Anterior ischaemic optic neuropathy

I. Terminology and pathogenesis

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In anterior ischaemic optic neuropathy (AION) there is a comparatively sudden loss of vision in the entire eye, or in one sector of the field of vision of the eye, initially associated with oedema of the optic disc, which results in optic atrophy within a month or two, leaving a permanent visual defect. A large number of such cases have been reported in the literature, but, although this clinical entity is well-known under different names, its pathogenesis and management have till recently been ill-understood. A full understanding of the pathogenesis of AION would make it considerably easier to understand its clinical pattern and management.

Terminology

This condition has been given different eponyms by various authors because of controversy as to its pathogenesis (Hayreh, 1974c).

The most popular term in the European literature has been “vascular pseudo-papillitis” (François, Verriest, and Baron, 1956, 1957) and in the English “ischaemic optic neuropathy”. As will be evident from the pathogenesis of this condition, perhaps the most suitable term is “anterior ischaemic optic neuropathy”; because the condition is ischaemic, involves both the optic nerve head and retrolaminar optic nerve (hence the terms defining it as a disease only of the optic disc are not correct), non-inflammatory (therefore all terms including the suffix -itis are incorrect), and there is nothing “pseudo-” about it.

Pathogenesis

Many theories have been postulated to explain the pathogenesis. A review of the literature (Hayreh, 1974c) reveals that the site of the lesion in AION is thought to lie in the optic nerve, although some authors considered it to be due to involvement of the retina. It is almost universally agreed that the condition is the result of interference with the circulation of one of these structures.

The vast majority of authors, while describing a circulatory lesion in the optic nerve, have made vague statements without being specific as to the exact lesion. However, François and co-workers (François and others, 1957; François, Verriest, Neetens, and De Rouck, 1961; François, Verriest, De Rouck, and Hanssens, 1962; François and Neetens 1969) postulated that AION was due to occlusion of the so-called “central artery of the optic nerve”, an artery they only assumed to exist (François and Neetens, 1954, 1956; François, Neetens, and Colette, 1955). My anatomical studies on the blood supply of the optic nerve and branches of the ophthalmic artery in about one hundred human specimens (Hayreh, 1958, 1962, 1963a,b; Singh and Dass, 1960a,b) and those of Beauvieux and Ristitch (1924) and Steele and Blunt (1956) failed to reveal the presence of any “central artery of

the optic nerve" corresponding to their description. Hence, occlusion of the "central artery of the optic nerve" can have no significance in the production of AION.

Various mechanisms have been postulated for the production of histopathological ischaemic necrosis seen in the anterior part of the optic nerve in AION. Kreibitz (1953) considered that the necrosis was due to a combined involvement of the axial and peripheral (from short posterior ciliary arteries) vascular systems as a result of occlusion of the ophthalmic artery and short posterior ciliary arteries. Spencer and Hoyt (1960) agreed with Kreibitz. Meadows (1954), Wagener and Hollenhorst (1958), and MacFaul (1967) thought that the necrosis was due to involvement of the short posterior ciliary arteries as they formed the circle of Zinn and Haller. According to Birkhead, Wagener, and Shick (1957), anoxic damage to the optic nerve is probably due to extreme narrowing of the lumen of the ophthalmic artery or central retinal artery.

Present studies

The concept of pathogenesis of AION which is presented below is based on:

(a) *The pattern of arterial supply of the anterior part of the optic nerve*

This was studied in man and experimentally in rhesus monkeys and is described in detail elsewhere (Hayreh, 1969, 1970, 1974b).

(b) *Clinical studies*

These consisted of ophthalmoscopic and fluorescein fundus angiographic studies on about 75 patients with AION of different aetiologies (mainly due to arteriosclerosis and temporal arteritis—Hayreh, 1974a).

(c) *Experimental studies*

AION was produced in rhesus monkeys and its evolution studied by ophthalmoscopy, fluorescein fundus angiography, and histopathology (Hayreh and Baines, 1972).

(d) *Histopathological studies on eyes of patients with AION*

These were obtained from the cases reported in the literature and very well summarized by Henkind, Charles, and Pearson (1970).

A complete knowledge of the anatomy and blood supply of the anterior part of the optic nerve, consisting of the optic nerve head and retrolaminar optic nerve, is an essential prerequisite to an understanding of the pathogenesis of AION. As far as the arterial supply of the optic nerve is concerned, the optic nerve head and retrolaminar region form a single unit.

