CYTOLOGICAL DIAGNOSIS OF PHACOLYTIC GLAUCOMA UTILIZING MILLIPORE FILTRATION OF THE AQUEOUS*†

BY

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ALTHOUGH the Millipore filtration technique of cytological analysis has been largely neglected in clinical ophthalmology (Goldberg, Erozan, Duke, and Frost, 1965; Jarrett, Goldberg, and Schulze, 1966), it can be of practical assistance in diagnosis and therapy. Documentaion of this usefulness is provided by the following report of morgagnian cataract with phacolytic glaucoma.

Case Report

An 88-year-old man of Ukrainian descent complained of decreasing vision of 20 years' duration. Vision had painlessly and progressively decreased in the right eye until 8 years before admission, when he had been struck in the right eye with a tree branch and sustained a laceration of the upper lid. Subsequently, there was further decrease in vision of the right eye. One week before admission, redness and mild pain were noted and topical corticosteroids were instituted by the patient's general practitioner. On the day of admission the patient's niece had discovered that the right cornea appeared to be white and opaque.

Examination.—The visual acuity was perception of light with good projection in the right eye and 20/60 (with -0.5D sph.) in the left. Except for early nuclear sclerosis of the lens, the left eye was normal.

On the right the conjunctiva was moderately and diffusely hyperaemic without discharge. The cornea had a cloudy white appearance, through which the pupil was barely discernible. Biomicroscopical examination showed oedema of the corneal epithelium, a normal stroma, and no keratic precipitates. The anterior chamber was of normal depth but was completely filled with milky material containing myriads of tiny, iridescent, pin-point particles. The anterior chamber angle could not be visualized with a gonioscope. No details of the iris were visible. After the instillation of glycerine drops, biomicroscopy revealed a barely visible iridescent cataract. A pinkish-white fundus reflex was obtained.

The intra-ocular pressure was 43.4 mm. Hg (Schiötz) in the right eye and 14.6 mm. Hg (Schiötz) in the left.

A clinical diagnosis of severe iritis was made; other possibilities included necrotic intra-ocular neoplasm, retained intra-ocular foreign body, metastatic endophthalmitis, glaucomatocyclitic crisis of Posner-Schlossman, and lens-induced glaucoma. The patient was treated with a systemic carbonic anhydrase inhibitor and topical l-epinephrine, atropine, and phenylephrine without relief. Systemic penicillin and chloramphenicol were started on the following day, and hourly CortisporinR eye drops were added to the therapeutic regimen. In the next 3 days there was no appreciable change.

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Radiological examination of the skeleton, para-nasal sinuses, and chest showed no active disease process. Routine orbital x rays were unremarkable. Bone-free dental x rays of the right orbit demonstrated two 1 × 2 mm. non-metallic, seed-like opacities in the extra-ocular orbit, possibly related to the earlier trauma, but the German foreign body locator did not react upon contact with the anterior surface of the globe, conjunctiva, or lids.

By the fourth day, phacolytic glaucoma was considered to be the most likely diagnosis.

Operation.—Cataract extraction was therefore performed in spite of the severe inflammatory signs in the anterior segment of the eye and the elevated intra-ocular tension. Mannitol 1 g./kg. body weight was administered intravenously 2 hours before retrobulbar anaesthesia and compression of the globe. Before the cataract extraction, a paracentesis was performed through the limbus, and approximately 0·2 ml. aqueous was removed and processed as described below. A sector iridectomy was performed superiorly, and the lens was then slid intracapsularly with forceps without loss of vitreous.

Progress.—On the first post-operative day the intra-ocular pressure was 35·8 mm. Hg (Schiötz). The cornea was clear, and the anterior hyaloid face was intact with minimal cream-coloured debris on its surface. The anterior chamber contained a moderate number of cobweb-like strands and minimal cells and flare. Systemic carbonic anhydrase inhibitor and topical cycloplegics were given.

By the eighth post-operative day the aqueous flare and cells had diminished, the cobweb-like strands had disappeared, and the anterior hyaloid face was transparent. The fundus appeared normal. The intra-ocular pressure was 4·9 mm. Hg (Schiötz), and the carbonic anhydrase inhibitor was therefore discontinued.

