Cogan-Guerry Microcystic Corneal Epithelial Dystrophy: A Clinical and Electron Microscopic Study

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Over the past two decades various authors have described changes such as "fingerprint lines," grayish-white microcysts, and geographic or map-like patterns in the corneal epithelium of apparently healthy eyes. As further papers have been published on these types of corneal changes, they have appeared to be very similar in clinical presentation, clinical course, and histopathology.

In 1950, Guerry described the ocular findings of two patients with "peculiar wavy lines, extremely fine in character" which were best seen by retro-illumination (2). Their whorl-like pattern appeared similar to fingerprints and were located in or near the epithelium. Vision was 20/20 in both eyes. A histologic study was not performed.

Cogan *et al.* in 1964, described five cases, two with histopathologic correlation, that had "grayish-white, discrete but sometimes confluent spheres, measuring usually 0.1–0.5 mm in diameter and situated in the superficial portion of the cornea (1)." If present in the pupillary area, a slight reduction of vision may have been present, and these changes were usually found in asymptomatic healthy eyes. Histologic examination revealed discrete intraepithelial cysts which contained pyknotic nuclei and cytoplasmic debris. A thickened anomalous basement membrane within the epithelial layers was also seen. All the cases reported were in women, an etiology could not be found, and the condition was described as "benign and usually asymptomatic."

In 1966, Guerry reported nine cases of microcystic dystrophy of the corneal epithelium similar to that described by Cogan and found associated with the grayish-white dots "many irregular, faintly gray configurations varying in size from a millimeter or so to several millimeters . . . The border of these map-like areas appeared a darker gray than did the background (3)." In one case, corneal epithelium was obtained for histopathological examination. The pathological changes were similar to those reported by Cogan *et al.* The author stressed that these map-like or geographic changes could easily be missed unless diffuse illumination was used. These changes seemed to appear more frequently in women since seven of the nine cases reported were females.

In 1966, Wolter *et al.* reported an additional case of microcystic dystrophy (5) and in 1972, Trobe *et al.* reported a series of 35 patients which manifested some combination of the dot, fingerprint, or map-like patterns (4). The histopathology in these 35 patients was the same as that reported by Cogan *et al.*, and Guerry. Ocular pain in the form of foreign

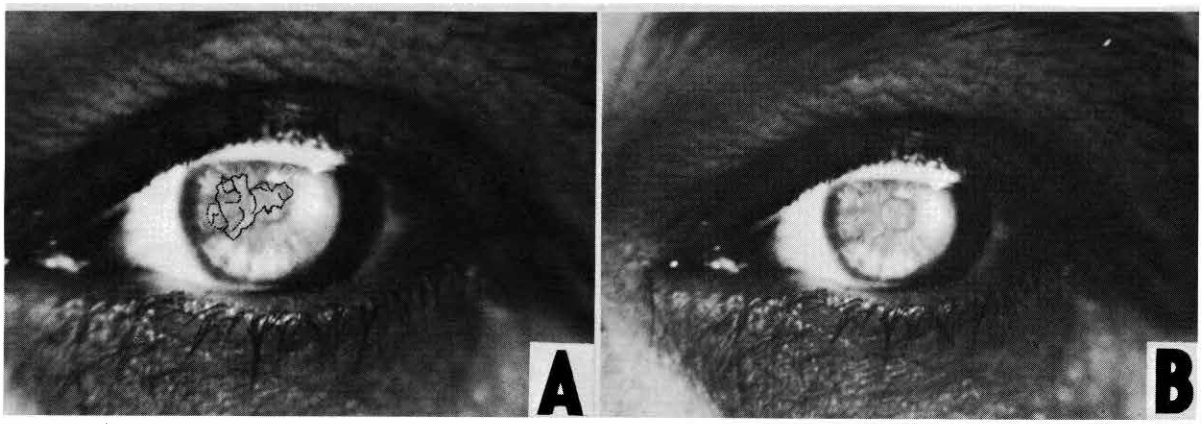

Fig. 1—Identical photographs of the corneal epithelial lesion of the left eye. Photograph A has the outlines of the corneal lesion drawn in. Photograph B shows lesion outlined by the pooling of the topical fluorescein.

body sensation was the presenting symptom of 54% of the patients in their series, and the treatment the authors felt to be most successful was hypertonic sodium chloride ointment. When the pain persisted, mechanical debridement and pressure dressing were effective.

