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ENDOTHELIOMA OF THE OPTIC NERVE

BY

HUMPHREY NEAME AND EUGENE WOLFF

Clinical Report by E. Wolff

F.H., a man, *aet.* 27, came under the care of Sir J. H. Parsons, to whom acknowledgments are made for permission to report the case, at University College Hospital in March, 1924. He stated that for the last six years his right eye had been growing more prominent.

On examination the eye was found to be proptosed to a marked degree (see Figs. 1 and 2). The proptosis was straight forward. All movements were somewhat limited and rather worse upwards. On palpating between the orbital margin and the globe a firm lobulated mass could be felt all round the eyeball and fixed to it. The right pupil was larger than the left and reacted sluggishly to light directly, but was brisk to consensual illumination.

R.V.—He could only “count fingers” at a metre with his right eye, but the retinoscopy showed him to be hypermetropic to the extent of 7.5D. With this correction he read 6/36. The hypermetropia definitely increased while he was under observation, and was presumed to be due to flattening of the globe by a tumour pressing on it behind. The right fundus showed a papilloedema of 3.4D. and, a very curious feature of the case, there was some scattered black pigment down and out from the disc (see Fig. 3). This latter was most probably due to interference with the short

FIGS. 1 and 2.

Photograph of patient, showing proptosis of right eye.

FIG. 3.

Drawing of fundus, showing blurring of disc margin, congestion of disc, and marked arching forwards of the retinal vessels.

ciliary arteries; for it has been shown that tying these vessels in the rabbit produces a similar condition. The left eye was emmetrope; the fundus normal and the vision 5/5.

An X-ray examination of the orbit and accessory sinuses of the nose showed nothing abnormal. The Wassermann reaction was negative. Nothing abnormal was felt in the renal fossae.

A diagnosis of tumour of the optic nerve was made. On March 31, 1924, an operation for the removal of the tumour was done under general anaesthesia. The conjunctiva was incised all round close to the limbus and dissected up.

The external rectus was divided and a finger put into the orbit to determine the extent of the growth. Local excision was found impossible and after the external canthus had been slit up the eye and the tumour adhering to it were removed as one.

There was no recurrence ten months later.

Pathological Report by Humphrey Neame

F.H., March 31, 1924. Pathological O.P., No. 1628, Royal London Ophthalmic Hospital.

Macroscopic examination.—The specimen, in 10 per cent. formaldehyde, consisted of eyeball and an ovoid mass firmly attached to the posterior part of the globe and partly enveloping it. The posterior surface of the mass showed a flat surface, approximately circular and of 18 mm. diameter, with the cut surface of the optic nerve near the centre of this surface. A slice was removed from the posterior end of the mass, 5 mm. in thickness, and transferred to Müller's fluid, for a period of over six weeks, with several changes of fluid during that time, during which the fluid was kept warm on a paraffin-embedding chamber. The specimen was divided, after freezing, into three parts horizontally, the central portion including all the optic nerve. The cut surface showed the ovoid mass to be attached to the outer surface of the sclera for about $\frac{1}{3}$ of the total circumference of the eyeball. The cut surface of the remainder of the mass measured 22 mm. antero-posteriorly, from immediately behind the sclera at the posterior pole to its posterior limit. The greatest transverse diameter was 29 mm. The surface of the mass was homogeneous and of a yellow-white colour. A few red-brown spots and flecks and some thin fibrous strands were visible. The Müller-fixed tissue was embedded in paraffin and stained: (1) with glychaemalum and eosin; (2) with Weigert's iron haematoxylin and van Gieson's picric acid fuchsin; (3) with Weigert-Pal's method of showing medullary sheath. The main central horizontal slice was embedded in celloidin and serial sections cut of the optic nerve portion. These were stained with glychaemalum and eosin, and with Weigert's iron haematoxylin and van Gieson's stain.

Sections stained by the Weigert-Pal method show the uniform presence of medullary sheath throughout in this posterior part of the optic nerve.

Serial celloidin sections.—Stain, glychaemalum and eosin, Weigert's iron haematoxylin, and van Gieson's as above. Between fifty and sixty serial sections were cut, including the whole thickness of the optic nerve head. In these sections the cornea, anterior chamber, iris, lens, ciliary body, and choroid are all normal in situation and appearance. The retina is moderately detached (artefact), but, apart from very slight cystic degeneration near the ora serrata, appears of normal structure. The nerve head is somewhat swollen and the thickness of the retina at the edge of the optic disc is about 0.75 mm. in section through the middle of the disc. There is no extension of neoplasm into the retina or through the sclerotic into the eyeball.

