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HISTOLOGICAL DESCRIPTION OF AN EYEBALL, WITH DROPSICAL DEGENERATION OF THE NUCLEI AND PROTOPLASM OF THE ROD AND CONE VISUAL CELLS OF THE RETINA WHICH CLINICALLY SIMULATED GLIOMA.

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The following case presents features, both clinical and pathological, of sufficient interest to render its record worthy:

A boy, aged two years, was brought to one of us (Dr. de Schweinitz) on January 20, 1900, by his physician, Dr. William L. Estes.

History. The boy is the youngest of six children, all the others being girls. He has always been puny, but has never suffered from any serious illness; he has much trouble with his digestion. The cause of death of the child's paternal grandmother is not known except that it occurred from some acute disease; his maternal grandmother is said to have "died of exhaustion." The paternal grandfather died from a complication of liver and renal affections; the maternal grandfather, now over seventy-five years of age, is in excellent condition, suffering only from occasional attacks of gout. The child's father is an active business man; his mother is somewhat nervous, but in fair condition. She and one daughter suffer from chronic blepharitis.

About two weeks prior to the child's visit for ocular examination it was noted that the pupil of the right eye was slightly dilated, and that through it a yellowish-brown mass was visible. There was no history of injury and none of any affection, local or general, to which this change in the eye could be attributed.

Examination. The child was distinctly undersized and exceedingly pallid, but physical examination failed to reveal chronic disorder of any of the organs of the body, with the exception of the diseased eye, and the only constant menace were attacks of indigestion, which doubtless were frequently brought on by ill-considered diet.

Examination of the Right Eye. Vision was lacking, and light perception could not be demonstrated. The external appearance of the eye presented no anomalies. The pupil was semi-dilated and fixed, but the iris was of good color, resembling that of the opposite side; synechiæ and inflammatory deposits were wanting. The iris responded to a mydriatic, although the pupil did not dilate *ad maximum.* Well forward in the vitreous chamber and behind the pupil space could be seen a yellowish or rather yellowish-pink mass, over which some large vessels could be detected. This apparently filled the entire ophthalmoscopic

field, and no red reflex could be demonstrated, nor was there any sign of undetached retina. The tension of the eye was normal or about equal to that of the eye upon the opposite side. The clinical appearances were those of glioma, and the opinion was expressed that the eye should be enucleated. The patient was also examined by Dr. Herman Knapp, who thought the disease was glioma, and, in any event, recommended the enucleation of the eyeball.

Examination of the Left Eye. This was normal in all respects.

The eyeball was enucleated on January 27, 1900; chloroform narcosis. The healing was prompt, and there was absolutely no unfavorable sign at any period of the convalescence. After the original shock attending the operation of enucleation had passed away, and the necessity for frequent dressings of the eye had disappeared, the child seemed to gain in nutrition. This improvement was in a measure attributed to the removal of the eye. A recent letter, however, from Dr. Estes, the child's physician, states that "he has not improved in nutrition or growth markedly since the operation." He further states, however, that much of the child's indigestion, from which he still suffers, is due to injudicious feeding and indulgence in sweets. There has been no sign of recurrence *in loco* and no metastasis. Once, for a short time, a small œdematous swelling appeared at the bottom of the orbit. This, however, has entirely passed away, and was probably due to the pressure of the edge of the artificial eye. At the present writing, eighteen months after the operation, the child appears to be normal in all respects.

The enucleated eye was immediately placed in a solution of formalin, and after hardening divided and submitted to macroscopical and microscopical examination.

Pathological Report.

Macroscopical Examination. The eyeball measured 21 mm. in its antero-posterior and 22 mm. in its vertical and horizontal diameters. It was divided into two halves by a section passing in a horizontal plane through the centre of the cornea and the optic nerve. The retina was folded closely together in the centre of the globe, attached only at the optic nerve entrance and at the ora serrata. It was moderately thickened, but presented no distinct trace of tumor formation. (Fig. 1.) The subretinal space was filled with a grayish-white exudate; the choroid was in its normal position, and showed on its inner surface on the temporal side a narrow linear pigment mass. Aside from this, no cause could be seen for the retinal detachment. One-half of the specimen was mounted in glycerin jelly, the other half embedded in celloidin for microscopical section.

