Infarction in the optic nerve¹

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Infarction in the optic nerve is a well-known complication in cases of giant-cell arteritis, but may not be diagnosed when it is related to atherosclerosis. The three patients to be reported were referred during the same year with papilloedema and a diagnosis of suspected brain tumour. Two underwent extensive radiological procedures to exclude an intracranial tumour. The three patients illustrate the syndrome of infarction in the optic nerve and provide a basis for the suggestion that, when this diagnosis is suspected, a short period of observation appropriately may replace some of these procedures. In addition, studies were made of the vasculature of selected optic nerves at necropsy.

CASE 1

A 52-year-old man noted sudden, painless onset of right inferior altitudinal hemianopsia. The defect remained unchanged. A year later, he consulted an ophthalmologist immediately after an identical defect occurred on the left. On admission to the hospital, vision was 20/30 on the right, 20/20 on the left. Intraocular tension was normal. The right optic disc was pale and the arterioles narrowed. The left disc was slightly elevated, had indistinct margins, but was not hyperaemic. Retinal arterioles on the left were narrowed in segments, and a few small haemorrhages radiated from the nerve head. Evidence of retinal vascular occlusion was not seen. Inferior altitudinal fibre bundle defects were present bilaterally (Fig. 1). Blood pressure 160/100, but the remainder of the physical examination was normal. Fasting blood sugar, VDRL, erythrocyte sedimentation rate (ESR), cerebrospinal fluid (CSF), electroencephalogram (EEG), bilateral carotid arteriograms, and pneumoencephalogram were normal. Biopsies of temporal artery, skin and muscle, and examination of bone marrow were also normal. One month, and again two years later, bilateral pallor of the discs was noted, but visual acuity and fields were unchanged.

COMMENT A hypertensive, middle-aged man presented with a Foster Kennedy syndrome. Extensive studies did not give evidence for an intracranial lesion. Sudden onset of symptoms, permanent bilateral altitudinal field loss, and prompt disappearance of disc swelling are

important features suggesting infarction in the optic nerve.

CASE 2

A 29-year-old woman suffered sudden decrease of vision in the left eye and was seen by an ophthalmologist who diagnosed 'papillitis'. Acuity improved over a few months. At the age of 41, she noted episodic blurring of vision for three days, and then sudden painless onset of a superior altitudinal field defect on the right. Another ophthalmologist diagnosed papilloedema and recommended neurological evaluation.

On admission, no history of other previous neurological deficit was obtained. Blood pressure and general examination were normal. Vision with glasses was 20/40 in both eyes. Intraocular tension was normal. The right optic disc was elevated two dioptres, had indistinct margins, but was not hyperaemic. A small linear haemorrhage radiated from the disc. Retinal veins were dilated, tortuous, and segmented, and arterioles extremely narrowed. The left disc was pale, had sharp margins and the left retinal arterioles were small in calibre. Superior altitudinal fibre bundle defects were noted in both fields (Fig. 2).

Moderate iron deficiency anaemia and an abnormal glucose tolerance curve were found. Fluorescent treponeme antibody (FTA-ABS) test was negative. ESR was normal. Electrocardiogram demonstrated changes of ischaemia, and biopsy of the temporal artery revealed mild atherosclerosis. Radiographs of the skull with views of the optic foramina, EEG, CSF, and brain scan were normal. Papilloedema disappeared within a

FIG. 1. Visual fields in Case 1 demonstrating inferior altitudinal fibre bundle defects bilaterally. Test objects: 1/330 and 3/1000, white.

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FIG. 2. Visual fields in Case 2 demonstrating superior altitudinal fibre bundle defects bilaterally. Test objects: 1/330 and 2/1000, white.

month, and the disc became pale. Acuity and fields did not change during the following year.

COMMENT A middle-aged, diabetic woman presented with a Foster Kennedy syndrome. Evidence for atherosclerosis was found on ECG and arterial biopsy, but an intracranial mass was not found. Sudden onset of symptoms, permanent altitudinal field loss and prompt disappearance of disc swelling again favoured infarction in the optic nerve rather than raised intracranial pressure. Preserved acuity is not consistent with demyelinative disease, and no clinical evidence for multiple sclerosis was found. The cause of the initial episode of 'papillitis' is uncertain.

CASE 3

A 37-year-old woman with a history of diabetes mellitus for 14 years noted sudden onset of visual field defect in the upper nasal quadrant on the left. Onset was not accompanied by pain or systemic symptoms.

