The basic change is senile, but the process may be aggravated by proteolytic enzymes (Lysins) in the aqueous, the product of glaucomatous metabolism.

REFERENCES

1. WOLFRUM.—*Handbuch des. Augenheilkunde, Graefe-Saemisch-Hess.* Teil 1, Band 1, Abt. 2, Kap. 3, p. 197.
2. EISLER.—*Anat. des Auges. Kurzes Handbuch der Augenheilk.*, Vol. I, p. 91.
3. WOLFF, E.—*Anatomy of the eye.* Second edition, p. 65.
4. SCHMITT.—*Klin. Monatsbl. f. Augenheilk.*, Vol. LXVIII, p. 214, 1922.
5. DRABKIN.—*Ibid.*, Vol. LXXI, p. 188, 1923.
6. SANDER.—*Ibid.*, Vol. LXXIV, p. 729, 1925.
7. VOGT.—*Ibid.*, Vol. LXXVII, p. 710, 1926.
8. SCHOENBERG.—*Arch. of Ophthal.*, Vol. LXVI, p. 538, 1927.
9. IMRE, J.—*Ibid.*, Vol. LXVI, p. 539, 1927.
10. DOLLFUS, A.—*Bull. Soc. d'Ophtal. de Paris*, p. 170, 1927.

PERIARTERITIS NODOSA AFFECTING THE EYE*

BY

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PERIARTERITIS nodosa is a rare and usually fatal disease of blood-vessels first described by Kussmaul and Maier in 1865, and subsequently treated at considerable length in the literature, chiefly, in consequence of its baffling symptomatology, by pathologists. It is exceptional for recognition to be possible during life unless subcutaneous nodules occur which on biopsy show the characteristic changes.

Occasionally the ophthalmologist is given an opportunity to assist in the diagnosis, but there are very few of the published cases where the ophthalmoscope has revealed more than a quite ordinary albuminuric retinitis. Yet in a very important percentage of the eyes which the pathologists have examined, they have discovered inflammatory disease of the choroidal and ciliary vessels, and it is a matter for regret that more ophthalmoscopic observations have not been made. The case we shall describe may throw some light on the ophthalmoscopic appearances which may occur in the disease.

It is not intended in this paper to enter into a discussion of periarteritis nodosa in its general manifestations. There is no agreement on the pathogenesis of the condition, but as to the pathological changes which occur there is no difference of opinion. The name is descriptive of the changes seen in the larger vessels, particularly those with vasa vasorum, but the ophthalmologist is concerned rather with vessels of smaller calibre.

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In small vessels, the initial lesions are found in the inner media, and consist of a coagulative necrosis which may involve part or the whole of the vessel circumference. The wall of the vessel becomes thickened by oedema and fibrinous exudate, the endothelium over the affected area becomes swollen and may desquamate, and a fibrin clot may form in the lumen. Soon the media and adventitia become infiltrated with lymphocytes, polymorphs, large mononuclears and plasma cells, and there is much exudation throughout the vessel wall and in the perivascular tissues. Aneurysms may result, or the vessel wall may rupture, but there is no definite record of such developments in the ocular vessels.

In the absence of these catastrophes, repair begins, the vessel wall being replaced by granulation tissue which invades any thrombus in the vessel lumen, and the endothelium undergoing considerable proliferation. There is some confusion regarding the relation of this proliferation to the severity of the medial disease, but the problem is resolved satisfactorily by Arkin (1930), who points out that the endothelial proliferation extends longitudinally beyond the area of medial necrosis, so that sections may show no other change than intimal proliferation if taken peripheral to the main lesion.

When healing is complete the vessel and its lumen may be replaced by scar tissue which extends into the area around for a variable distance.

The eye may be affected in either of two ways, indirectly by the toxic processes associated with the renal lesions which are so usual in this disease; or directly by the involvement of the arteries of the region in the arteritis.

The frequency of renal impairment in periarteritis nodosa is put at 80 per cent. by Arkin; 83 out of 115 cases by Gruber; and all cases coming to necropsy by Spiegel (1936). The types of kidney lesion are detailed by Gruber and Spiegel:

	Gruber	Spiegel
Renal infarcts and aneurysms ...	35	8
Glomerulonephritis ...	21	3
Focal degeneration ...	5	1
Interstitial inflammation ...	2	—
Acute periarteritis nodosa ...	—	2
Arteriosclerosis ...	—	1
Malignant sclerosis ...	—	2

Hypertension and urea nitrogen retention are present in the vast majority of cases. Hence it is not surprising that the most common ocular finding in periarteritis nodosa is albuminuric retinitis with no special features to distinguish it from the retinopathy of nephritis due to other causes.