The purpose of this paper is to present a case of microcystic corneal epithelial dystrophy with light and electron microscopic studies of the pathological corneal epithelium.

Case Report. A 44-year-old married caucasian female secretary was first seen during October, 1971, with the complaint of blurred vision in the left eye for the last four months.

Past medical history revealed a normal ocular examination during March, 1970. Vision at that time in the right eye was correctable to 20/15 with a −1.25 sphere. Vision OS was correctable to 20/15 −2 with a −1.25 −0.75 ax 135 sphero-cylinder. For many years, she gave a history of an occasional foreign body sensation of short duration in the right eye upon awakening which never required medical treatment. She had recently been examined by another ophthalmologist who found decreased vision in the left eye but no pathology to explain it.

Ocular examination at the time of complaint of blurred vision OS revealed a vision OD of 20/15 with correction and a vision OS of 20/25, described as very distorted by the patient, with a −1.75 −1.25 ax 115 correction. Both corneas revealed pooling of fluorescein solution on the surface but no staining. The irregular fluorescein pattern on the right cornea was a superior temporal small area and on the left cornea a large apical area (fig. 1). In these areas on the cornea, the image of the Placido disc and the keratometer mires were also distorted. Slit lamp examination by direct illumination appeared normal; however, retro-illumination revealed superficial thin gray lines producing a geographic pattern on the cornea. Mild central corneal guttata was present in both eyes. Corneal sensation and Schirmer tear test were normal in both eyes. The intraocular pressure by applanation was 18 mm Hg OU. The retina and disc were unremarkable in each eye; however, the view of the left posterior pole was distorted because of the corneal pathology.

The patient symptomatology remained unchanged as did the geographic or map-like corneal areas during follow-up visits. During this time small, round microscopic, epithelial grayish deposits surrounding the geographic area were visualized in the right cornea. These deposits remained, but they changed in location, size, and number.

Four months after the patient's initial visit, she elected to undergo corneal epithelial curettage of the left eye since the blurred vision bothered her during work. The corneal epithelium was scraped after 4% cocaine ophthalmic solution was instilled for anesthesia. The peripheral epithelium required more manipulation for removal than the central epithelium which lifted off easily. The eye was patched with antibiotics, cycloplegic drops, and pressure dressing. Re-epitheliation occurred in three days without complication.

Over the past eight months, the corneal lesion of the right eye has persisted with only slight variation.

The left cornea appears normal with direct and retro-illumination. Vision OS with the patient's original corrective lens is 20/15.

Materials and Methods. After removal of the corneal epithelium in one piece it was immediately fixed in 10% formalin, dehydrated in increasing concentrations of ethanol, and embedded in paraffin. Sections were cut 8μ thick and stained with hematoxylin and eosin, Masson's trichrome, and by the periodic acid-Schiff reaction. When approximately half of the epithelium had been sectioned and stained in this way, an examination of the fine structure became desirable, as an afterthought. The remaining epithelium was de-paraffinized, osmicated, and re-embedded, partly in Epon, partly in Durcupan ACM, according to the method described by Zimmerman *et al.* (6). Sections approximately 1μ thick were mounted on glass slides and stained with toluidine blue. Thin sections 80–100 mμ thick were collected on unfilmed copper grids and stained with uranyl acetate for 6–8 minutes and lead citrate for 10 minutes. The sections were viewed with a RCA 3-G electron microscope and photographed on Kodak EM film #4498.

Results and Comments. *Light Microscopy.* The paraffin and 1μ epoxy sections showed apparently normal corneal epithelium with an anomalous basement membrane (fig. 2), as described first by Cogan *et al.* (1) and confirmed and extended by Guerry (3). In some areas the thickened basement membrane extended into the epithelium between the deeper layers of the cells. In a few sections the basement membrane appeared interrupted with the loose ends forming a knob or curl. Several cysts of different sizes located at different levels were found. Some were underneath the insinuated basement membrane and a few immediately under the surface. (figs. 3 and 4). These cysts contained cell debris.