Result.—After 6 weeks all therapy was stopped. Visual acuity in the right eye was then 20/40 (with +8·5D sph., +4·25D cyl., axis 15°). The intra-ocular pressure was 14 mm. Hg with the Goldmann applanation tonometer. Gonioscopy showed a healed limbal incision anterior to Schwalbe's line. The angle was of aphakic width, and no recession or peripheral anterior synechiae were present. There was 1 to 2+ pigment in the region of Schlemm's canal. About twenty tiny, punctate, iridescent spots were seen scattered throughout the trabecular meshwork, resembling those particles seen in the aqueous pre-operatively. Normal ciliary processes were seen through the surgical coloboma of the iris. Ophthalmoscopy and biomicroscopy showed crystal-clear media.

Aqueous Studies

Giemsas and Gram stains of unfiltered aqueous showed no cellular or crystalline elements. Approximately 0·15 ml. aqueous was sucked through a 47 mm. white plain cellulose (Millipore) filter of 0·45 μ pore size. The entire filter was fixed in 95 per cent. ethyl alcohol for 30 minutes, stained only with the Papanicolaou technique, and mounted in Eukitt (Goldberg and others, 1965; Jarrett and others, 1966).

Several hundred large rounded macrophages were seen singly and occasionally in clumps (Fig. 1, opposite). The small round nuclei were located centrally or eccentrically. The swollen cytoplasm was filled with granular material. Several of the cells were well over 40 μ in diameter. These cells were indistinguishable from those previously reported in histological studies of phacolytic glaucoma (Flocks, Littwin, and Zimmerman, 1955). A large number of erythrocytes and only one polymorphonuclear leukocyte were also present, but no lymphocytes, plasma cells, or fibroblasts were observed. The virtual absence of inflammatory cells, other than the characteristic large macrophages, was especially striking.

Histopathological and Histochemical Studies

Macroscopically, the lens was morgagnian in type, with a brown nucleus floating in a clear sac of fluid (Fig. 2, opposite). The capsule was intact and had many small greyish-white opacities on its surface.
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Fig. 1 (a-c).—Phacolytic macrophages demonstrated by Papanicolaou stain after filtration of aqueous through Millipore sheet. Smaller, ovoid objects scattered on mottled surface of Millipore filter are erythrocytes (b). × 465.

Fig. 2.—Macroscopic appearance of morgagnian cataract with nucleus floating within intact capsule. Note focal opacities in capsule and compare with microscopic appearance in Fig. 3.
Microscopically, the lens capsule was considerably wrinkled and focally reduplicated (Fig. 3). The reduplicated areas contained amorphous collections of basophilic granular material, probably corresponding to the greyish-white opacities seen with the naked eye. This material stained positively for calcium with von Kossa stain. Only rare epithelial cells were present beneath the capsule. No phacolytic macrophages were seen on the surface of the lens or beneath the capsule. The cortex was completely absent, and only a sclerotic nucleus remained.

Birefringent crystals, which were insoluble in 2N acetic acid, were present within the nucleus (Fig. 4a, b). Treatment of a deparaffinized and micro-incinerated section with concentrated sulphuric acid produced immediate and total dissolution of the crystals with liberation of gas bubbles, substantiating the impression that the crystals were composed of...
calcium oxalate (Zimmerman and Johnson, 1958). No cholesterol clefts were present. Colloidal iron and Alcian blue staining revealed no acid mucopolysaccharide around the calcium oxalate.

The iris showed normal structure with very rare phacolytic macrophages within its crypts (Fig. 5).

Discussion

The idea that a morgagnian cataract might cause intractable secondary glaucoma was first correctly postulated by Gifford (1900), who noted that total spontaneous resorption of cataractous lenses occasionally occurred with restoration of clear ocular media, but that useful vision might never return:

That a spontaneous cure of senile cataract sometimes occurs is well enough known. I have seen four such cases, and it is highly probable that if cataract patients lived longer and could keep out of the hands of the oculists, a large portion of them would be more or less completely relieved in this way. But unfortunately for Nature's statistics, I have to report that in three of my four cases, the eye has been lost by glaucoma.

