RETINAL VASCULITIS*

BY

T. KEITH LYLE AND KENNETH WYBAR

London

IN 1880 Henry Eales described, in a number of young adult males, a condition of recurrent haemorrhages within the retina and vitreous, which he considered to be the result of some primary retinal disorder in the absence of any obvious constitutional upset; he entitled his paper "Primary Retinal Haemorrhage in Young Men". Many similar cases have been described since that time, and it is now generally recognized that the condition is essentially an inflammatory affection of the retinal veins (periphelebitis), although in some cases there may be involvement also of the retinal arteries (periarteritis). It is therefore more accurate to describe the disease as a retinal perivasculitis, or better still as a retinal vasculitis, since the vessel wall itself is involved and not merely its surrounding connective tissues. There is little understanding of the true nature of the inflammation, and, although some reports indicate a tuberculous aetiology (Axenfeld and Stock, 1911; Gilbert, 1935), it is likely that the condition is not an expression of a single disease but a clinical phenomenon common to several diseases (Ballantyne and Michaelson, 1937).

The authors of the early descriptions of the condition considered that the brunt of the disease was borne by the veins in the periphery of the retina, and that any involvement of the veins in the central part of the fundus was the result of spread from the veins in the periphery (Eales, 1880, 1882; Ballantyne, 1909; Davis, 1912; Igersheimer, 1912), but sporadic reports have since appeared which indicate that in some cases there is a primary involvement of the central retinal vein within the optic nerve-head (Gilbert, 1913; Siegrist, 1913; Davis, 1920; Ballantyne and Michaelson, 1937). It is the purpose of the present communication to draw attention to this latter group of cases which show certain characteristic features: oedema of the optic nerve-head and adjacent retina, generalized dilatation of the retinal veins, little or no involvement of the retinal arteries, a variable amount of retinal haemorrhage, and an almost complete absence of vitreous haemorrhage, and, therefore, of retinitis proliferans. Furthermore, these cases are seldom associated with any gross disturbance of vision, unless there is obvious involvement of the macula by oedema or haemorrhage, and, even when vision is affected, more or less normal vision is usually restored within a relatively

* Received for publication May 10, 1961.

short time. In this way the disease tends to run a fairly benign, although protracted, course, without the development of serious complications. The condition is usually confined to young adults, although it may occur in middle age, and it is commoner in men than women. It often, but not invariably, occurs in apparently healthy persons; for example, several cases were encountered by one of us (T.K.L.) among apparently fit young adult males serving in the R.A.F. during the second world war. On the other hand, in one typical case, a man was found to be suffering from active pulmonary tuberculosis.

Case Reports

The following six cases represent examples of this specialized group of cases which may be included within the generic title of retinal vasculitis.

Case 1, a married woman aged 39, complained in April, 1955, of attacks of blurred vision of the left eye lasting about half an hour. She said she had noticed this on several occasions during the last fortnight, but admitted that she had also experienced transient attacks of defective vision in her left eye for the last 10 years.

Examination.—The visual acuity in each eye was 6/5 with no refractive error. The right optic disc was unusually pink and the edges were not clearly defined, but there was no evidence of abnormality in the fundus generally and the appearance was considered to be within the physiological limits of normal.

The left optic disc showed considerable oedema, associated with oedema of the surrounding retina. The blood vessels, especially the veins, were distended and tortuous and there were numerous small haemorrhages along their entire course, even out to the extreme periphery of the fundus (Fig. 1). The patient had already been seen by another ophthalmologist and a neurologist, who had diagnosed the presence of oedema of both discs ("papilloedema") affecting the left eye more than the right, and, suspecting raised intracranial pressure, had instituted investigations to discover the underlying cause.

FIG. 1.—Case 1. Copy of fundus painting of left eye, showing oedema of the optic disc and surrounding retina, and dilatation and tortuosity of the retinal veins. The retinal arteries are slightly affected.

