Two cases of glioma of the retina / by G. E. de Schweinitz and E. A. Shumway.

Reprinted from the Proceedings of the Pathological Society of Philadelphia, 1900.]

TWO CASES OF GLIOMA OF THE RETINA.

G. E. DE SCHWEINITZ, M.D.,
AND
E. A. SHUMWAY, M.D.

As a certain amount of interest always attaches itself to glioma, the following cases are deemed worthy of record:

CASE I.—L. E., a male Hebrew child, aged three and a half years, was brought to one of us (Dr. de Schweinitz) on the 29th of June, 1900, for an opinion on the left eye, which was blind, painful, and prominent.

History. There was nothing important in the clinical history of the child, who is the only one, and who had been in sturdy health until recently, when great restlessness developed, particularly at night, doubtless due to pain in the affected eye. The right eye was normal in all respects, as far as could be ascertained by ophthalmoscopic examination. Eight months prior to his visit, that is to say, when the child was not yet three years old, a white spot appeared in the pupil of the left eye, and the child was taken to several of the hospitals of this city, but failed to follow the advice there given. Within the last few months the eyeball became distended and masses began to appear in the orbit.

Examination showed a greatly enlarged eyeball, a wide pupil, behind which all interior examination was obscured by the cataractous lens. The episcleral and posterior conjunctival vessels were enormously enlarged and distended. The tension of the eyeball was + 3. Below and to the outer side, and apparently adherent to the floor of the orbit, were several large episcleral nodules. The diagnosis of intraocular growth, almost certainly glioma, in the stage of extraocular tumor formation, was readily made, and evisceration of the contents of the orbit was advised. This operation was performed on the 2d of July at the Jefferson College Hospital, the entire contents of the orbit with the periosteum being removed in a single mass.

Convalescence from this operation was uneventful, and the child was dismissed from the hospital about the 15th of August. There is no note that there was any recurrence of the growth at this time. On the 15th of September of the present year the child, after a day or two of great restlessness, was seized with convulsions and was hurriedly conveyed to the Pennsylvania Hospital. The convulsions ceased very soon, but recurred the same evening, when the child was again taken to this hospital, where he died in a few hours. The note on the book of the hospital is the following: Unilateral spasms, clonic in character, and coming on in paroxysms; internal strabismus of the right eye; twitching of the fingers and toes; rapid, feeble pulse; marked cyanosis; hurried respiration." Unfortunately an autopsy was not obtained. On interviewing the father as to recurrence *in loco*, it was ascertained from him that the orbital cavity had healed completely; but that a small button, as he expressed it, was visible at the bottom of the pit. This may or may not have been a recurrence, as it is common to find a small mass of granulation in the orbit after exenteration, and we are inclined to think that this should be so regarded.

The clinical symptoms point to intracranial involvement or metastasis. This is rendered the more likely, inasmuch as the brain, after the cranial and facial bones, is the most frequent region for the appearance of metastatic deposits.

The eyeball was placed in a 5 per cent. formalin solution, and subsequently cut in two, one half being mounted in glycerin jelly, and the other embedded in celloidin, and cut in sections parallel to a horizontal plane passing through the cornea and optic nerve. Its anteroposterior diameter measures 26 mm., the vertical 22 mm., and the horizontal 22 mm. The posterior half is filled with a grayish-white mass, which has broken through the sclera, and forms an extraocular nodule, closely investing the optic nerve at its entrance into the ball. The anterior part of the tumor mass stains less well than the posterior. It is composed of a mass of round cells, the majority of which have undergone degeneration, and shows in places dense deposits of lime salts. Certain portions of the growth, especially the better staining ones, show the usual tubular arrangement which glioma cells assume: thick mantles of well-preserved cells surrounding the bloodvessels and projecting