Involvement of the bloodvessels of the eye and orbit is not often described, but these parts are apt to escape examination. Typical periarteritis nodosa has been recorded with greatest frequency in the choroidal arteries and the short ciliary vessels. I have been able to find 7 cases of choroidal and 5 of ciliary vessel periarteritis in the American and English literature. The retinal vessels are seldom affected, although retinal haemorrhages, oedema and exudates are common; but these are more likely to be due to the hypertension than to the periarteritis, and the only descriptions, all microscopic, of what appears to be typical arteritis of the retinal vessels are those of Muller (1899), King (1935) and Von Heřrenschwand (1929). In addition, one case of occlusion of the central retinal artery has been reported by Evans (1943). King's case also showed papilloedema for some months, most probably a result of increased intracranial pressure caused by periarteritis of the cerebral vessels. Iridocyclitis, episcleritis, and orbital cellulitis have also been seen rarely, and are an expression of the direct involvement of the arteries of these regions. Chemosis of the conjunctiva, which may disappear spontaneously in a few days, has also been noticed, as in the case described below.

Case Report

A young airman, aged 20 years, was admitted to an R.A.F. Hospital with generalised clonic convulsions followed by unconsciousness which lasted some hours. Thereafter he ran a pyrexial temperature and complained intermittently of pains in the abdomen, muscles and joints. The blood pressure at the end of two weeks was 180/110, but fell a little later and varied between 140 and 160 systolic till the end. He became steadily more anaemic and emaciated, and left ventricular failure developed eight weeks after admission. Clonic fits recurred a few days before his death after an illness of three months.

Pathological examination demonstrated well marked periarteritis nodosa affecting arteries in all systems, and particularly the coronary arteries (Fig. 1). There were infarcts in both kidneys. The Wassermann reaction was negative, and blood cultures showed no growth. No conclusion could be formed as to the aetiology.

Ophthalmic examination was requested late in the disease, four weeks before death, and provided appearances of great interest.

There was a concomitant divergent strabismus of about 15 degrees, and convergence was absent.

Right Eye:—The retinal vessels were of normal calibre. There was generalised retinal oedema, more marked in the temporal half of the fundus, and the edges of the disc were blurred but not noticeably swollen. Lateral to and above the level of the macula

FIG. 1.

Heart showing nodules along coronary vessels.

FIG. 2.

Right fundus, early stage. Tubercle-like nodules in choroid and wide-spread retinal oedema. The retinal elevations overlying the nodules could not be reproduced on the drawing.

FIG. 3.
Right optic papilla showing hyaline vessels.

FIG. 4.
Low power view of choroidal and ciliary vessels. Numerous choroidal vessels with hyaline walls.

FIG. 5.
Low power view of choroidal cicatricial nodule.

were several areas of retinal detachment of small extent, with no vitreous haze, and deep to the retina in these areas were greyish-white nodules of oval or branching shape, somewhat resembling miliary tubercles of the choroid (Fig. 2).

Left Eye:—The left retina was oedematous, and there was a large, globular retinal detachment far out on the temporal side, commencing half-way between the macula and the equator. It had all the appearances of an exudative detachment, and there was no hole or tear.

On the next day the eyes were examined again. Now there was considerable oedema of the conjunctivae. The areas of detachment in the right fundus had become confluent, forming a total area of about six disc diameters, and two or three new patches of whitish choroidal exudate were visible nearer the ora serrata. The left eye, in addition to the large detachment, showed a few similar whitish patches above and below the macula.

Four days later the conjunctival oedema had gone. There was a great reduction in the general oedema of the right retina, although the localised detachment remained, and the macula was more oedematous. The left detachment had almost disappeared except inferiorly, and in the area where the detachment had been were a number of hazy white lines running radially to the disc, possibly choroidal vessels obscured by exudate. The left macula was more oedematous. (The patient then complained of misty vision, his first and only ocular symptom.) The divergent squint was no longer noticeable.

Two days later, a week after the first ophthalmoscopic observation, the right detachment had diminished, and the left detachment was no longer visible. Both maculae were less oedematous.