General examination had, however, revealed no abnormal physical signs, and an x-ray examination of the skull and an air encephalogram had shown no abnormality. The

blood pressure was 140/80. X-ray examination of the chest showed no evidence of pulmonary disease. The blood count and erythrocyte sedimentation rate were normal. The electro-encephalogram showed no evidence of any focal cerebral lesion. The cerebrospinal fluid was of normal pressure and its constituents were normal. The blood Wassermann reaction was negative.

There appeared to be no doubt that the patient was suffering from retinal vasculitis of the left eye.

Subsequent History.—The visual acuity of the left eye deteriorated to 6/60 2 months later because of a haemorrhage in the macular region, but it subsequently recovered; one year later it was 6/18, 2 years later 6/9, and 3 years later 6/6 and N5. During this period the patient remained well, and the condition of the left fundus gradually cleared, leaving sheathing of the veins (Fig. 2), an ill-defined disc with some new vessels on the nasal part, and some pigmentary changes around the macula (Fig. 3). It is now 5 years since she was originally seen at the hospital and she remains symptom-free.

FIG. 2.—Case 1. Fundus photograph 3 years later, showing sheathing of retinal veins.

FIG. 3.—Case 1. Fundus photograph, showing pigmentary disturbance at the macula and new vessel formation at the nasal edge of the disc.

Case 2, a man aged 49, had noticed a sudden onset of defective vision in the right eye in September, 1954. Examination at that time showed a visual acuity of 6/60 in the right eye, and 6/5 in the left. There was a paracentral temporal scotoma extending from the blind spot towards the point of fixation in the right visual field. The left visual field showed no abnormality. The right fundus was described by another ophthalmologist as showing the typical appearance of a *partial thrombosis of the central retinal vein*. The blood pressure was 140/90. He was admitted to hospital and treated as a case of thrombosis of the central retinal vein. He was given anti-coagulant therapy, but this caused severe melaena and had to be discontinued after a few days.

X-ray examination of the skull and chest showed no abnormality. The blood count and the erythrocyte sedimentation rate were normal. The Wassermann reaction and gonococcal complement-fixation test were negative, and the Mantoux test was negative to 1:10,000 O.T.

The patient was then seen by one of us (T.K.L.), who suggested that the diagnosis was that of retinal vasculitis, the veins being affected to a considerably greater extent than the arteries.

Subsequent History.—The fundus condition (Fig. 4) remained unchanged until July, 1955, when the haemorrhages began to be absorbed and central vision improved. By November, 1956, the haemorrhages had disappeared and the visual acuity of the right eye had recovered to 6/6 and N5. The condition of the fundus had almost returned to normal except for the presence of sheathing of the retinal vessels and some new vessel formation on the disc (Fig. 5). When the patient was last examined, 6 years after the onset of the disease, there had been no recurrence of the condition.

FIG. 4.—Case 2. Fundus photograph of right eye, showing massive oedema of the optic disc, multiple retinal venous haemorrhages, and dilatation and tortuosity of the retinal veins. The condition resembles that of a central retinal vein thrombosis.

FIG. 5.—Case 2. Fundus photograph 1 year later. The fundus is almost normal except for sheathing of the retinal vessels and some new vessel formation at the nasal edge of the disc.

Case 3, a young man aged 24, who had previously enjoyed normal vision, suddenly became aware of a slight blurring of the vision of the right eye on waking each morning, which cleared completely within a few hours.

Examination.—2 weeks later the retinal veins of the right eye were found to be markedly dilated along their entire length from the optic disc to the periphery of the fundus. There were a few scattered retinal haemorrhages and pronounced oedema of the optic disc and surrounding retina. The left fundus was normal. Apart from some emotional instability, general examination showed no abnormality and serological investigations proved to be negative.

