and presumably

the microcirculatory changes which are characteristic features of the occipital cortex may also occur in the optic nerve vessels. In one case optic disc ischaemia followed a severe migraine headache (McDonald and Sanders, 1971), and in the other patient in this group the ischaemia may have been related to migraine therapy.

(2) ABNORMALITIES IN THE CIRCULATING BLOOD

Emboli, Polycythaemia, Leukaemia

The incidence of embolic occlusion of short ciliary arteries is difficult to assess unless concomitant embolization of the retinal arteries also occurs. In two patients in this series a careful search revealed retinal emboli. In both instances there were atheromatous plaques within the carotid artery and in none were calcific emboli from the heart detected.

Factors affecting the flow in blood vessels are complex and difficult to measure owing to the non-Newtonian behaviour of blood. Viscosity, which is a measure of fluid friction, may be increased by an increase in the plasma proteins (especially fibrinogen), the red blood cells, or to a lesser extent the white cells. Although viscosity measurements were not made in this series, it is probable that these were elevated in the patients with polycythaemia and leukaemia. Detection of these conditions is important because of the different therapeutic requirements.

(3) ABNORMALITIES OF THE BLOOD FLOW

Perfusion of the optic disc depends on an adequate arterial pressure and a normal venous pressure. Dramatic reduction in blood flow may be seen after acute blood loss, with resultant optic nerve infarction (Gowers, 1879). Hypotensive episodes, myocardial infarcts, and carotid occlusion may also produce sudden visual loss. In our patient with complete carotid occlusion, the ophthalmodynamometry readings were equal on each side because of the development of collateral channels.

Impaired perfusion is also produced by elevation of the intraocular pressure and there are several reports of raised intraocular pressure and ischaemic papillopathy (Foulds, 1969). The field loss in glaucoma is probably due to impaired perfusion of the disc (Hayreh, Revie, and Edwards, 1970), and a similar mechanism has been postulated in low tension glaucoma. Hypoxia in the territory of the short posterior ciliary arteries obviously contributes to the pattern of field loss in chronic simple glaucoma, low tension glaucoma, and ischaemic papillopathy, but it seems important, for clinical, diagnostic, and therapeutic reasons, to regard them as separate nosological entities. In the present series only one patient presented with a pallid swollen disc which was subsequently found to be associated with chronic simple glaucoma. The administration of Diamox (250 mg. four times a day) would seem of therapeutic benefit and provides a safe and harmless way to improve ocular perfusion.

Differential diagnosis

The accurate diagnosis of ischaemic papillopathy depends on the association of sudden arcuate field loss and a characteristic pattern of disc swelling with confirmation by fluorescein angiography. In the absence of disc oedema sudden visual loss may be produced by compressive, infiltrative, demyelinating, or vascular lesions of the retrolaminar optic nerve.

Unilateral disc oedema with sudden visual loss may occur in papillitis and, although the characteristic visual field defect is a central scotoma, there are no positive methods of differentiating this from ischaemic papillopathy. The visually evoked response may

demonstrate reduced amplitude and delayed latency in both conditions (Halliday, personal communication).

Carcinomatous optic neuropathy may present with visual loss and disc oedema and this diagnosis should be considered if resolution fails to occur.

Finally, symmetrical dilatation of the papillary and peripapillary capillary plexus with symmetrical leakage of dye should raise suspicions of an alternative diagnosis.

Conclusions

The present report indicates the complexity of the pathogenesis, diagnosis, and treatment of ischaemic papillopathy. The causes are numerous and in a given case may be multifactorial. Investigations include assessment of the circulatory and microcirculatory systems, specific examination to exclude any form of arteritis, and sophisticated immunological, haematological, and rheological tests. In patients with arteriosclerotic disease, a minor polycythaemia or mild elevation of the intraocular pressure may suffice in combination to impair disc perfusion. Thus, one patient with a carotid occlusion presented with an ischaemic papillopathy only after a severe epistaxis (Cullen, 1967). The high incidence of bilateral involvement makes extensive medical investigations paramount, and the treatment of minor contributory factors crucial. The clinical and fluorescein angiographic appearances and the natural history have been well documented, so that in most instances accurate diagnosis is feasible. Therapy therefore assumes particular importance. In the absence of any double-blind controlled trial on the efficacy of steroid therapy, only arbitrary measures can be taken. There is unequivocal evidence for the immediate administration of steroids in high dosage in cases of giant cell arteritis, but steroids may be contraindicated in syphilitic arteritis if not combined with antibiotics, and they may not be beneficial in polycythaemia vera.