Electron Microscopy. Before the findings on the ultrastructural level are reported, the limitations of the applied method should be mentioned. Because of the unusual tissue preparation outlined in materials and methods, a certain degree of artifactual change of the tissue can be assumed to have taken place, primarily in the cytoplasm. The empty spaces

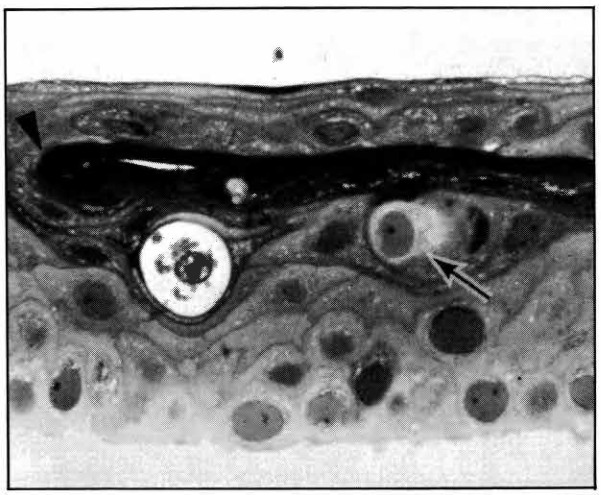

Fig. 3—Insinuated and folded basement membrane (arrowhead) near surface of corneal epithelium, large microcysts with cellular debris and beginning cyst (850×).

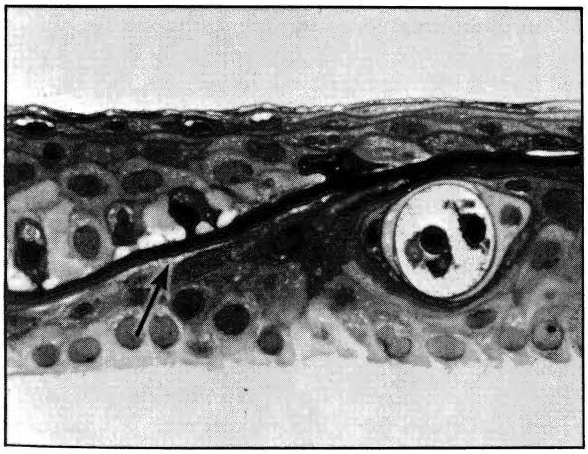

Fig. 2—Corneal epithelium with anomalous basement membrane (arrow) and microcyst (600×).

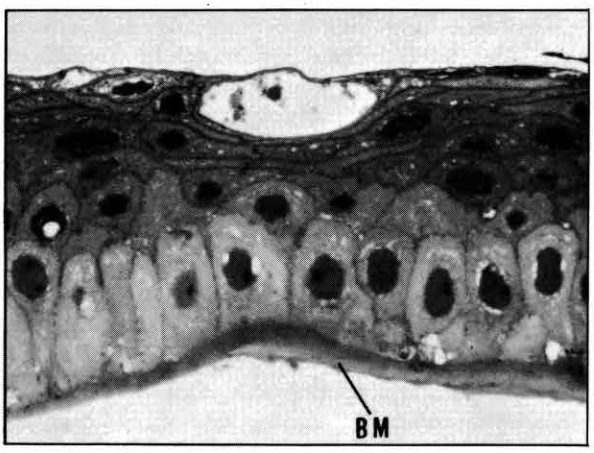

Fig. 4—Corneal epithelium with thickened basement membrane (BM) and microcyst about to break through the surface (900×).

which are normally present in the corneal epithelium, particularly in the cytoplasm of the surface cells, appeared enlarged and more numerous. Since the tissue was fixed immediately after removal, post mortem changes are very unlikely. However, it is not possible to determine whether the appearance of the cytoplasm is due primarily to the preparation of the tissue or due to the pathologic condition, that is, the dystrophy. Therefore, no conclusions will be made about the fine structure of the cytoplasm, the mitochondria, and the Golgi apparatus. On the other hand, the granular or rough endoplasmic reticulum (rER), fibrils, and desmosomes appeared to be normal. For these reasons, this preliminary ultrastructural study is limited mainly to the two characteristic features of the dystrophy, namely the microcysts and the thickened basement membrane.

The cysts ranged in size from 5μ to 50μ. A portion of such a cyst underlying the aberrant basement membrane is shown in figure 5. It contains a homogeneous substance, surrounded by the same dense material that forms the border of the cysts (fig. 6). No definite membrane enclosing the cysts can be recognized.

If this fact could be confirmed in a future exclusively ultrastructural study, it would mean that these cysts are not true membrane bound cysts which by some mechanism migrate to the surface, but instead represent pseudocysts, that is, holes, with some debris from degenerated cells, which are transported to the surface with the surrounding cells. Whether those cysts seen underneath the aberrant basement membrane remain "trapped" or also reach the surface, and how they "escape" is not known. Similarly, it should be interesting to know whether the aberrant basement membrane also moves to the surface with the cells that are constantly formed in the basal layer. A slit lamp examination at regular intervals could perhaps provide an answer.