The optic nerve head is composed of (from the front backwards):

- (a) The surface nerve fibre layer continuous with the nerve fibre layer of the retina;
- (b) The prelaminar region composed of nerve fibres and glial tissue septa;
- (c) The lamina cribrosa containing nerve fibres, glial tissue, and dense compact connective tissue septa (Hayreh, 1974b).

The posterior ciliary arteries (PCAs) are the only source of blood supply to the lamina cribrosa and prelaminar region and the main (if not the only) source to the retrolaminar region, and they may also supply the temporal part of the surface nerve fibre layer (Hayreh, 1969, 1970, 1974b). The PCAs are therefore extremely important in the blood supply to the optic nerve head and the adjacent retrolaminar optic nerve; this is the crucial factor to be recognized before one can understand the pathogenesis of AION. There are usually two or three PCAs (designated medial

and lateral PCAs) arising from the ophthalmic artery (Hayreh, 1962). The main lateral or medial PCA usually supplies half of the choroid and optic nerve head (Fig. 1) (Hayreh, 1970). Smaller divisions of the main PCAs would supply smaller sectors (Fig. 2).

FIG. 1 Fluorescein fundus angiogram of left eye of 78-year-old man 23 days after onset of bilateral deterioration of vision and a negative temporal artery biopsy for temporal arteritis. Retinal arterial phase shows nasal part of the choroid and optic disc (supplied by the medial posterior ciliary artery) filling with fluorescein, while the temporal part of the disc and choroid (supplied by the lateral posterior ciliary artery) is empty

Basing my argument on these studies of the blood supply of the optic nerve head, I pointed out that the basic lesion in AION is the occlusion of the PCAs (Hayreh, 1969), which produces infarction not only of the optic nerve head but also of the retrolaminar part of the optic nerve, by virtue of their distribution to the prelaminar, lamina cribrosa, and retrolaminar regions. In patients with cilio-retinal arteries, the retinal area supplied by these vessels is also infarcted (Fig. 17 in Hayreh, 1969; and Fig. 3). Foulds (1969) also attributed AION to interference with PCA circulation.

Fluorescein angiographic studies in patients with AION confirmed the presence of occlusive disorder of the PCAs (Hayreh, 1974a), because these eyes showed a very slow and poor filling of the choroid, or on occasion, complete absence of filling, and also non-filling of the optic disc.

Experimental studies were conducted in rhesus monkeys to investigate the pathogenesis of AION, in which the various PCAs were occluded (Hayreh and Baines, 1972). These eyes developed AION which ophthalmoscopically showed swelling of the optic disc soon after occlusion of the PCAs and optic atrophy within 5 to 6 weeks. Histological examination of these eyes shows the involvement of the optic nerve head and retrolaminar region (Fig. 6 in Hayreh and Baines, 1972). Lessell (1974), in a recent review of these experimental AION studies, has stated that there are obvious differences between the clinical picture of AION in humans and the lesions we produced in monkeys by occlusion of the PCAs.

FIG. 2 *Fluorescein fundus angiogram of a normal human right eye, showing sectoral filling of the choroid and adjacent prelaminar region of the optic nerve head*

FIG. 3 *Right eye of a 71-year-old woman with temporal arteritis, anterior ischaemic optic neuropathy, cilio-retinal artery occlusion, and no perception of light in that eye, 4 days after onset of blindness. This fundus photograph shows chalky-white swelling of the entire optic disc with oedema (infarction) of upper half of retina*

I do not understand the basis for his impression. Nor do I agree with Anderson and Davis (1974) that AION must represent disease of more than just the PCAs, as is discussed in detail elsewhere (Hayreh, 1974c).

These fluorescein angiographic studies in patients, and experimental studies in rhesus monkeys, have established the role of occlusion of the PCAs in the production of AION. A review of the histopathological studies of AION in patients (Henkind and others, 1970) further confirms this, because the infarct involved the optic nerve head and retrobulbar region (Fig. 6 in Hayreh and Baines, 1972) in all eyes, and frequent involvement of the PCAs was found in these eyes (ten out of sixteen case reports mention PCA involvement, while five make no mention of the absence of PCA involvement; presumably the changes in the PCAs were not recorded). The possible role of PCA occlusion in the production of AION was also postulated by some workers on the basis of their histopathological findings of PCA occlusion in these cases (Kreibig, 1953; Meadows, 1954; Wagener and Hollenhorst, 1958; MacFaul, 1967).