into the other masses of cells which have lost their staining power. The two portions are separated partially by the proliferating pigment epithelial layer of the retina, and represent respectively the original retinal growth, and the secondary deposit, in the choroid. The retina is attached as far back as the ora serrata; here it bends abruptly inward, and widens out into the tumor mass. The latter springs from the inner nuclear layer, as the outer nuclear layer continues for a short distance undisturbed. The bloodvessel walls are much thickened, and show hyaline degeneration to a marked degree. The anterior part of the globe shows the effect of the increased tension, all of the tunics being relatively thin. The ciliary processes are stretched forward and are atrophied; there are also marked atrophy of the iris, and a well-developed intercalary staphyloma. The cornea is thinned and staphylomatous, but is otherwise normal. The lens shows beginning cataractous changes in its cortical layers. Both anterior and posterior chambers are quite deep, but the filtration angles are blocked by the firm adhesion of iris and cornea. The optic nerve is replaced partly by the infiltrating tumor cells, which have passed along the lines of the nervous bundles and also through the intervaginal space. The uninfiltrated part of the nerve shows a conversion of its entire structure into hyaline connective tissue. The sclera is very much thinned, and its fibers are separated by lines of glioma cells. None of the rosets described by Wintersteiner are present in the tumor. Pieces of orbital tissue were also cut for microscopic examination. They show extensive infiltration with glioma cells; in places this infiltration is diffuse, in others the cells are grouped in dense masses, and exhibit a decided tendency to cell death. In both the orbital and intraocular portions of the growth there are a great many karyokinetic figures. These are especially notable around the bloodvessels, where the cell growth is most rapid. Sections of the lacrimal gland show mononuclear, round-cell infiltration around the bloodvessels, and between the acini, but no glioma cells are present.

Case II.—E. B., aged nine years, male. Patient of Dr. George E. Rohrer, of Lancaster, Pa. The boy was first seen by Dr. Rohrer in February, 1900, but the ocular symptoms appeared one year before. At this time the eye became weak and watery, and some pain was complained of, but the symptoms subsided in a

week's time. Similar attacks recurred, however, and several months later the pupil was found dilated ad maximum, and vision was reduced to zero. In the back part of the eye whitish patches were seen, and, later, the whole of the retina presented a yellowish-white appearance. Despite the occurrence of these attacks, the boy attended school regularly until, at Christmas, the eye began to bulge. When seen by Dr. Rohrer there was marked exophthalmos, the tension of the globe was elevated, and vision was nil. The anterior chamber was filled with a yellowish mass, which prevented any view of the fundus. Enucleation was immediately advised and performed. During the operation an attempt was made to cut well back of the optic nerve entrance, and, as the orbit was involved, the tissue was removed as far as it seemed to be diseased. There was, however, a very rapid recurrence, which soon filled the orbital cavity, and the boy died about three months later.

The eyeball was placed in alcohol at the time of enucleation, and was subsequently frozen and cut in a horizontal plane. The macroscopic specimens show that the globe is filled with a grayish-white mass, the central part of which is necrotic. In addition to the intraocular mass there is a large extraocular nodule, the sclera running as a narrow band, with a pigmented inner border, between the two portions. The globe has become shrunken and distorted in the alcohol, presenting a ring-shaped depression in the ciliary region, which allows the cornea to project forward in the form of a nipple. The anterior chamber is filled with a yellowish-white mass; the lens is crowded forward in front of the ciliary processes and jams the iris against the cornea at its periphery. The globe measures 24 mm. in its anteroposterior diameter, 21 mm. vertically, and 21 mm. horizontally.

Sections stained with hematoxylin and eosin show macroscopically that the mass is composed of two parts—a poorly staining one, occupying the anterior part of the eyeball, and a well-staining mass posteriorly, which includes the extraocular nodule. The poorly staining portion, when examined under the microscope, is seen to be made up of a mass of necrotic tissue, the greater part of its cells refusing the stain. Here and there are groups of round cells which stain faintly with hematoxylin, the nuclei of which are undergoing fragmentation. In contrast with this mass of un-

stained tissue the bloodvessels stand out prominently, their lime-infiltrated walls staining dark blue with the hematoxylin. This is evidently the original tumor. The retina can be traced only as a line of degenerated tissue, extending inward from the ora serrata, and the growth has advanced too far to determine the layer of the retina from which it has sprung. The posterior well-staining portion represents the secondary infiltration of the choroid. It shows moderately well the tubular arrangement typical of glioma. The bloodvessel walls have undergone marked hyaline change and the mass is infiltrated with scattered masses of pigment, part of which represent the remains of the stroma cells of the choroid, but the greater part is evidently the result of previous blood extravasation. The sclera is infiltrated, and the optic nerve is entirely replaced by the growing tumor. Anteriorly the ciliary bodies are stretched forward and are quite atrophic. The lens is pushed forward in advance of them; it shows extensive cataractous changes: proliferation of the capsule epithelium, separation of the fibers by a coagulated fluid, with destruction of individual fibers. The iris is pressed firmly against the corneal periphery, entirely blocking the filtration angle, and is to a high degree atrophic. The cornea is stretched, but is otherwise normal, neither Descemet's nor Bowman's membrane showing any break in its continuity. The mass in the anterior chamber is composed of degenerated glioma cells, only a few retaining their staining power. In no part of the tumor mass are there any of the so-called rosets.