Subsequent History.—The retinal veins remained dilated for several months and then gradually improved, but a certain degree of dilatation has persisted despite an interval of over 3 years from the onset of the condition. The retinal haemorrhages remained more or less unchanged for 6 months, but then slowly absorbed, and had completely disappeared 4 months later. A few weeks after the onset of the condition the oedema surrounding the optic disc spread to the macular region, but thereafter there was a gradual reduction of the oedema over a period of about 12 months, leaving only the residual appearances of an ill-defined disc margin and a characteristic “pseudo-hole” at the macula. At the first examination the visual acuity of the right eye was normal (6/5), despite the subjective awareness of transient blurring of the vision, but 6 weeks later the vision deteriorated to 6/12 and, after a slight improvement, it has remained at 6/9 partly. It is likely that this permanent slight defect in the central vision is the direct result of the oedema of the macula.

Case 4, a man aged 34, who had previously had no trouble with his eyes, noticed a slight blurring of the vision of the right eye.

Examination.—A few days later he was found to have pronounced oedema of the right optic disc and macular area, together with massive dilatation of the retinal veins extending to the periphery of the fundus, and several scattered retinal haemorrhages (Fig. 6). The corrected visual acuity of the right eye was 6/9. The left eye was normal in all respects. Neurological, serological (Wassermann reaction, Kahn test, and blood count), and radiological tests (x rays of chest and orbits) proved to be negative.

Subsequent History.—2 weeks after the onset of the condition there was a temporary deterioration of the visual acuity of the right eye to 6/18, but the vision returned to a normal level within 5 weeks. The retinal haemorrhages disappeared in 2 months, with some reduction of the dilatation of the retinal veins and of the degree of oedema of the optic disc (Fig. 7). This was followed by further resolution of the dilatation of the retinal veins, so that the fundus appearance became almost normal within 5 months of the onset of the condition. The right eye has remained unchanged since that time, and there has been no similar involvement of the left eye.

FIG. 6.—Case 4. Fundus photograph of the right eye, showing massive oedema of the optic disc, multiple retinal venous haemorrhages, and dilatation and tortuosity of the retinal veins. The condition resembles that of a central retinal vein thrombosis.

FIG. 7.—Case 4. Fundus photograph 2 months later, showing haemorrhages absorbed and retinal veins less dilated.

Case 5, a married woman aged 49 years, noticed occasional generalized blurring of the vision of the right eye when she bent her head downwards; this was followed by a restoration of normal vision within 30 seconds of resuming an upright position, the restoration starting in the centre of the field of vision and spreading rapidly to the periphery.

Examination.—One month later she was found to have obvious oedema of the right optic disc which extended about one disc diameter around the disc (Fig. 8, opposite). There was also a marked dilatation of the retinal veins throughout their whole length from the optic disc to the periphery of the retina. There were no retinal haemorrhages and the visual acuity of the affected eye was normal (6/5). There was no disturbance of the visual field, except for a slight concentric enlargement of the blind spot, and in all other respects the eye was normal. The left eye was unaffected. A neurological examination, serological (Wassermann reaction, Kahn test, and blood count), and radiological tests (x rays of chest and orbits) proved to be negative.

Subsequent History.—4 months later the disc oedema and venous dilatation had increased slightly and a few fine haemorrhages were present in the central part of the retina (Fig. 9). The haemorrhages disappeared within a further 2 months. One year after the onset of the condition the right eye was unchanged in appearance (Fig. 10), but the left fundus showed a small degree of oedema of the optic disc, with some dilatation of the retinal veins which involved particularly the small veins on the optic disc which showed nodular dilatations (Fig. 11). Since that time there has been a gradual decrease in the oedema of the right optic disc, but only a very slight decrease in the dilatation of the retinal veins although 2 years have elapsed since the onset of the condition. On the other hand, the early changes noted at one stage in the retina of the left eye, disappeared completely within 6 months.

FIG. 8.—Case 5. Fundus photograph of right eye, showing gross oedema of the optic disc and surrounding retina, and dilatation of the retinal veins.