One of the important points to be stressed is that *it is not essential for the PCAs to be completely occluded to produce AION*. In fact, I feel, in the majority of the eyes there is never a complete occlusion of the PCAs. We demonstrated that the circulation in the optic disc, peripapillary choroid, and choroid is dependent upon the difference between the intraocular pressure and perfusion pressure* in the PCAs (Hayreh, Revie, and Edwards, 1970). When such imbalance is produced between the perfusion pressure and intraocular pressure, by either lowering the perfusion pressure or raising the intraocular pressure, the susceptibility of the intraocular blood vessels to obliteration varies considerably:

(a) The vessels in the prelaminar part of the optic disc are most susceptible to obliteration and are usually the first to be obliterated.

(b) The peripapillary choroid is either equally or slightly less susceptible to obliteration. The obliteration of the peripapillary choroid itself would in turn involve the blood supply to the prelaminar region of the disc and retrolaminar optic nerve as well (Fig. 4), particularly in arteriosclerotic individuals with poor collateral circulation.

(c) The rest of the choroidal circulation is also susceptible to obliteration but much less so than (a) and (b). In the choroid it is most marked in the watershed areas where the territories of distribution of the medial and lateral PCAs meet.

(d) The retinal circulation does not show any obliteration unless the intraocular pressure is higher than the perfusion pressure in the central retinal artery. Thus, the retinal circulation is the last to be obliterated.

In the light of these observations it is evident that, once the perfusion pressure in the PCAs falls, the optic disc circulation is the first to be involved, then the peripapillary choroid, and the rest of the choroid last of all (Fig. 4). In these cases the PCAs may still be patent. Thus, the determining factor for the production of AION is the level of the perfusion pressure in the PCAs as compared to the intraocular pressure and not the absence or presence of complete occlusion of the arteries. This is demonstrated by means of angiography which reveals the frequent presence of some choroidal circulation in the absence of any circulation in the optic disc and peripapillary choroid in these cases (Fig. 4) (Hayreh, 1974a). The other very important factor to consider, when interpreting fluorescein angiographic filling of the PCA circulation in these cases, is the time-lapse between the onset of AION and fluorescein angiographic examination. This is because, even in eyes with

* In this paper perfusion pressure denotes blood pressure in the vessels.

FIG. 4 Right eye of a 72-year-old woman with temporal arteritis, anterior ischaemic optic neuropathy, and no perception of light, 3 days after onset of anterior ischaemic optic neuropathy and on day of loss of perception of light
(a) Fundus photograph, showing chalky-white swelling of right optic disc, with no haemorrhages

complete absence of filling of the PCA circulation at the onset of the disease, a slow restoration of circulation occurs fairly soon so that a significant filling defect is no longer seen within a few days or weeks (Hayreh, 1974a). Thus, the fact that no filling defect in PCA circulation is seen on intravenous fluorescein angiography does not prove that there has been no earlier filling defect, as I have also demonstrated in cases of retinal vascular occlusions (Hayreh, 1971).

This imbalance between the perfusion pressure in the PCA circulation and intraocular pressure has also been pointed out by Foulds (1968, 1969). If the imbalance is of a chronic nature, it produces so-called "low tension glaucoma", but when it is of a sudden onset, it results in AION. The fall in perfusion pressure in the PCAs may be due to several causes:

(1) LOCAL VASCULAR CAUSES

The important factors in this category include occlusion or stenosis of PCAs, ophthalmic, internal carotid, or common carotid arteries due to any cause, particularly in an arteriosclerotic individual. In this group may be included temporal arteritis, marked atherosclerosis and arteriosclerosis, hypertension, carotid artery disease, diabetes, collagen diseases, syphilis, hypercholesterolaemia, thromboangiitis obliterans, Raynaud's disease, migraine, Takayasu's disease, etc. By far the commonest cause of AION among these is arteriosclerosis. Temporal arteritis is an important, but by no means a common, cause.