Microscopical Examination. The cornea, anterior chamber, ciliary bodies, choroid, and sclera are entirely normal. The iris is partly adherent to the lens, but is otherwise normal and shows no sign of previous infiltration. The retina is in close apposition to the posterior surface of the lens, and the very small vitreous cavity contains a few fine, homogeneous bands, crossing between the inner surface of the retina, which include an occasional oval cell.

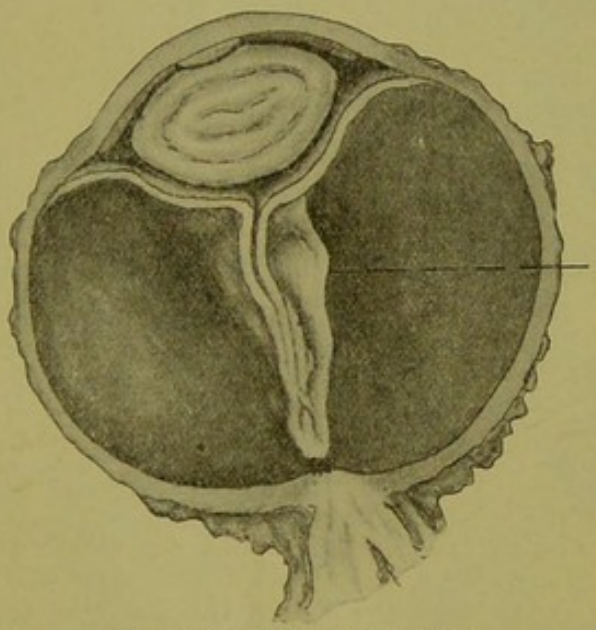
The subretinal space is filled with a homogeneous exudate which stains pink with the eosin. Embedded within it are a large number of enor-

mously swollen cells, each of which possesses a shrunken, distorted nucleus, coarse, highly refractive granules, and masses of pigment. The pigment is in fine rods, and distinctly of the type peculiar to the retinal pigment cells. In many places all that can be recognized of the cell is a large, oval vacuole in the exudate, which contains an isolated nucleus and scattered pigment granules. These cells are especially numerous on the temporal side. They have remained attached to the outer edge of the exudate, and consequently have been separated from the choroid by the shrinking of the former, but they evidently represent the line of pigment described on the surface of the choroid in the macroscopical report. The retinal pigment cells form a regular layer, which has remained adherent to the surface of the choroid.

The optic nerve is partially atrophied, but the majority of nerve-fibres retain the Weigert nerve-sheath stain.

The principal changes occur in the retina. It is moderately thickened. The nerve-fibre layer is œdematous, and the supporting fibres of

Fig. 1.