In connection with these cases of glioma of the retina, which present no features distinguishing them from the many cases now on record, it may be well to review the subject of the etiology of the growth in question, especially as there has been little mention in American literature of the very animated discussion that has been called forth on the Continent by Wintersteiner's monograph.[1] For many years the scientific world has been divided into two camps—those defending Virchow's views,[2] that glioma develops from the neuroglia or supporting tissue of the retina—among them Hirschberg,[3] Iwanoff,[4] Knapp,[5] etc.; and, on the other hand, those who take the ground that it is a round-cell sarcoma, or plexiform, or tubular angiosarcoma (Delafield,[6] Vetsch,[7] Straub,[8] Mazza,[9] Van Duyse,[10] Becker[11]). Virchow's stand-point has recently re-

ceived strong support from Greef,[12] who, by means of the Golgi-Cajal silver method, was able to show the presence of long protoplasmic processes in connection with the cells, thus demonstrating their neurogliar character. These results were confirmed by Hertel,[13] although he did not succeed when employing the Weigert neuroglia method. Both Greef and Hertel found also numerous ganglion cells, and the former has proposed to call the growth neuroglioma ganglionare, following Klebs,[14] who had chosen the name of neuroglioma, not only for the retinal tumors, but also for the gliomata of the central nervous system.

Wintersteiner, however, lays especial weight upon the epithelial rosets, described by Flexner,[15] Eisenlohr,[16] Becker,[11] and Van Duyse,[10] which he found in 11 out of 26 cases of glioma investigated by him. These peculiar structures consist of closed or partly closed rings of 10 to 12 narrow, wedge-shaped, cylindric cells, the lumen of the roset being lined by a distinct basement membrane. In places, rod-shaped protoplasmic processes extend into the lumen, through the basal membrane. He considers that these cells, with their processes, are rudimentary rod and cone cells, that the basal membrane represents the limitans externa retinæ; and as he found them in a beginning glioma nodule in the external nuclear layer, where they could not be present normally, he believes that glioma arises from embryonally misplaced cells of the neuro-epithelial layer of the retina. He described these roset formations in two malformed eyes, which were free from tumor formation, and in one case he was able to show a direct transition of the cells to the rod-cone fibers and to the limitans externa retinæ. He further mentions that Salzmann has also described similar rosets in an eye with a conus below the optic nerve entrance, and as clinical observation permits no doubt as to the influence of congenital disturbances upon the production of the tumor, Wintersteiner suggests the name of neuro-epithelioma retinæ. That the rosets were found in only one-third of his cases was not considered important by him, as it is not necessary that the misplaced cells should, in every case, reach the height of development necessary to produce the fully formed rosets. He does not deny the presence of glia cells in the growth, but claims that they do not decide the nature of the growth, because such cells are present normally, and the support-

ing tissue may be increased without, however, constituting the essential element of the tumor.

On the other hand, Ginsberg[17] has described groups of cells in the displaced and partly detached retina, in the micro-ophthalmic eye of a new-born child, which showed transition to the cells of the pars ciliaris retinæ. Such rosets have also been found in micro-ophthalmic, or otherwise malformed eyes, by Dötsch,[18] Bernheimer,[19] Pichler,[20] Bock,[21] Rubinski,[22] and Helfreich.[23] Ginsberg thinks that Wintersteiner's claim that the neuro-epithelium is involved in the formation of the roset has not been proven, but that they more closely resemble the cells of the pars ciliaris retinæ, and as the latter are found before the division of the cells of the future retina into spongioblasts and neuroblasts, he believes that the origin of the growth must be from cells which have remained upon this low stage of embryologic development. In any case the cells composing the tumor are epiblastic in origin, and not mesoblastic, so he suggests the name "carcinoma retinæ" in place of neuroepithelioma retinæ. Pichler's work confirms that of Ginsberg, and his conclusions are identical.