Examination of the serial sections under a 2-inch objective, shows the whole mass attached to the back of the eyeball to be thicker in transverse diameter on the temporal than on the nasal side of the optic nerve (see Fig. 4). On the temporal side, the mass is intimately adherent to the sclera for about 1/2 of its thickness on this side, and only for about 1/3 on the nasal side. The greatest thickness on the temporal side (in the sections examined) is 15 mm., and the greatest on the nasal side is 10 mm., whereas for a considerable part of the latter it is only 5 mm. thick. Study of the van Gieson stained sections gives evidence strongly suggestive that on the narrower (nasal) side of the nerve the dural sheath remains to a considerable extent intact, with a thin layer—about 0.5 mm. in thickness—of new growth between dural and pial sheaths. Here and there, the layer of fibrous tissue, which presumably represents the dural sheath, is perforated by growth cells which connect the thin layer beneath it with the mass covering it. On the temporal side of the nerve, lying on the pial sheath, there is a layer of growth from 2 to 3 mm. thick, along the greater part of the nerve, which is comparatively free from red-stained collagen fibrous tissue, and which is bounded peripherally by a much broken line of fibrous tissue, probably from the deepest layers of the dural sheath. Anteriorly, where the mass is attached to the sclera, strands of red-stained collagen fibrous tissue from the posterior layers of the sclera pass backwards subdividing into thinner strands to become lost in the mass. Posteriorly, the mass ceases abruptly at the line of section at which the layer—5 mm. thick—was cut off for fixation in Müller's fluid. Peripherally, the boundaries of the mass show in section an irregularly sinuous outline. Nowhere is there evidence of growth extension through the pial sheath into the nerve itself.

The mass, in sections stained by glychaemalum, is of a general purple colour; in sections stained by Weigert's iron haematoxylin and van Gieson's stain, it is of a grey or yellowish-grey colour, with many strands of bright red-stained fibrous tissue by which it is subdivided. This fibrous tissue stroma carries a moderate supply of blood-vessels and is continuous with strands of similar

FIG. 4.

Drawing of section, showing the eyeball with the growth attached to it posteriorly: (a) Detached retina; (b) papilloedema; (c) incomplete fibrous partition in the growth, probably part of dural sheath, within which the growth has expanded the subdural space and further extended through splitting of the dural sheath into multiple lamellae.

tissue from the sclera and from the dural sheath of the optic nerve. There is a sufficiency of fibrous tissue to be seen in the sections to warrant the opinion that there is more fibrous tissue than could have arisen merely by permeation of growth into the dural sheath and sclera, and expansion of these tissues. In other words, there has been some proliferation of fibrous tissue to form supporting stroma and to carry blood-vessels to the neoplasm.

The paraffin sections of the posterior part of the mass (Müller fixed) show in part a whorl-like arrangement of cells and in part the formation of small spaces so typical of endotheliomata (Kettle

and Ross⁽¹⁾; see Figs. 5 and 6). The smallest of the spaces appear to lie within the cytoplasm of individual cells close up against the nucleus in many cases. This vacuole formation is, to a less extent, to be seen in the thinnest parts of the celloidin sections also; but in these it gives more the appearance of a delicate sponge-work structure, as of numerous minute vacuoles lying adjacent to one another in different layers in the thickness of the section, when examined under 1/12 oil immersion objective. This vacuole

FIG. 5.

Microphotograph $\times 160$ diam., shows portion of the growth near its surface. In the centre of the picture is a well-defined whorl-like arrangement of cells, with several others less well-marked. Among the cells are numerous spaces of various sizes, some between groups of cells, some within individual cells.

formation is studied only in the surface portions at the margins of the sections, where the action of the fixing fluids should have had an early effect and avoided the development of shrinkage.

The specimen above described bears a considerable macroscopic resemblance to two specimens in the Moorfields Hospital Museum. One is Mr. Goulden's case (Path. No. 1061 of April 22, 1910, Museum No. IV, G.2), examined and described by Mr. A. C. Hudson as a typical endothelioma. Sections of the above, kindly lent by Mr. Hudson and compared with the writer's case, show an identical type of cellular growth. The other is Sir J. H. Parsons' case⁽²⁾ (Moorfields Hospital Museum, No. IV, G.3), which

was grouped by Hudson as one of fibromatosis, in his exhaustive investigation into and analysis of cases of optic nerve tumour.⁽⁴⁾ For comparison, two microphotographs of parts of the fibromatosis specimen are reproduced, for the use of sections of which the writer is indebted to Sir J. H. Parsons. In one, under low power magnification, the posterior part of the eyeball and the anterior part of the growth are shown in section. The mass is seen to consist of a fibrous structure enclosing darkly stained islands of

FIG. 6.