The left disc was oedematous, but not hyperaemic, and the margins were indistinct. One small haemorrhage was near the disc, and retinal veins were engorged, but evidence of retinal vascular occlusion was not seen. Vision with glasses was 20/20 bilaterally. A left sectoral field defect, mainly in the nasal quadrant, and enlargement of the left blind spot were noted (Fig. 3). The remainder of the examination was normal.

FIG. 3. Visual fields in Case 3 demonstrating upper nasal sectoral defect on the left. Test objects: 3/330 and 1/1000, white.

ESR, FTA-ABS test, radiographs of the skull with views of the optic foramina, and tomograms of the sella turcica, EEG, brain scan, and CSF were normal. No abnormalities were seen in the left carotid arteriogram. This procedure was followed by dysphasia and dyslexia, improving slowly over two months. The patient refused pneumoencephalography. Two weeks and again two months after discharge from the hospital, the left disc was flat, had distinct margins, and was slightly pale. Acuity and fields remained unchanged.

COMMENT A 37-year-old diabetic woman presented with unilateral papilloedema. The sudden onset, sectoral visual field deficit, and prompt disappearance of disc swelling are consistent with infarction in the optic nerve. Evidence for an intracranial mass was not found. Preservation of visual acuity and permanent field defect make demyelinative disease unlikely.

DISCUSSION

Infarction in the optic nerve, also called ischaemic optic neuritis (Hollenhorst, Brown, Wagener, and Shick, 1960), ischaemic optic neuropathy (Miller and Smith, 1966) or vascular pseudopapillitis (François, Verriest, Neetens, De Rouck, and Hanssens, 1962) has been reported frequently in the French and German medical literature for more than a decade, but has only recently been considered as a nosological entity in the English literature (Miller and Smith, 1966). Involvement of the eye in many systemic vascular diseases is generally recognized, but infarction in the optic nerve on the basis of arteriolo- or atherosclerosis is seldom diagnosed. The resulting choked disc may be mistaken as evidence of increased intracranial pressure, and, when the process later occurs on the other side, the finding of a Foster Kennedy syndrome may suggest a mass in the anterior fossa.

Infarction in the optic nerve probably occurs more frequently than generally realized, and may account for some cases of 'low tension glaucoma', optic neuritis of unknown origin and 'chiasmatic arachnoiditis'. It is a frequent result of giant-cell arteritis, whether typical (Hollenhorst *et al.*, 1960) or 'occult' (Cullen, 1967), and has occurred in association with polyarteritis nodosa (Kimbrell and Wheliss, 1967), lupus erythematosus (Lasco, 1961), syphilitic arteritis (Smith, Israel, and Harner, 1967), acute blood loss (Piper and Unger, 1957), and polymyalgia rheumatica (Fessel and Pearson, 1967). We have observed one case after subarachnoid haemorrhage (University of Virginia Hospital, Case No. 54-05-45). Nevertheless, infarction in the optic nerve is probably most common with atherosclerosis (François *et al.*, 1962).

The syndrome, as recently described also by Miller and Smith (1966), begins with sudden onset

of a visual field defect which may include central vision. Pain is usually not present when atherosclerosis is the cause. Permanent visual deficit may occur after several attacks of transient ischaemia. Initially, the process is often unilateral, but it may eventually occur in the other eye within days to years. Twenty-four to 36 hours after the onset, the appearance of the optic disc may be indistinguishable from papilloedema resulting from raised intracranial pressure. More commonly, however, the disc, although oedematous, is not hyperaemic, and may even be pale. Frequently, only a segment of the disc is elevated, and occasionally it is normal. Small linear haemorrhages may radiate outward from the disc, and the pattern of nerve fibre bundles be accentuated by oedema. Elevation gradually disappears in two or three weeks, leaving a flat, pale disc.

Evidence for retinal arteriosclerosis is usually present. In addition, in the acute stage, retinal veins may be dilated, tortuous and segmented, and arterioles narrowed, sometimes to thread-like calibre.

An important distinguishing sign of infarction in the optic nerve is the abnormality of the visual field. Sudden onset of a large fibre bundle defect, particularly an altitudinal hemianopsia, should suggest a vascular mechanism for the elevated disc. Fibre bundle defects are not characteristic of this entity alone; they are common in glaucoma, for example. Total loss of vision, sectoral defects, and scotomas also occur frequently. Visual acuity may not be diminished.