Observation was continued till the day of his death, although in the last few days only fleeting glances could be obtained since the mere light stimulus was enough to start a generalised convulsion. A week before death the fundi looked normal except that there were small, lightly pigmented scars at the sites of the choroidal lesions previously noted. No sign of albuminuric retinopathy occurred.

The eyes and orbital contents were obtained for examination, which was kindly performed for me by Dr. A. J. Ballantyne, and the following notes are derived from his very detailed report.

No definite pathological changes were found in the orbital structures, although the muscles were unduly bulky on account of oedema.

Macroscopically both optic discs were ill defined, and situated in the midst of a wide area of pale, opaque retina, without definite boundary. The retinae were thrown into ridges and folds, some of which at least might be a post-mortem change, but from the

appearance of exudate between the retina and choroid at the cut edge of the specimens, it was clear that some of the elevations were due to exudate. In the examination of the specimens with the slit-lamp and binocular microscope no changes could be detected in the visible retinal vessels. The anterior halves of the globes also showed irregular elevations of the retina produced by subretinal exudate as far forward as the ora serrata. Lens, iris and choroid were normal. In the left eye, in the upper temporal quadrant, a melanoma of the choroid was discovered by transillumination, about 3 mms. in diameter.

Microscopically the subretinal exudate consisted of an albuminous-looking coagulum containing a few red blood cells, fragments of pigmented cells, probably derived from the pigment epithelium, and fat granule cells. The neuro-epithelium was largely destroyed, probably the result of post-mortem change.

Examination of specimens of retina unstained in bulk revealed no changes in the retinal vessels, and no haemorrhages.

In the nerve fibre and ganglion cell layers there were many vacuoles, probably representing a true retinal oedema.

In sections passing through the right disc there was definite papilloedema. Some of the retinal vessels showed thickening and rigidity of their walls. Both arteries and veins in the papilla had thickened hyaline walls (Fig. 3), and similar smaller vessels were found on the outer surface of the sclera, adjoining the entrance of the optic nerve. None of the vessels in the retina showed any cellular infiltration in or adjacent to their walls.

The optic nerve sheath of the right eye was distended, and there was a small haemorrhage just in front of the lamina cribrosa. A thrombus was seen in the central vein.

Many of the choroidal vessels had thickened walls, and some of them had a hyaline character (Fig. 4). In Fig. 5 there is a cicatricial nodule occupying the whole thickness of the choroid, and apparently due to thrombosis of one of the large vessels. The choroid was richly pigmented especially in its outer layers, and this richness of pigmentation was also seen accompanying the ciliary vessels and nerves in their passage through the sclera.

The microscopic examination of the melanoma of the choroid in the left eye showed cells of various types, but mainly type A, and the reticulin was No. 1 grade, pointing to a low-grade malignancy.

Sections of the anterior part of the left eye showed iris, cornea, lens, ciliary body and angle of the anterior chamber to be normal.

Discussion

Certain features of the post-mortem findings refer to appearances not seen ophthalmoscopically, and obviously developed during the last few days of life. It is likely that there was some increase

of intracranial pressure when his convulsions recurred, and consequently slight but definite papilloedema was found post-mortem, but some of the disc change may have been due to the local arteritic changes in the vessels. There was no acute change in either the retinal or choroidal vessels to account for the subretinal exudate, which was very widespread but everywhere shallow, and may have persisted although undetected ophthalmoscopically when cellular infiltration passed off.

The main interest lies in the finding of healed arteritis in many of the choroidal vessels. Similar appearances were in evidence in the retinal vessels in the disc of the right eye and in some of the extra-scleral vessels.

The copious subretinal exudation noted four weeks before death, and the whitish choroidal nodules, were without much doubt clinical observations of active choroidal periarteritis nodosa, first in the exudative stage, and later during the subsidence of the acute phase and in the period of repair. The changes in the retinal vessels, which were slight, were not noticed during life.

The clinical picture seen in this case was surmised with much accuracy by Goldstein and Wexler (1929) in their paper which described the histology of the choroid in a similar case. Arkin (1930) in one case, observed multiple retinal detachments, but did not describe the microscopic ocular findings. Friedenwald and Rones (1931) have demonstrated oval nodules of inflammatory tissue in the choroid in a case of streptococcal septicaemia complicated by chronic nephritis, hypertension and syphilitic aortitis, but they definitely excluded periarteritis nodosa from the diagnosis. The nodules were related to thrombosed and sclerosed arterioles, and resembled the nodules which they demonstrated in another case undoubtedly suffering from periarteritis nodosa.