FIG. 9.—Case 5. Copy of fundus painting 4 months later. The disc oedema has increased.

FIG. 10.—Case 5. Fundus photograph of right eye 1 year later, showing condition unchanged.

FIG. 11.—Case 5. Fundus photograph of left eye, showing slight disc oedema and moderate dilatation of the retinal veins.

Case 6, a boy of 14, who had had no previous eye trouble, became aware of a small cloud in the centre of the field of vision of the right eye, which, although initially more or less transparent, developed into a generalized mistiness within 2 weeks, with a deterioration of the central and peripheral vision of that eye. There was no disturbance of the vision of the left eye.

Examination.—3 weeks after the onset of these symptoms, the right eye showed massive oedema of the optic disc, moderate oedema of the macula, and well-marked dilatation and tortuosity of the retinal veins along their entire course from within the optic disc to the periphery of the retina. There were scattered retinal haemorrhages in all parts of the fundus including the paramacular region, and some sheathing of the veins in the periphery (Fig. 12). The corrected visual acuity of the right eye was 6/24. At the same time the left eye showed slight localized dilatations of the retinal veins in the periphery and also some tortuosity of part of the inferior temporal vein mid-way between the optic disc and the equator. There were localized patches of sheathing of the left retinal veins in the periphery of the fundus and a few haemorrhages beyond the equator, particularly in the nasal part of the fundus. There was no oedema of the left optic disc and no change in the retinal veins near the disc (Fig. 13). The unaided visual acuity of the left eye was 6/5.

FIG. 12.—Case 6. Copy of fundus painting of the right eye, showing disc oedema, widespread retinal haemorrhages, and dilatation of the retinal veins.

FIG. 13.—Case 6. Copy of fundus painting of the left eye, showing peripheral haemorrhages and localized dilatation and sheathing of the retinal veins.

Progress.—2 weeks later a few cells were present in the anterior chamber of both eyes, and this was followed by the development in the right eye of a fine vitreous haze. At the same time a raised circular nodule ringed by a few dilated iris vessels appeared on the central part of the iris of the right eye at 9 o'clock. The appearance of the right eye changed significantly within a very few weeks of the onset of the condition; there was a considerable increase in the extent of the retinal haemorrhage, which involved a wide area of the peripheral and central retina particularly below and temporal to the optic disc; there was an increase in the oedema of the optic disc and of the macular area and in the isolated areas of sheathing of the retinal veins in the periphery of the fundus. The iris nodule completely disappeared and the cells circulating within the anterior chamber gradually reduced in number.

Subsequent History.—Within 5 months, the following changes occurred: gradual reduction in the disc oedema, disappearance of the macular oedema (followed, however, by the development of fine pigmentary changes at the macula), reduction in the degree of dilatation of the retinal veins and in the extent of their sheathing, almost complete disappearance of the retinal haemorrhages, and development of a small area of new vessel formation of venous origin in the lower temporal periphery of the retina (Fig. 14). The visual acuity of the right eye improved from the original 6/24 to normal (6/5) within 10 weeks of the onset of the condition, despite the presence of obvious pigmentary changes in the macula as a result of the previous oedema. The appearance of the left eye did not alter significantly in the first few weeks of observation, except for a slight increase in the degree of retinal vein dilatation, and subsequently, within this period of 5 months, the retinal haemorrhages almost completely disappeared with a reduction in the degree of dilatation of the retinal veins and in the extent of their sheathing (Fig. 15). The central vision of the left eye remained normal throughout the period of observation.

FIG. 14.—Case 6. Copy of fundus painting of the right eye 5 months later, showing haemorrhages mostly absorbed, retinal veins less dilated, and new vessel formation of venous origin in the lower temporal periphery of the fundus.

FIG. 15.—Case 6. Copy of fundus painting of the left eye 5 months later, showing haemorrhages mainly absorbed and less dilatation and sheathing of the retinal veins.