An expanding intracranial or intraorbital lesion compressing one optic nerve is most important in the differential diagnosis of infarction in the optic nerve. Some expanding lesions, particularly aneurysms, may rarely cause sudden loss of vision, and even altitudinal hemianopsia (Mitts and McQueen, 1965). Thrombosis of a retinal branch of the central retinal artery may cause similar abnormalities of the visual field, particularly sectoral or fibre bundle defects. These defects, however, are more likely to radiate from the blind spot rather than from the centre of fixation (as in Case 3), and also are usually more sharply demarcated at the horizontal line because the superior and inferior halves of the retina are supplied by separate branches of the central artery. Similar field defects may result from trauma to the optic nerve (Turner, 1943), probably because the same vessels, the pial arterioles of their branches, are involved. These arterioles, being on the outer surface, may be more vulnerable than the central vessels.

Preservation of visual acuity frequently aids in

distinguishing infarction in the optic nerve from demyelinating diseases in which severe loss of vision is common.

A helpful diagnostic point illustrated by the present cases is the resolution of disc elevation within two or three weeks. After recognition of a static visual deficit, adequate reason exists to postpone arteriography and pneumoencephalography for the short time necessary to observe the disc.

Occlusion of a 'central artery of the optic nerve' has been a frequent explanation of this syndrome (Piper and Unger, 1957; François *et al.*, 1962; François and Neetens, 1965). François and Neetens (1965) have cited the occurrence of lower altitudinal hemianopsia as evidence for existence of this artery thought to supply the upper half of the optic nerve by these authors (François *et al.*, 1962), macular fibres by others (Wolff, 1954).

The pattern of arterial supply of the optic nerve is a controversial subject. The concept of a central artery of the optic nerve has been strongly supported by François and Neetens (1954, 1963, 1965), on the basis of latex injection and microradiographic studies, and has become widely accepted. These authors stated that nutritive branches of the central retinal artery supplying the optic nerve do not exist, and maintained that the nerve is supplied by perforating arterioles from the pia, and a separate axial system that enters the nerve to supply the upper half (Fig. 4a). In 10 of 31 specimens, François *et al.* found the axial system to be a discrete central artery of the optic nerve; in the remainder, more than one axial artery was present.

Hayreh (1963) stressed the variability of the blood supply to the optic nerve. Using latex injection, he demonstrated nutritive branches from the intraneural part of the central retinal artery in 75% of 64 specimens, but noted absence of these branches from the distal third of the artery (Fig. 4b). The section of optic nerve just behind the lamina cribrosa was supplied only by branches from the circle of Zinn. Although Hayreh found abundant anastomoses between the central retinal artery and pial plexus, he found none between this artery and branches of the circle of Zinn immediately behind the lamina cribrosa. This may be a relatively vulnerable location for infarction. Several other authors have found intraneural branches of the central retinal artery and have denied the existence of a central optic nerve artery (Wybar, 1956; Steele and Blunt, 1956; Blunt, 1963). Present clinical and pathological evidence does not support the concept of occlusion of a central optic nerve artery as being the cause of infarction in the optic nerve in all cases.

FIG. 4. (a) Scheme of the arterial supply of the optic nerve, according to François and Neetens (1954). (b) The scheme of Hayreh (1963). Note central artery of the optic nerve (CAO) in (a) only, intraneural branches of central retinal artery (CAR) in (b) only.

(Figures redrawn from and by permission of the *British Journal of Ophthalmology*.) C, choroid. CAO, central artery of optic nerve. CAR, central artery of retina. CZ, circle of Zinn. D, dura. ON, optic nerve fibres. PCA, posterior ciliary artery. Pia, pia mater. R, retina. S, sclera.

The variety of visual field defects resulting from infarction in the optic nerve suggest that more than one small blood vessel may be involved.

Several pathological studies of ocular lesions in giant-cell arteritis are available (Cardell and Hanley, 1951; Kreibitz, 1953; Crompton, 1959; Spencer and Hoyt, 1960; Rodenhäuser, 1964; Wolter and Phillips, 1965) but optic nerves have not been studied in cases of infarction resulting from arteriolo- and atherosclerosis. The location of the lesions in both instances may be similar, however. Narrowing of arterial lumens by cellular infiltration and intimal proliferation is frequently seen in the ophthalmic and central retinal arteries, mainly in their most

proximal parts, and, almost invariably, in the long and short posterior ciliary arteries, and their pial branches. The central retinal artery is usually patent in these cases. A localized region of opticomalacia immediately posterior to the lamina cribrosa has been noted in a few cases of temporal arteritis (Kreibitz, 1953; Spencer and Hoyt, 1960) but other reports describe total destruction of nerve fibres just behind the disc (Rodenhäuser, 1964; Wolter and Phillips, 1965), 'gross degeneration' (Cardell and Hanley, 1951), or a normal nerve.