(2) SYSTEMIC CAUSES

(a) Systemic arterial hypotension

Many diseases may produce a sudden and marked systemic arterial hypotension, *e.g.* shock of any aetiology, surgical hypotension, heart failure, myocardial infarction, ischaemic

heart disease, severe haemorrhages, recurrent haemorrhages, etc. In a patient with poor perfusion pressure in the PCAs due to local vascular factors, even a small fall in systemic blood pressure may be enough to produce AION. It is not uncommon to find that AION is noticed by a patient on waking up in the morning because systemic hypotension during sleep can be enough to produce the imbalance between perfusion pressure and intraocular pressure in already diseased and narrowed PCAs. Thus, systemic arterial hypotension is an important precipitating factor.

(b) Embolic phenomenon

An embolus originating anywhere in the cardiovascular system may become lodged in the PCAs.

(c) Haematological disorders

Vascular occlusion may be produced by polycythaemia, sickle cell disease, thrombocytopenic purpura, leukaemia, and, possibly, the contraceptive pill. In this category can also be

included the severe anaemias, because oxygenation of the optic nerve head depends not only upon the amount of blood flow but also upon the oxygen-carrying capacity of the blood (Foulds, 1969). Low-grade optic disc oedema and diminution of central vision in severe anaemias and chlorosis, resembling AION, were described nearly a century ago by Gowers (1904). Unrecognized visual disturbances in severe anaemia may be due to some degree of AION (Foulds, 1969). In chronic bronchitis with polycythaemia, poor oxygenation of the blood and slow circulation because of increased viscosity may produce AION (Foulds, 1969).

(3) OCULAR CAUSES

The most important factor in the eye itself which may produce AION is elevated intra-ocular pressure, which compromises the circulation in the optic disc. Thus, a patient with chronic simple glaucoma has a higher chance of developing AION than one with a low intraocular pressure. This has been reported by Foulds (1968, 1969), Begg, Drance, and Sweeney (1970, 1971), Drance and Begg (1970), and Sanders (1971). Drusen in the optic nerve head could produce AION by direct pressure on the vessels.

While discussing the blood supply of the optic nerve head, it was shown that two or three PCAs usually arise from the ophthalmic artery and that each PCA then subdivides into multiple short PCAs. The occlusive disorder may involve only one PCA or short PCA, thus producing only a sectoral and not a generalized AION. The AION may start as a sectoral change but may soon progress to complete AION because the development of oedema in one part of the optic nerve may, by raising the tissue pressure, slowly compromises the small blood vessels in the parts adjoining the oedematous part, and thus the oedema may gradually creep to involve other parts. Similarly, Foulds (1969) postulated that optic disc oedema might occur before the onset of symptoms because anoxic damage might be severe enough to cause capillary dilatation and increased permeability without interrupting the function of the optic nerve fibres; increased permeability → a rise of local tissue pressure → either direct damage to the optic nerve fibres or further impairment of the circulation in the optic nerve head → AION.

Thus, AION, glaucoma, and low tension glaucoma are manifestations of ischaemia of the optic nerve head and retrolaminar optic nerve caused by interference with PCA circulation as a result of an imbalance produced between the perfusion pressure in the PCAs and the intraocular pressure. If the process is sudden, it produces AION with infarction of the optic nerve head and retrolaminar region, but if it is chronic (as in glaucoma and low tension glaucoma) it produces slow degeneration of neural tissue in the optic nerve head and retrobulbar region, resulting in cupping of the optic disc and cavernous degeneration of the retrolaminar optic nerve.

Summary

The clinical entity comprising sudden loss of vision, initially associated with oedema of the optic disc, which resolves to optic atrophy within a month or two, leaving a permanent visual defect, has been given many different names. It is suggested that the term "Anterior Ischaemic Optic Neuropathy" (AION) gives an accurate description. A theory of its pathogenesis based on clinical, experimental, and histopathological evidence is discussed. The evidence shows that interference with the posterior ciliary artery (PCA) supply to the anterior part of the optic nerve is responsible for AION, without involvement of the central retinal artery. It is not essential for the PCAs to be completely occluded to produce AION,

because, as soon as the perfusion pressure in the PCAs falls below the intraocular pressure for any reason (*e.g.* local vascular, systemic, and ocular causes), the blood supply to the anterior part of the optic nerve is cut off because of its special vulnerability to such an occlusion. The mechanism of this process is discussed.

I am grateful to my wife Shelagh for help in the preparation of this manuscript and to Mrs. Maria Warbasse for secretarial help.

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