General and neurological investigations, serological investigations (Wassermann reaction, Kahn test, erythrocyte sedimentation rate, and general blood picture), lumbar puncture, and radiological examinations (x rays of teeth, sinuses, and chest), and calf muscle biopsy, all produced negative results, except for some enlargement of the left tracheo-bronchial gland and a positive Mantoux reaction (1 in 100,000). Tests for toxoplasmosis and brucellosis were negative.

Treatment was carried out as an in-patient on sanatorium lines for nearly 3 months, with the use of the following drugs: prednisolone 5 mg. five times daily, reduced after 12 weeks to a maintenance dose of 5 mg. three times daily; potassium chloride 7.5 gr. once daily; isoniazid 50 mg. and PAS 3 g. each four times daily for 4 weeks at the beginning of the treatment.

An interesting aspect of this sixth case has been the investigation (carried out by Dr. G. B. Arden at the Institute of Ophthalmology) of the metabolic function of the retina. In the acute stage of the condition there was a gross functional

disturbance of the right eye and a less marked functional disturbance of the left, but 6 months later there was a complete return of normal metabolic function in both eyes. There is, therefore, a close correlation between the clinical appearance of the eye and the assessment of its metabolic function in the laboratory. The method used by Dr. Arden is to be described by him in a later publication.

This last case is of particular importance because it endorses the main purpose of this paper, which is to emphasize the existence of a form of retinal vasculitis due primarily to an involvement of the central retinal vein within the optic nerve-head, in contrast to the more usual form of the condition in which the brunt of the disease is borne by the periphery of the retina. The occurrence in the same patient at the same time of the central type of retinal vasculitis in one eye and of the peripheral type of the disease in the other eye appears to provide evidence that the two conditions, although clinically different, are manifestations of the same underlying cause, namely, an inflammatory affection of the retinal venous system.

Differential Diagnosis

It is important to consider other conditions of the eye which may simulate these cases of retinal vasculitis:

(1) *Thrombosis of the Central Retinal Vein*.—The fundus in certain cases of retinal vasculitis resembles, at first glance, the appearance in typical cases of thrombosis of the central retinal vein, although in the latter condition the haemorrhages are usually more extensive, particularly in the central part of the fundus, with marked involvement of the macula and consequent disturbance of the central vision. The essential points of difference, however, are these: retinal vasculitis tends to occur more in younger patients than thrombosis of the central retinal vein; cases of retinal vasculitis show no evidence of generalized arteriosclerosis or vascular hypertension; if retinal vasculitis is confined to one eye, the fundus of the unaffected eye shows no abnormality, whereas in cases of central retinal vein thrombosis there is invariably evidence of arteriosclerosis and hypertension in the other eye.

The importance of differentiating between retinal vasculitis and central retinal vein thrombosis has been emphasized recently by another case seen by one of us (K.C.W.).

Case 7, a young man aged 24 years, gave a history of a vague disturbance of the vision of the right eye in August, 1960, and he was treated 3 months later with dindevan because he was considered to be suffering from a thrombosis of the right central retinal vein. When he was first seen a few weeks after starting the anti-coagulant therapy, the eye showed the typical appearances of a retinal vasculitis, with oedema of the optic disc and massive dilatation of the retinal veins from the optic nerve-head to the retinal periphery, and there was also an unusually large amount of haemorrhage scattered over a wide area of the retina with involvement of the macula. The left fundus was completely normal, and the general cardio-vascular system was also normal. The dindevan was discontinued immediately and the patient was given systemic steroids. 4 weeks later there was an obvious reduction of the retinal haemorrhages and an absence of any fresh haemorrhage (Fig. 16, opposite), and the central vision had improved from "counting fingers" to 6/36.

It appears likely that in this case the retinal haemorrhages were accentuated by the treatment with an anti-coagulant, and this is scarcely surprising in view of the nature of the inflammatory changes which are presumed to be present within the walls of the retinal veins.