Involvement of vessels supplying the optic nerve by atherosclerosis is a reasonable possibility, because this disease is so generalized. However, the nature and extent of vascular disease in the optic nerve has received little attention, this nerve being relatively inaccessible in the routine necropsy.

Battastini and Caffi (1959) examined optic nerves from 14 elderly patients and found thickening of arterial walls due to invasion of media and adventitia by connective tissue and 'sclerosis'. The intima was also thickened, causing narrow lumens. Atheromata and other degenerative changes were not found. Brooser, Börzönyi, and Áhi (1967) noted irregular regions of fibre destruction in optic nerves of diabetic patients, and PAS-positive material in the walls of vessels in and around the nerve.

To extend our own observations, 40 optic nerves were removed from 20 cadavers after injection of embalming fluid into the cranial arteries. All patients were older than 45 years. The entire length of the nerves was obtained by removing the roofs of the orbits and optic canals with a chisel. Nerves were fixed in 10% formalin, embedded in paraffin, and sectioned in either sagittal or transverse planes. Sections were stained with haematoxylin and eosin, phosphotungstic acid, and by Weigert's method for elastic tissue.

Three changes were present in various degrees of severity in almost all optic nerves examined. Intimal thickening, usually diffuse and minimal, was present in many of the posterior ciliary arteries, but was less marked in the central retinal artery. A more frequent finding was the thickening of the walls of arterioles lying in the pia (Fig. 5) and within the substance of the nerves. In addition, increase in the amount of fibrous connective tissue was observed in the septae of many optic nerves, structures that consist only of capillary walls in the newborn. In some cases, this increase of fibrous tissue was excessive, even though present in patients without visual complaints (Fig. 6). Focal opticomalacia was not found in our specimens.

The results of the present pathological study

FIG. 5. A typical arteriole with thickened walls (arrow) in the pia of an optic nerve. Haematoxylin-eosin. $\times 400$.

FIG. 6. Longitudinal section of an optic nerve from an elderly patient without visual complaints, showing striking increase of fibrous tissue in septae. Phosphotungstic acid-haematoxylin. $\times 250$.

suggest that the arterial supply of the optic nerves is subject to athero- and arteriosclerosis no less than other vessels of similar size. These changes provide a limited pathological basis for the syndrome of infarction in the optic nerve. Although not found by us, emboli lodged in small arterioles may have an effect similar to thrombotic occlusion. Routine examination of optic nerves at necropsy would yield more definite data.

The name 'infarction of the optic nerve' is more specific and descriptive than 'ischaemic optic neuropathy' or 'vascular pseudopapillitis', and is in accord with current nomenclature. 'Neuropathy'

designates primary disease of neural tissues rather than of its blood supply. Only infarction, not ischaemia, can account for permanent visual loss. 'Pseudopapillitis' is one more addition to a long list of confusing terms describing the appearance of the optic disc in various conditions, and has been used, as has 'pseudopapilloedema', to designate congenital anomalies of the disc. Infarction may occur in the optic nerve without causing abnormalities of the disc.

SUMMARY

Three cases are presented to illustrate a syndrome,

infarction in the optic nerve, which most probably results from arteriolo- and atherosclerosis of vessels supplying the nerve. Sudden onset of a static visual field defect, particularly of the altitudinal fibre bundle type, and transient, pale swelling of the optic disc are salient features of this syndrome. When infarction in the optic nerve is suspected, the patient should be observed for a short time with particular reference to optic disc and visual fields. Such innocuous studies may replace more hazardous diagnostic procedures for exclusion of an intracranial mass. Atherosclerosis and arteriolosclerosis of the arterial supply and thickening of connective tissue septae of the optic nerve were demonstrated in a small series of necropsy specimens.