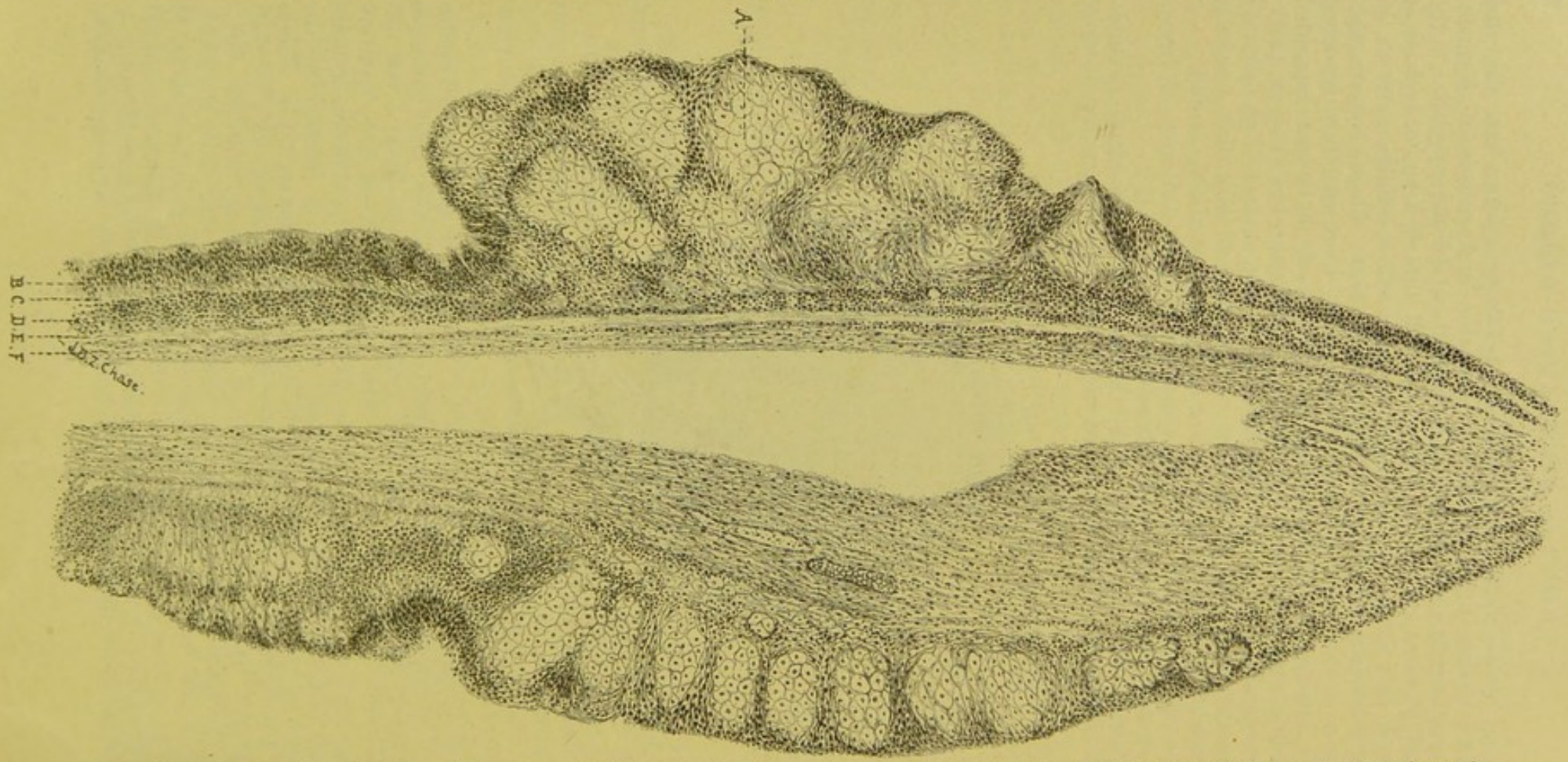


Detached and thickened retina.

Müller are prominent. The ganglion cells are in an advanced condition of chromatolysis; they are distorted and shrunken, their processes are broken abruptly off, the Nissl granules are absent, and the cell bodies show numerous vacuoles. The rods and cones have entirely disappeared, and the fibres of Müller extend in the form of fine arcades a short distance beyond the limitans externa, and in places show the presence of nuclei similar to those in the external nuclear layer. (Compare Deutschmann's[1] article, *Archiv f. Ophthalmologie*, xxv. 3, and Tartuferi's,[2] in *Centralblatt f. die med. Wissenschaften*, 1882, xx. 801.)

In the nasal half of the retina, commencing 1 mm. from the nerve entrance and running for a distance of about 1.5 mm., is a series of cyst-like spaces, each measuring 0.16 to 0.25 mm. in diameter, situated in the position of the external nuclear layer, which is here absent. A similar series begins in the temporal leaf 3 mm. from the nerve entrance