The random administration of steroids in our group has not produced satisfactory guidelines for therapy and we are currently undertaking a more detailed trial. The classification of patients into aetiological groups would seem important before the therapeutic efficacy of drugs can be assessed. Reduction of oedema in the distal optic nerve remains one of the main objectives of treatment in an effort to preserve functioning neurones, and in some cases the administration of steroids has produced dramatic results. We therefore suggest that, in our present state of knowledge, even a patient without arteritis should be given the benefit of either systemic or retrobulbar steroids.

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References

- ALM, A., and BILL, A. (1972) *Acta physiol scand.*, **84**, 306
- ANDERSON, D. R., and HOYT, W. F. (1969) *Arch. Ophthalm. (Chicago)*, **82**, 506
- ASHTON, N. (1953) *Brit. J. Ophthalm.*, **37**, 282
- (1972) *Trans. Amer. Acad. Ophthalm. Otolaryng.*, **76**, 17
- (1974) *Brit. J. Ophthalm.*, **58**, 344
- BEGG, I. S., DRANCE, S. M., and SWEENEY, V. P. (1971) *Ibid.*, **55**, 73
- BLUMENTHAL, M., GITTER, K. A., BEST, M., and GALIN, M. (1970) *Amer. J. Ophthalm.*, **69**, 39
- CHESTER, E. M., and BANKER, B. (1967) *Arch. intern. Med.*, **120**, 397

- CROMPTON, M. R. (1959) *Brain*, **82**, 377
- CULLEN, J. F. (1967) *Trans. ophthal. Soc. U.K.*, **87**, 759
- ELLENBERGER, C., KELTNER, J. L., and BURDE, R. M. (1973) *Arch. Neurol.*, **28**, 182
- and NETSKY, M. G. (1968) *J. Neurol. Neurosurg. Psychiat.*, **31**, 606.
- FOULDS, W. S. (1968) "Ischaemic optic neuropathy", in "Wm. Mackenzie Centenary Symposium on the Ocular Circulation in Health and Disease", ed. J. S. Cant, p. 136. Kimpton, London
- (1969) *Trans. ophthal. Soc. U.K.*, **89**, 125
- FRANÇOIS, J., VERRIEST, G., and BARON, A. (1957) *Acta ophthal. (Kbh.)*, **35**, 32
- , ———, and DELAEY, J. J. (1968) *Soc. belg. Ophtal.*, **149**, 470
- FRIEDENWALD, H. (1919) *Contrib. to Med. and Biolog. Res.*, **1**, 495
- GOWERS, W. R. (1879) "A Manual and Atlas of Medical Ophthalmoscopy", pp. 184–188. Churchill, London
- GREENFIELD, J. G. (1951) *Proc. roy. Soc. Med.*, **44**, 855
- HARNISH, A., and PEARCE, M. L. (1973) *Medicine (Baltimore)*, **52**, 483
- HAYREH, S. S. (1969) *Brit. J. Ophthal.*, **53**, 721
- (1970) *Ibid.*, **54**, 289
- , REVIE, I. M. S., and EDWARDS, J. (1970) *Ibid.*, **54**, 461
- HENKIND, P., CHARLES, N. C., and PEARSON, J. (1970) *Amer. J. Ophthal.*, **69**, 78
- JENNINGS G. H. (1938) *Lancet*, **1**, 424
- KIMBRELL, O. C., and WHELISS, J. A. (1967) *J. Amer. med. Ass.*, **201**, 61
- KING, E. F. (1935) *Trans. ophthal. Soc. U.K.*, **55**, 246
- LINDENBERG, R., WALSH, F. B., and SACKS, J. G. (1973) "Neuropathology of Vision." Lea and Febiger, Philadelphia
- MCDONALD, W. I., and SANDERS, M. D. (1971) *Lancet*, **2**, 521
- MEADOWS, S. P. (1954) *Trans. ophthal. Soc. U.K.*, **74**, 13
- MERRITT, H. H., ADAMS, R. D., and SOLOMON, H. C. (1946) "Neurosyphilis." Oxford Univ. Press, New York
- MILLER, S. J. H. (1972) *Trans. ophthal. Soc. U.K.*, **92**, 563
- NICOL, C. S. (1973) In "Price's Textbook of the Practice of Medicine", 11th ed., ed. R. B. Scott. Oxford Univ. Press, London
- PARSONS-SMITH, G. (1959) *Brit. J. Ophthal.*, **43**, 204
- SANDERS, M. D. (1971) *Trans. ophthal. Soc. U.K.*, **91**, 369
- WALSH, F. B., and HOYT, W. F. (1969) "Clinical Neuro-Ophthalmology", 3rd ed. Williams and Wilkins, Baltimore
- TEXON, M. (1974) *Med. Clin. N. Amer.*, **58**, 257
- UHTHOFF, W. (1924) *Ber. dtsh. ophthal. Ges., Heidelberg*, **44**, 196