Microphotograph $\times 400$, shows the central portion of Fig. 3, and greater detail of the whorl-like collection of cells. Note that some of the spaces are definitely within the cell-protoplasm and in close contact with nuclei.
(Photographs by Mr. F. Welch.)

cells. The second photograph shows, under high magnification, one such island of cells, which is largely formed of small round cells and is surrounded by concentrically arranged layers of fibrous tissue (collagen, stained a brilliant red by van Gieson's fuchsin stain). Some of these nodules are arranged with small round cells in the periphery, a few plasma cells, and epithelioid cells in the centre.

As stated above, there is considerable macroscopic resemblance between these two types of growth which do not arise in the nerve fibre part of the optic nerve.

Microscopically, there are well-marked differences. These are tabulated as follows :

(1) The fibromatosis case (*a*) is essentially a fibrous tissue mass. The tissue is intimately blended with the superficial layers of the sclera and with obliteration of Tenon's capsule. It blends in exactly the same manner with the surface only of the dural sheath. In a similar manner, it infiltrates the sheath of the

FIG. 7.

Microphotograph showing posterior part of eye in section, and anterior part of tumour (fibromatosis; case of Sir J. H. Parsons). The mass is composed mainly of cellular fibrous tissue and encloses islands of cell-infiltration which appear very dark in the photograph.

orbital muscles and in parts apparently destroys the muscle fibres, with infiltration of orbital fat.

(b) There are nodules or islands of cell-infiltration among the cellular fibrous tissue. These are mainly arranged with small round cells in the periphery, and a few plasma cells and epithelioid cells in the centre.

(c) There is endothelial proliferation in some of the small vessels, and, in parts, marked perivascular infiltration, which indicates inflammation.

(2) (*a*) The above described tumour (endothelioma) is essentially a cellular growth, with distinct separation between a large part

of the growth and the eyeball. There is no scleral involvement, but the growth is present in the subdural space and splits up the dural sheath.

- (b) There are no nodules of cell-infiltration and only a minimum amount of new fibrous tissue.
- (c) There is no visible vascular abnormality.

FIG. 8.

Microphotograph (magn. $\times 70$), shows a small area of the same section (on opposite side of optic nerve). There is a darkly stained group of cells which are mostly small round cells, surrounded by concentric layers of fibrous tissue. The rest of the photograph shows cellular fibrous tissue with diffuse cell-infiltration. Some of the larger nodules contained plasma cells and epithelioid cells.

The means of differentiation on clinical grounds between Hudson's group of cases of endothelioma of the optic nerve and of gliomatosis and fibromatosis are tabulated in a previous paper by the writer.⁽²⁾ The most important distinguishing features are that in the endothelioma group, the age of incidence is such that more than 50 per cent. start after the age of thirty years, whereas in the other group, more than 75 per cent. start in the first decade of life; and in the former group, there is a slight excess of cases in which exophthalmos precedes visual defect, whereas in the latter group, the primary defect is visual, in the majority; and that there is usually more limitation of movement in the eyeball in endothelioma than in gliomatosis or fibromatosis.

Conclusion

The growth described is a typical endothelioma. There is some evidence suggestive of the presence of a thin layer of growth which lies between the dural and pial sheaths on the nasal side of the nerve and that this layer of growth, wrapped around the nerve superficial to its pial sheath, much thicker on the temporal side, has on that side grown more rapidly and spread more freely into and through the dural sheath. On the other hand, it may quite well be stated that the growth arose as an extra-dural endothelioma, or from lymph channels in the dural sheath, and that it extended inwards into the subdural space. The neoplasm has extended to such dimensions that a decision as to this is impossible. However, as shown in a previous paper⁽²⁾, an endothelioma arising in the endothelium of the subdural space, either superficial or deep to the arachnoid sheath, may at an early stage spread into and through, and largely destroy the arrangement of the dural sheath. Further, the subdural space is a recognized source of endothelioma of the optic nerve. It is probable, therefore, that the growth in this case originated from the endothelium of the subdural space.

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GLAUCOMA SECONDARY TO CHOROIDAL SARCOMA. THE TREATMENT OF PAINFUL BLIND GLAUCOMATOUS EYES

BY

HUMPHREY NEAME AND WAJID ALI KHAN, M.B., B.CH.

THE occurrence of several cases of sarcoma of the choroid in eyes that were excised on account of pain and loss of vision with glaucoma, at Moorfields Hospital, led to the investigation of the incidence of new growth of the choroid in glaucomatous eyes that were excised during a period of eleven years from 1903 to 1911 and 1922 to 1924. Acknowledgments are due to the following surgeons for their kind permission to report their cases:—Mr. W. Lang; Mr. Flemming; Mr. Lawford; Mr. Spicer; Mr. Collins; Mr. Worth; Mr. Fisher; Mr. B. Lang; Mr. Whiting; and to Mr. Greeves for facilities given for the examination of sections