The case we have described was not complicated by arterio-sclerosis, albuminuric retinopathy, or any inflammatory disease of the uveal tract apart from the arteritis. The ocular lesions produced remarkably few symptoms, and it would have been easy to neglect ophthalmoscopy altogether had there been no cerebral symptoms.

The main ophthalmoscopic features were the widespread retinal oedema, the exudative detachments of the retina, the transience of these detachments as of oedema in other parts such as the conjunctiva and the characteristic nodular, tubercle-like choroidal lesions, which evolved rapidly and disappeared, unlike tubercles, in a matter of days, leaving small, white pigmented scars.

Summary

A case of periarteritis nodosa is described in which the choroidal arteries were severely, and the retinal and ciliary vessels slightly, affected. In the absence of albuminuric retinopathy the exudative

phase of the choroidal arteritis could be observed ophthalmoscopically, and the appearances are described.

I am deeply indebted to Dr. A. J. Ballantyne for his most valuable help with the pathology of this case, and my thanks are due to Air Marshal Sir H. E. Whittingham, Director General of Medical Services, R.A.F., for permission to publish this report.

REFERENCES

- ARKIN.—*Amer. Jl. Path.*, July, 1930.
 BENNETT and LEVINE.—*Jl. Amer. Med. Assoc.*, Vol. CLXXVII, June, 1929.
 BOCK.—*Zeitschr. f. Augenheilk.*, Vol. LXIX, June, 1929.
 ——— *Ibid.*, Vol. LXXVIII., July, 1932.
 CHRISTELLER.—*Arch. f. Verd.*, Vol. XXXVII, 1926.
 EVANS.—*Proc. Roy. Soc. Med.*, Vol. XXXVI, No. 2, p. 40, December, 1943.
 FRIEDENWALD and RONES.—*Arch. of Ophthal.*, Vol. V, February, 1931.
 GAYNON and ASHBURY.—*Amer. Jl. Ophthal.*, Vol. CXXVI, No. 10, p. 1072.
 GOLDSTEIN and WEXLER.—*Arch. of Ophthal.*, Vol. II, September, 1929.
 GRUBER.—*Arch. f. Path. Anat.*, Vol. CCLVIII, p. 441, 1925.
 HANSSEN and KNACK.—*Klin. Monatsbl. f. Augenheilk.*, Vol. LIX, p. 263, 1917.
 HELPERN and TRUBEK.—*Arch. Path.*, Vol. XV, January, 1933.
 HERRESCHWAND.—*Klin. Monatsbl. f. Augenheilk.*, October-November, 1929.
 KING.—*Trans. Ophthal. Soc. U.K.*, 1935.
 KRAHULIK, ROSENTHAL and LOUGHLIN.—*Amer. Jl. Med. Soc.*, September, 1935.
 KUSSMAUL and MAIER.—*Deutsches Augenheilk. f. Klin. Med.*, Vol. I, p. 484, 1866.
 LICHTMAN, STICKNEY and KERNOHAN.—*Proc. Staff Meetings, Mayo Clin.*, Vol. XVIII, p. 500, December, 1943.
 MULLER.—*Festschr. d. Stadt. Krankenh.*, Dresden-Friedrichstadt, 1899.
 SPIEGEL.—*Arch. Inter. Med.*, 1936.
 TERTSCH.—*Zeitschr. f. Augenheilk.*, Vol. LXXVII, p. 294, 1935.

OBSERVATIONS ON THE EFFECT OF RIBOFLAVIN ON THE ORAL LESION AND DYSPHAGIA, AND OF RIBOFLAVIN AND BREWER'S YEAST ON DARK ADAPTATION IN A CASE OF SO-CALLED PLUMMER-VINSON SYNDROME*

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THIS report concerns a male patient admitted with a Plummer-Vinson syndrome including dysphagia, angular stomatitis, glossitis, achlorhydria, koilonychia and hypochromic anaemia. The oral lesion and the dysphagia during the first part of observation responded to riboflavin. The finding of impaired dark adaptation (DA) later seemed to offer an opportunity for testing the possible effect of riboflavin and allied factors.

These observations are part of a larger study on dark adaptation undertaken in an attempt to use this method for detecting disturbances in general metabolism, and studying quantitatively their possible relation to dietary factors.

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