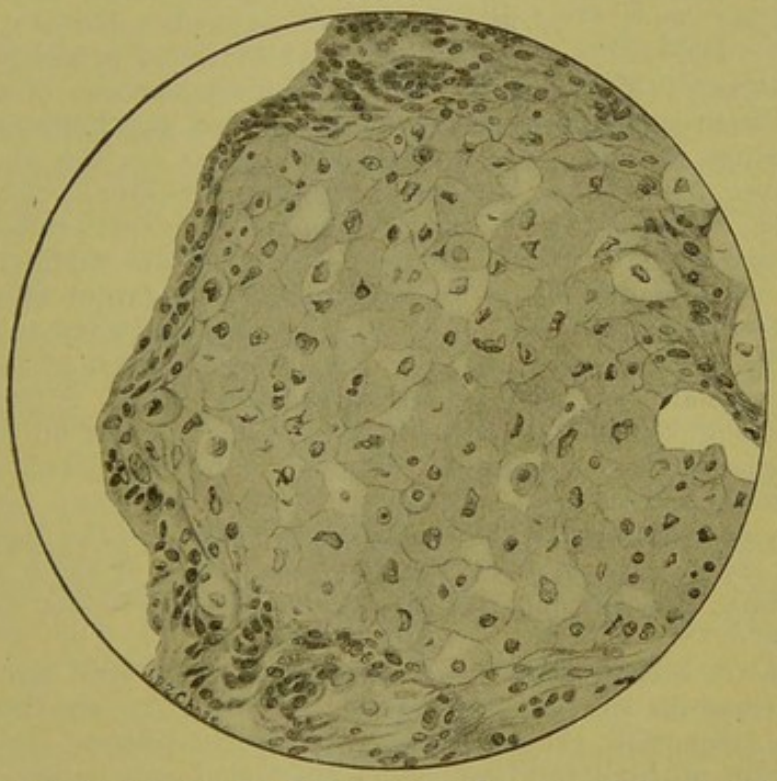
FIG. 2.



A. Cavities in the external nuclear layer of the retina. B. External nuclear layer. C. External granular layer. D. Internal nuclear layer. E. Internal granular layer. F. Ganglion and nerve-fibre layer. Leitz-Wetzlar objective 3, oc. 3.

and extends for a distance of 4 mm. (Fig. 2.) For convenience, these spaces have been represented in the drawing as being exactly opposite. In these positions the retina is thickened to nearly double its normal width. The cavities are bounded laterally by the thickened fibres of Müller and externally by the limitans externa retinæ. They are crossed by a fine reticulum, which at first glance gives the appearance of a network of anastomosing fibres of supporting connective tissue. More careful examination, however, showed that this reticulum represents the walls of large, flat cells measuring between 15μ and 30μ in diameter, each of which contains a distorted and degenerated nucleus either at the centre or near the periphery; the cell body has a finely granular appearance, more prominent in some cells than in others, but contains no large refractive granules. (Fig. 3.)

FIG. 3.



Detail of structure from A, Fig. 2, showing large flat cells with degenerated nuclei Leitz-Wetzlar objective 7, oc. 3.

In sections stained by the Weigert fibrin-method the cell outlines do not retain the stain. The half of the eyeball which was mounted in the jelly for a macroscopical specimen was subsequently removed from the cup, and a portion of the retina was stained with osmic acid, but the cells were not blackened. The condition was traced through a series of sections, and the same changes were found in approximately the same position. The retina exhibits no sign of inflammatory process.

The explanation of these changes is difficult. The following possibilities have been suggested:

1. They represent a fine network of fibrin such as has been frequently described in retinitis albuminurica. The entire absence, however, of signs of inflammation in the retina, of round-cell infiltration about the vessels, of exudation or hemorrhage, and the negative reaction of the

fine network to the Weigert stain, as well as the complete difference in the appearance of the cavities, render this theory untenable.

2. The condition is due to œdema of the retina, the spaces representing cavities between the separated fibres of Müller. Such cystic cavities have been very frequently described in the fibre layer of the retina, in detachment of this membrane, by Leber,[3] Müller,[4] Nordenson,[5] Poncet,[6] Caudron,[7] etc.; but in only two cases have there been found in the outer layers changes similar to those existing in our specimen. In 1882 Tartuferi[2] described, in a case of hemorrhagic glaucoma, "vacuole formation in the cones, due to œdema, which later may widen out and communicate through openings in the limitans externa with spaces in the external nuclear layer, which are likewise filled with serum and surround the cone nucleus on all sides, so that the latter is separated from the neighboring elements." In a case published by Webster,[8] in 1887, Van Gieson speaks of "numerous small, spheroidal cavities in the outer nuclear layer filled with fluid and containing delicate, flattened connective tissue fibres, with wing-like anastomosing processes. These are the fibres of Müller, exposed by the disappearance of the outer nuclei. These small cysts are enclosed between the limitans externa and the inner nuclear layer. There are similar cavities in the inner nuclear layer, but fewer in number." No plates accompany either paper. In our case, however, the minute spaces do not represent cavities formed by the separation of the fibres of Müller, but are distinct cellular elements. In this opinion we are supported by Professors Simon Flexner and George A. Piersol, of the University of Pennsylvania, who have studied the sections carefully. The cellular nature of the process is shown especially where the peculiar formation begins. A few isolated, swollen cells appear in the midst of the cells of the outer nuclear layer, and they gradually become more numerous until they fill out the large spaces described above.

