Unusual Idiopathic Lipid Keratopathy: A Newly Recognized Entity?

Diseases of the cornea can be attributed to inflammation; degeneration; dystrophies; and, rarely, neoplasms. A yellowish discoloration of the cornea usually is associated with a deposition of lipids that in most instances arises from neovascularization secondary to inflammation. In most cases, no systemic lipid abnormalities are found.

Report of a Case. In March 2002, a 35-year-old patient from Saudi Arabia presented with a massive corneal clouding that had been slowly progressive over the last 5 years. He said he had been practically blind for 2 weeks. When we first saw him, his visual acuity was light perception in both eyes. His history was uneventful, in particular with regard to ocular trauma or infectious diseases. No specific ointment or eye drops had been applied. The only remarkable detail was a cerebral tumorous lesion of unknown origin in the sella region, necessitating a replacement of glucocorticoids.

On examination, both corneas were thickened by irregular dense yellow infiltrates replacing almost all of the regular stroma (Figure 1). Only fairly mild neovascularization within these masses was present; otherwise, no evidence of inflammation could be noted. In particular, the subtarsal conjunctiva was inconspicuous. Intraocular structures could not be visualized. Thus, we performed a high-frequency ultrasound, revealing a marked corneal thickening predominantly toward the anterior chamber (Figure 2) with presumed penetration of the Descemet membrane in the right eye. Ultrasound of the posterior segments was unremarkable. A medical-rheumatologic exam as well as a neurologic investigation did not provide any diagnostic clues, apart from pituitary insufficiency and mild hypertriglyceridemia.

After careful consideration, we successfully performed a penetrating keratoplasty on the left eye with...
immediate improvement of visual acuity to 0.1.

Histologic Findings. Light Microscopy. The yellowish cornea was diffusely thickened (4 mm in height; Figure 3A) by a chronic xanthogranulomatous inflammatory cell infiltrate with occasional cholesterol clefts (Figure 3B). Inflammatory foci were present beneath the epithelium with destruction of most of the Bowman layer (Figure 3B) and throughout the stroma down to the Descemet membrane. There were numerous foam cells (Figure 3C) as well as pigment-containing macrophages that showed a positive reaction with Prussian blue. A Ziehl-Neelsen stain for acid-fast bacilli had negative results.

Immunohistochemistry. Labeling with anti-CD68 revealed numerous positive cells, and in few areas, there was also a positive reaction with anti-S100. No labeling was seen with anti–HMB-45.

Electron Microscopy. The ultrastructure of the intrinsic stromal cells demonstrated only few normal-looking keratocytes while the most prominent fraction of keratocytes was filled with lipid globules (Figure 4A-E), occasionally with features of dying cells (such as pyknotic nuclei). In some places, delicate new blood vessels were present, and occasionally extravasated erythrocytes could be found (Figure 4F). We also saw lipid-rich cells with heavily interdigitating cell processes without particular cell junctions, probably indicating a macrophage origin (Figure 4F), and in some of those, we found crystalline spaces (possibly lipid crystals). No preferred association between vessels and either lipid-laden macrophages or lipid-filled keratocytes could be detected; in contrast, those cells were present throughout the stroma, not related to any particular tissue or structure. Lipid granules were detected mostly in intracellular compartments and only rarely in extracellular compartments, where they seemed to originate from dying keratocytes. In few cells, typical mast cell granules were found, but no other specific organelles could be identified. In

Figure 3. Light microscopic findings. A, Low-power micrograph of the markedly thickened and diffusely infiltrated corneal button (hematoxylin-eosin, original magnification ×10). Arrows indicate irregular epithelium. The Descemet membrane shows folds on the right (arrowhead) and is largely missing on the left because of unfortunate sectioning. B, Separation from the epithelium and disruption of the Bowman layer (arrows) with adjacent cholesterol clefts (asterisk) (hematoxylin-eosin, original magnification ×320). C, Stromal infiltration by inflammatory cells and foamy cells (asterisks) (hematoxylin-eosin, original magnification ×320).
particular, no evidence of any microorganisms was seen.