As Axenfeld[24] remarks in his review of the subject in Lubarsch and Ostertag's *Ergebnisse* (1898), from which we have freely quoted, the purely sarcomatous conception of the tumor has certainly lost very much ground. Wintersteiner argues that its origin, in many instances, from the outer nuclear layer, where there are no mesodermal elements, precludes the use of the term sarcoma. Treacher Collins[25] also expresses himself strongly against this term. He shows that in the fourth fetal month the retina is composed of the same cells as those in glioma. That this morphologic proof of the epithelial nature of the growth is further supported by the clinical facts that glioma appears usually before the sixth year, that metastases in the liver are rare,* while the propagation in the lymph channels is the usual one; that sarcoma is never bilateral, and that histologically the glioma cells are

* Metastases in the liver are not exactly rare. Thus, in a recent paper by F. M. Wilson and Edgar S. Thompson (Archives of Ophthalmology, January, 1900), there is recorded a case of glioma of the retina and brain metastasis with autopsy, and a review of the literature. In a total number of 530 cases metastases were recorded 61 times, and of these 61, 7 appeared in the liver, the only other regions of the body more frequently affected by metastatic deposits being the cranial and facial bones, the brain, the lymphatic glands, and the parotid gland.

poorer in protoplasm, show fine protoplasmic processes, and are much more inclined to degenerate.

The discussion upon the subject is evidently not ended, but the newer work points toward the greater probability of the epithelial character of the growth. If the findings of Greef and Hertel be still further confirmed, especially by other methods, its neurogliar origin must be admitted. The silver method, however, is too uncertain in its results, and we must consider this proof as not yet thoroughly established.

BIBLIOGRAPHY.—(1) Wintersteiner: Das Neuroepithelioma retinæ, eine anatomische und klinische Studie, Leipzig und Wien, 1897. (2) Virchow: Onkologie, 1864, ii. 123. (3) Hirschberg: Der Markschwamm der Netzhaut, Berlin, 1869. (4) Iwanoff: Beiträge zur normalen u. patholog. Anatomie des Auges. Arch. f. Ophth., 1869, xv. 2, p. 1. (5) Knapp: Die intraocularen Geschwülste, Karlsruhe, 1868. (6) Delafield: Tumors of the Retina, Transactions of the American Ophthalmological Society, 1870, p. 73. (7) Vetsch: Ueber Glioma retinæ, Arch. f. Augenheilk., 1882, xi. 413. (8) Straub: Die Gliome des Sehorgans, Arch. f. Ophth., 1886, xxxii. 1, p. 205. (9) Mazza: Gliosarcoma della retina con speziali considerazioni sui processi progressivi e regressivi nucleari, Annali di Ottamol., 1888, xvii., Fasc. ii. p. 157. (10) Van Duyse: Du glio-angiosarcome tubuleux de la rétine, Arch. d'Ophtalm., 1893, xiii. p. 726. (11) Becker, A.: Beitrag zur Kenntniss des Netzhautglioms, Arch. f. Ophthal., 1893, xxxix., 3, p. 280. (12) Greef Der Bau und das Wesen des Glioma retinæ, Deutsche medicin. Wochenschrift, 1896, No. 21. (13) Hertel: Ein Beitrag zur Kenntniss des Netzhautglioms., Monatsbl. f. Augenheilk., October, 1897. (14) Klebs: Beitrage zur Geschwulstlehere, Prager Vierteljahrschrift, 1877, Bd. cxxxiii. p. 68. (15) Flexner: A Peculiar Glioma (Neuro-epithelioma?) of the Retina, The Johns Hopkins Hospital Bulletin, August, 1891, No. 15. (16) Eisenlohr: Beitrag zur Kenntniss des Glioms der Netzhaut, Virchow's Archiv, 1891, cxxiii. 3, p. 429. (17) Ginsberg: Ueber embryonale Keimverlagerung in Retina und Centralnervensystem, ein Beitrag zur Kenntniss des Netzhautglioms, Graefe's Arch. f. Ophth., xlviii. p. 1. (18) Dötsch: Anatomische Untersuchung. eines Falles von Mikrophthalmus congenitus bilateralis, Graefe's Archiv, xlvii. p. 1. (19) Bernheimer: Ein Beitrag zur Kenntniss der Missbildungen des Auges Schweigger's Archiv, xxviii. (20) Pichler: Zeitschrift f. Augenheilk., 1900, Bd. iii., Ergänzungsheft. (21) Bock: Die Angeborenen Kolobome des Augapfels, Wien, 1893. (22) Rubinski: Beitrag zu der Lehre von den angeborenen Cysten des unteren Augenlides mit Mikrophthalmus (Colobomcysten). Inaug. Dissertation, Königsberg, 1890. (23) Helfreich: Beitrag zur Lehre vom Glioma retinæ, Graefe's Archiv, xxi. p. 2. (24) Axenfeld: Ergebnisse der allgemeinen Pathologie und pathologischen Anatomie des Menschen und der Tiere, Wiesbaden, 1898. (25) Treacher Collins: Researches into the Anatomy and Pathology of the Eye, London, p. 68 ff. and 84 ff.

November 22, 1900.