FIG. 16.—Case 7. Copy of fundus painting of right eye, showing disc oedema, dilatation and tortuosity of the retinal veins, massive haemorrhages along the main tributaries adjacent to the optic disc, and scattered haemorrhages in the periphery of the fundus.

(2) *Oedema of the Optic Nerve caused by Increased Intra-cranial or Intra-orbital pressure.*—In retinal vasculitis the obvious oedema of the optic disc of the affected eye, particularly when it is associated with haemorrhages on and around it, may simulate a “choked disc”, but a mistake in diagnosis should easily be avoided if a thorough examination of the entire fundus of the affected eye is made. In cases of retinal vasculitis the dilatation of the retinal veins and the haemorrhages in the retina, when they occur, are *not confined to the disc, nor indeed to the area immediately around it, but are found throughout the fundus even in the extreme periphery*. However, in spite of this, on more than one occasion patients with retinal vasculitis have been suspected of having a cerebral tumour and elaborate and quite unnecessary investigations have been undertaken. It should be noted that it is not possible to distinguish between the two conditions by an assessment of the visual acuity, because, at least in the early stages, it is unusual for either to be associated with more than a slight and transient blurring of vision, although in both conditions there may be some further deterioration of visual acuity due to the development of macular oedema. In the later stages of disc oedema caused by raised intra-cranial pressure, however, there may be a marked loss of central vision as a result of the development of a consecutive form of optic nerve atrophy, and this is in contrast to cases of retinal vasculitis in which the final visual acuity is usually good.

(3) *Fulminating Hypertensive Retinopathy.*—Oedema of the optic disc, the occurrence of retinal haemorrhages adjacent to the disc, and dilatation of the

retinal veins are characteristic features of the central form of retinal perivasculitis and also of most cases of fulminating hypertensive retinopathy, but the latter condition is associated also with obvious calibre variations of the retinal arteries, concealment of the veins at the arterio-venous crossings, often with a star-figure at the macula and invariably with similar changes in the other eye: features which are not present in cases of retinal vasculitis.

Summary

Retinal vasculitis is generally described as a condition of the peripheral parts of the retina, involvement of the central part of the retina being a relatively rare secondary event. There is, however, a group of cases in which the central retinal vein appears to be involved primarily within the optic nerve-head with the production of a characteristic clinical picture: well-marked oedema of the optic disc and sometimes also of the macula; well-marked dilatation of the retinal veins throughout their entire course in the retina; a variable amount of retinal haemorrhage without any obvious vitreous haemorrhage. The condition is usually unilateral and tends to run a protracted although often relatively benign course. Six such cases are described and illustrated. The distinguishing features of central retinal vein thrombosis, plerocephalic disc oedema, malignant hypertensive retinopathy, and this form of retinal vasculitis are discussed.

REFERENCES

- AXENFELD, T., and STOCK, W. (1911). *Klin. Mbl. Augenheilk.*, **49** (n.s. **11**), pt. 1, p. 28.
 BALLANTYNE, A. J. (1909). *Ophthalmoscope*, **7**, 662.
 ——— and MICHAELSON, I. C. (1937). *Brit. J. Ophthalm.*, **21**, 22.
 DAVIS, A. E. (1912). *Trans. Amer. ophthalm. Soc.*, **13**, 235.
 ——— (1920). *Ibid.*, **18**, 55.
 EALES, H. (1880). *Birmingham med. Rev.*, **9**, 262.
 ——— (1882). *Ophthalm. Rev.*, **1**, 41, 139.
 GILBERT, W. (1913). *Ber. ophthalm. Ges. (Heidelberg)*, 39th meeting, p. 47.
 ——— (1935). *Klin. Mbl. Augenheilk.*, **94**, 335.
 IGGERSHEIMER, J. (1912). *v. Graefes Arch. Ophthalm.*, **82**, 215.
 SIEGRIST (1913). *In discussion of Gilbert (1913)*, p. 54.