REFERENCES

- Battastini, A., and Caffi, M. (1959). Alterazioni vascolari del nervo ottico nella senilità. *Ann. Ottal.*, **85**, 715-722.
- Blunt, M. J. (1963). Intraneural branches of the central retinal artery. *Brit. J. Ophthalm.*, **47**, 664-665.
- Brooser, G., Börzönyi, M., and Áhi, O. (1967). Die Schädigung des Fasciculus opticus bei Diabetes. *Acta ophthalm. (Kbh.)*, **45**, 211-219.
- Cardell, B. S., and Hanley, T. (1951). A fatal case of giant-cell or temporal arteritis. *J. Path. Bact.*, **63**, 587-597.
- Crompton, M. R. (1959). The visual changes in temporal (giant-cell) arteritis. Report of a case with autopsy findings. *Brain*, **82**, 377-390.
- Cullen, J. F. (1967). Occult temporal arteritis. A common cause of blindness in old age. *Brit. J. Ophthalm.*, **51**, 513-525.
- Fessel, W. J., and Pearson, C. M. (1967). Polymyalgia rheumatica and blindness. *New Engl. J. Med.*, **276**, 1403-1405.
- François, J., and Neetens, A. (1954). Vascularization of the optic pathway. I. Lamina cribrosa and optic nerve. *Brit. J. Ophthalm.*, **38**, 472-488.
- , ———. (1963). Central retinal artery and central optic nerve artery. *Brit. J. Ophthalm.*, **47**, 21-30.
- , ———. (1965). Vascularization of the intraorbital part of the optic nerve. *Amer. J. Ophthalm.*, **60**, 62-67.
- , Verriest, G., Neetens, A., De Rouck, A., and Hanssens, M. (1962). Pseudo-papillitis vasculaires. *Ann. Oculist. (Paris)*, **195**, 830-885.
- Hayreh, S. S. (1963). The central artery of the retina. Its role in the blood supply of the optic nerve. *Brit. J. Ophthalm.*, **47**, 651-663.
- Hollenhorst, R. W., Brown, J. R., Wagener, H. P., and Schick, R. M. (1960). Neurologic aspects of temporal arteritis. *Neurology (Minneapolis)*, **10**, 490-498.
- Kimbrell, O. C., and Wheliss, J. A. (1957). Polyarteritis nodosa, complicated by bilateral optic neuropathy. *J. Amer. med. Ass.*, **201**, 61-62.
- Kreibitz, W. (1953). Optikomazie die Folge eines Gefäßverschlusses im retrobulbären Abschnitt des Sehnerven. *Klin. Mbl. Augenheilk.*, **122**, 719-731.
- Lasco, F. (1961). Les affections vasculaires du nerf optique et leurs manifestations cliniques. *Ophthalmologica (Basel)*, **142**, 429-445.
- Miller, G. R., and Smith, J. L. (1966). Ischemic optic neuropathy. *Amer. J. Ophthalm.*, **62**, 103-115.
- Mitts, M. G., and McQueen, J. D. (1965). Visual loss associated with fusiform enlargement of the intracranial portion of the internal carotid artery. *J. Neurosurg.*, **23**, 33-37.
- Piper, H. F., and Unger, L. (1957). Hemianopsia horizontalis inferior bei akuten Durchblutungsstörungen des Sehnerven. *Ophthalmologica (Basel)*, **134**, 169-180.
- Rodenhäuser, J. H. (1964). Über pathologisch-anatomische Augenveränderungen bei generalisierter Riesenzellarteriitis. *Klin. Mbl. Augenheilk.*, **145**, 414-429.
- Smith, J. L., Israel, C. W., and Harner, R. E. (1967). Syphilitic temporal arteritis. *Arch. Ophthalm.*, **78**, 284-288.
- Spencer, W. H., and Hoyt, W. F. (1960). A fatal case of giant-cell arteritis (temporal or cranial arteritis) with ocular involvement. *Arch. Ophthalm.*, **64**, 862-867.
- Steele, E. J., and Blunt, M. J. (1956). The blood supply of the optic nerve and chiasma in man. *J. Anat. (Lond)*, **90**, 486-493.
- Turner, J. W. A. (1943). Indirect injuries of the optic nerve. *Brain*, **66**, 140-151.
- Wolff, E. (1954). *The Anatomy of the Eye and Orbit*, 4th ed., p. 352. H. K. Lewis, London.
- Wolter, J. R., and Phillips, R. L. (1965). Secondary glaucoma in cranial arteritis. *Amer. J. Ophthalm.*, **59**, 625-634.
- Wybar, K. C. (1956). Anastomoses between the retinal and ciliary arterial circulations. *Brit. J. Ophthalm.*, **40**, 65-81.