3. They are fat, granular cells, such as are found in the degenerative lesions of the central nervous system (in softening of the brain, etc.). They contain, however, no refractive granules, and are not stained by osmic acid.

4. They are inclosures in an obliquely cut and folded retina of the cells described in the subretinal fluid. Now, although they are of much the same size, they present an entirely different appearance. They contain no highly refractive granules, and only rarely any pigment, although the two forms of cells are separated in some places only by the limitans externa retinæ.

5. They are due to the burrowing of these cells into the retina, where they have undergone secondary proliferation and lost their pigment and refractive granules. Such a process, however, would be hard to understand.

6. They are a proliferation of the nuclei of the external nuclear layer, and represent a true tumor formation. Such a condition is especially suggested by the overlapping of portions of the retina, as though from an active cell proliferation. The change, however, has occurred in two remote portions of the retina at the same time, and the cells, with their degenerated nuclei, do not have the appearance of actual proliferating cells. A tumor of this character would be unique.

7. They are due to an œdematous or dropsical degeneration of the nuclei of the external nuclear layer. The latter are the nuclei of the

rod and cone visual cells, modified epithelial cells derived from the embryonic epiblast, and would be subject to the changes observed in such cells. That the condition is not a fatty metamorphosis is shown by the absence of granules and the negative reaction to osmic acid. Myxomatous degeneration may be likewise excluded, as the cells do not stain typically with hæmatoxylin or thionin. Œdema of the retina is one of the most frequently described conditions in detachment, and in this respect our case forms no exception to the rule. Therefore, it is possible that we have here a localized dropsical degeneration of the nuclei and surrounding protoplasm of the visual cells. This we believe to be the most probable explanation of a change which is certainly of great rarity, if it is not unique. At the same time we cannot exclude entirely the possibility that it is a true tumor formation, and must leave the matter for time and future observation to decide.

A word may be said in regard to the diagnosis from the clinical stand-point. As has been particularly pointed out by Mr. E. Treacher Collins, the following conditions may be mistaken for glioma: Persistence of the posterior part of the fœtal fibrovascular sheath of the lens, masses of tubercle in the choroid, and inflammatory or purulent effusion into the vitreous, following retinitis or cyclitis, usually with detachment of the retina. Although well-marked differential diagnostic points have been established between these affections and glioma of the retina, it is frequently very difficult to come to a definite decision, and, therefore, it is an excellent surgical rule that the eye should be enucleated in case of doubt.

In June, 1889, De Wecker[9] called the attention of the Society of Ophthalmology of Paris to a danger to which young subjects attacked with white degeneration of the retina, or retinitis circinata, are exposed, inasmuch as the disease may be mistaken for glioma. He believes that this affection is not necessarily confined to the eyes of adults, but may be seen also in infants. Among three observations he cited the case of a girl, aged six years, under his care for two years, during which time, although the lesions resembled glioma of the retina, they had not increased, and the intra-ocular tension had not been augmented. This eye was afterward enucleated by one of De Wecker's confrères, who, in addition to the plaques of atrophied choroid and degenerated retina described by De Wecker, found a small ossifying fibroma. In the present instance the clinical appearances were exactly those of glioma; and, although, fortunately for the child, this malignant form of growth was not discovered with the microscope, in the light of the report already cited, it is not absolutely sure that tumor formation is entirely absent. The enucleation, therefore, was a wise procedure.

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