A relatively small cyst, about the size of a single cell, is seen in figure 7. This illustration also shows that, although cell membranes are not prominent, cisternae of rER, interdigitating cell processes, intercellular spaces, and desmosomes are intact and normal. Also visible is the difference in the density of the cytoplasm between wing cells and surface cells.

The basement membrane is shown at high magnification in figure 8. Two slightly different regions can be recognized. The anterior portion has a marbled appearance, with fibrous material surrounded by irregular strands of a homogeneous sub-

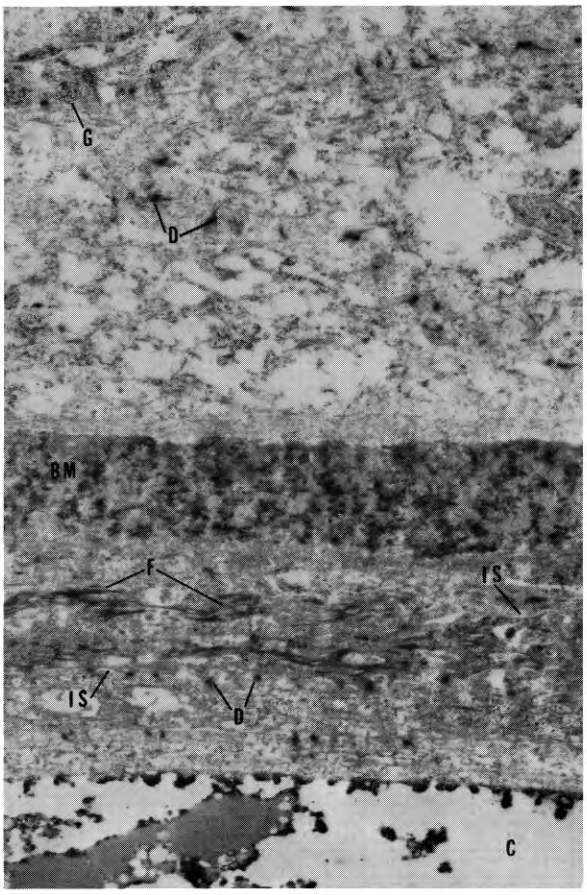

Fig. 5—Portion of corneal epithelium showing thickened and insinuated basement membrane (BM) and border of a microcyst containing homogeneous material (16,000×). IS-intercellular spaces, D-desmosomes, F-fibrils, G-glycogen, C-cyst.

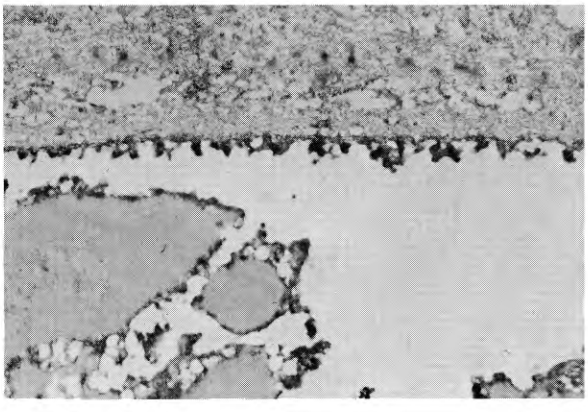

Fig. 6—Portion of microcyst with homogeneous material. No membrane surrounding cyst can be seen (25,000×).

stance. The posterior portion consists of tufts of fibrous material. The thickness of the anomalous membrane ranges from 2μ to 6μ, that is, approximately 100 times the regular thickness of the normal basement membrane.

Previous histopathological case reports of this dystrophy have demonstrated reduplication of the basement membrane (1, 3) but not actual loss of basement membrane as seen in this patient's epithelium. This loss of basement membrane does not appear to be an artifact since the edges of the remaining membrane are curled and interdigitated between the corneal epithelial cells. This loss of basement membrane may be due to a degenerative process and could produce some of the debris containing "cysts."