Over 50 years later Gifford's pathogenetic explanation that "the detritus of the cortex might block the outlets" of aqueous humour was substantiated by histological study of eyes which had been unsuccessfully treated medically and subsequently enucleated (Irvine and Irvine, 1952; Flocks and others, 1955; Fenton and de Buen, 1964; Smith and Zimmerman, 1965). It is now recognized that mechanical blockade of the anterior chamber angle structures is effected by proteinaceous debris and by characteristic large macrophages which have ingested hyper-mature cortical protein of the lens. An expected decrease in the facility of outflow of aqueous humour has been recorded (Grant, 1951). To this syndrome the name phacolytic glaucoma has been applied (Flocks and others, 1955).

Although the histopathological characteristics of this syndrome have been described in detail, some puzzling aspects remain open to conjecture. Strikingly
refractile, punctate, iridescent opacities were prominent in the turbid aqueous of the current patient. Similar opacities have been described previously (Safar, 1928; Kaufman, 1933; Knapp, 1937; Scott, 1953; Hubberstey and Gourlay, 1953; Ballen and Hughes, 1955; Leigh, 1955; Flocks and others, 1955). The nature of these aqueous opacities remains obscure, although some have considered them to be cholesterol crystals (Safar, 1928, Kaufman, 1933; Hubberstey and Gourlay, 1953). Such crystals in the aqueous, however, occur in “needle-like or rectilinear” shapes (Berliner, 1949), rather than in punctate pinpoint forms. It seems, therefore, that each of these tiny opacities might more likely represent an individual macrophage swollen with protein granules.

Another puzzling feature of this syndrome is the characteristic presence of calcium oxalate crystals in the nucleus of the morgagnian cataract (Cogan, Kuwabara, Silbert, Kern, McMurray, and Hurlbut, 1958; Zimmerman and Johnson, 1958; Fenton and de Buen, 1964). Although these crystals may occur in over 18 per cent. of such lenses (Flocks and others, 1955), their pathogenesis also remains obscure.

Therapeutically, lens extraction is the only feasible means of eliminating the anterior chamber reaction and glaucoma. This viewpoint has been accepted and substantiated by numerous authors (Gifford, 1900, 1918, 1927; Schwenck, 1917; Knapp, 1927; Safar, 1928; Irvine and Irvine, 1952; Ballen and Hughes, 1955; Irvine, 1957; Chandler, 1958). If the diagnosis of phacolytic glaucoma were universally unequivocal, there would be no hesitation in removing the lens. However, a certain amount of clinical courage is required to perform cataract surgery on an intensely and acutely inflamed eye which is simultaneously involved by a severe glaucomatous process. In the series of Focks and others (1955), 138 enucleated eyes with phacolytic glaucoma were studied, and only 21 (15 per cent.) of these were correctly diagnosed clinically. In this regard, it is of interest that the pre-operative differential diagnosis applied to the patient here reported included several of those incorrect diagnoses made in the series reported by Focks and others (1955)—intra-ocular neoplasm, intra-ocular foreign body, endophthalmitis, and inflammatory glaucoma. The need for further diagnostic techniques is self-evident.

Anterior chamber aspiration with filtration of the aqueous through a Millipore filter can be of definite diagnostic value by demonstrating the highly characteristic phacolytic macrophages. At worst, the eye will have been subjected to a simple paracentesis. At best, the correct diagnosis will have been made, and lens extraction can be performed forthwith without trepidation. It is possible that unfiltered aqueous may not be suitable for the cytopathological demonstration of the phacolytic macrophages. No cells were demonstrated in four previously reported aspirations in phacolytic glaucoma (Safar, 1928; Sugar, 1949; Hubberstey and Gourlay, 1953; Leigh, 1955); neither were they seen in unfiltered specimens from the present case. Therefore, it is recommended that such aqueous samples be filtered through Millipore sheets before cytological staining and microscopical inspection.

Summary

Phacolytic glaucoma may result in subtle and bizarre physical signs, and diagnosis may be correspondingly difficult, but correct clinical evaluation often enables an otherwise doomed eye to be saved.
A clinically and histopathologically documented case of phacolytic glaucoma has been presented, in which cytological study of an aqueous filtrate revealed characteristic macrophages. It is concluded that the Millipore filtration technique of cytological analysis may provide useful and benign assistance in diagnosing phacolytic glaucoma.

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