Diagnosis. The corneal changes when mild are very difficult to recognize as has been pointed out by the authors. The most useful examination procedure to detect these corneal changes is to apply topical fluorescein to the lower cul-de-sac, have the patient blink a few times, and then hold the lids open for 30 to 60 seconds to allow the fluorescein to pool. The dystrophy pattern then becomes very apparent when viewed with the slit lamp and blue light. It should be noted that this pooling of fluorescein is entirely different from the break up of tear film in sicca problems which is also seen with the lids held open.

In summary, microcystic epithelial dystrophy of the cornea as described by Cogan and Guerry has become a well documented clinical entity. In this paper, a case report and preliminary electron microscopic findings of a patient with this dystrophy were presented. This case showed a thickened, two-layered basement membrane which was completely missing in some areas. The second characteristic change was that of cystic epithelial areas containing debris. The possible significance of these findings

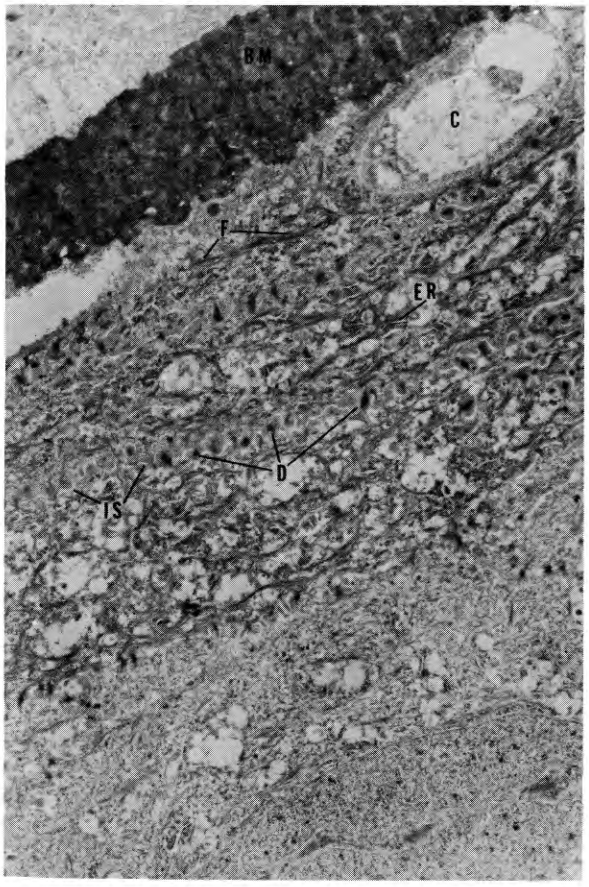

Fig. 7—Portion of corneal epithelium with insinuated basement membrane (BM) and small microcyst (C) (12,000×). IS-intercellular spaces, D-desmosomes, ER-endoplasmic reticulum, F-fibrils.

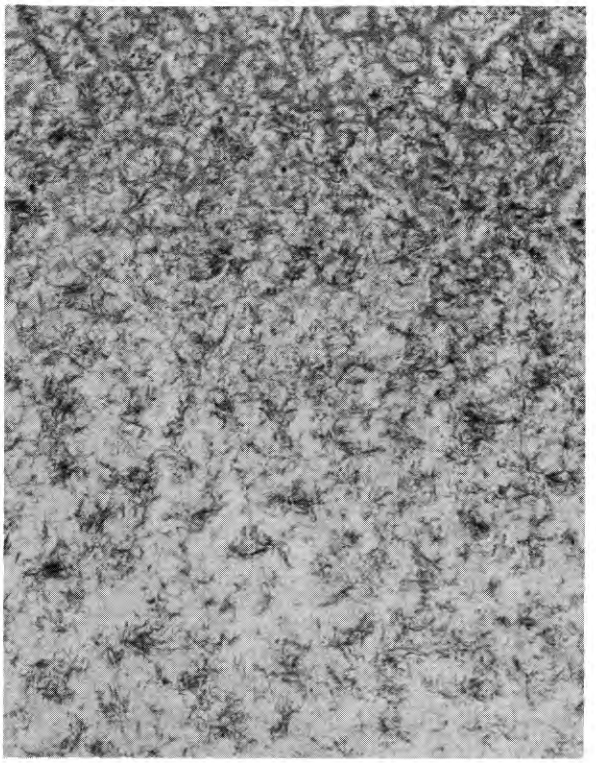

Fig. 8—Section of thickened basement membrane showing two different regions (20,000×) (see text).

and a diagnostic technique for detection of these corneal changes were discussed.

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