Comment. Lipid keratopathy is a rare disease. It has a primary and a secondary form, the secondary being the more common entity because of leakage from lipids out of newly formed corneal vessels after inflammation.1

In our patient, the bilaterality and rather symmetrical localization indicate a generalized problem. However, no evidence was found for a systemic (eg, sarcoid) or an infectious disease, nor did the patient admit to the application of a specific topical treatment. The articles that first brought to our attention the possibility of an independent corneal dystrophy were from Alfonso et al2 and Croxatto et al3 with almost identical clinical and histologic findings. Another case report by Fine et al4 also reveals striking similarities, especially the bulging of the cornea posteriorly toward the anterior chamber. In all 4 cases, the patients developed bilateral disease without evidence of preexisting corneal lesions or signs of a significant systemic illness. Although these 4 patients were male, one was of Mexican origin,2 one a white Argentinian,3 and one an Iranian,4 and our patient was of Arabic background. Friedlaender et al5 described a female patient also with bilateral disease who was probably white. Several other markedly similar albeit unilateral cases have also been published about women (Chinese,6 white7,8), and one could speculate about factors producing asymmetry in an eventually bilateral disease (Table).

Hypothesizing that none of these patients suffered from the same undisclosed systemic disease, the primary defect has to lie in the keratocytes. If, on the other hand, one speculates about a hormonal disturbance, a systemic intoxication, or a misregulation by the central nervous system giving rise to a bilateral disease, one could well imagine the presence of additional hitherto undetected systemic manifestations as can be observed in pseudoexfoliation syndrome.9 These symptoms obviously do not have clinical relevance because none of the case reports described a serious health disorder.

It is intriguing to speculate by which mechanism the deposition of lipid occurred in our patient. Following the suggestions of Croxatto et al,3 we also feel that an intrinsic metabolic defect in the keratocyte causes lipoidal degeneration, thereby initiating an inflammatory re-

Figure 4. Electron microscopic findings. A-D, Ultrastructural appearance of the corneal stroma showing keratocytes with intracellular lipid globules (asterisks). Note the fragment of the Bowman layer (arrowheads) in C (uranyl acetate–lead citrate). Bar indicates 5 µm. E, Cellular detail of lipid-laden keratocyte between stromal lamellae (uranyl acetate–lead citrate). N indicates nucleus; bar, 1 µm. F, Lipid-laden cells with numerous intercellular interdigitations (arrows). Note also the extravasated erythrocyte (e) (uranyl acetate–lead citrate). Bar indicates 1 µm.
sponse. This concept would be supported by the finding of numerous lipid-laden keratocytes throughout the cornea and not necessarily adjacent to vessels, pointing to a primary disturbance of this cell population rather than a simple inflammatory response. An ultrastructural study of a more conventional case of lipid keratopathy also demonstrated intracellular and extracellular lipid droplets and pyknotic keratocytes but revealed much fewer lipid-laden keratocytes.

Although the precise nature and pathogenesis of the corneal disease in our patient remain speculation, our case together with other case reports previously published in the literature (under different names) strongly supports the concept of an independent disease process. Data to corroborate our theory would be the bilaterality, the lack of previous inflammatory episodes, the normal appearance of the conjunctiva, fairly normal blood lipids, and massive involvement of the whole cornea. Should simple neovascularization be the trigger of such a lipid keratopathy, one would expect to see many more patients with this problem. Perhaps one could, even under the aspect of its hypothetical nature, apply the name idiopathic lipid corneal dystrophy to such a disorder and thereby stimulate more publications of otherwise neglected cases where further molecular studies of the families might shed more light on this disease.

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Giant Cell Angiofibroma
of the Ocular Adnexae

Giant cell angiofibroma (GCA) is a rare tumor. It was originally described by Dei Tos et al1 as an orbital tumor. These tumors are characterized by a patternless proliferation of spindle cells, multinucleated giant cells, and pseudovascular spaces. The stroma is collagenized or myxoid. Tumor cells stain positively for CD34 and vimentin. The morphologic appearance is similar to that of solitary fibrous tumor (SFT) and

Table. Summary of Cases With Corneal Lipid Deposition Quoted

<table>
<thead>
<tr>
<th>Source</th>
<th>Sex/Age, y</th>
<th>Country or Race</th>
<th>Site</th>
<th>Clinical Findings and Tissue Lipid Types</th>
<th>Blood Lipids</th>
<th>Systemic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfonso et al2</td>
<td>M/52</td>
<td>Mexico</td>
<td>Bilateral</td>
<td>Idiopathic; bulging toward anterior chamber; cholesterol, neutral fats, phospholipids</td>
<td>Normal</td>
<td>None (treated for hypertension)</td>
</tr>
<tr>
<td>Croxatto et al3</td>
<td>M/41</td>
<td>Argentina</td>
<td>Bilateral</td>
<td>Idiopathic; cholesterol, neutral fats, phospholipids; extracellular and intracellular</td>
<td>Normal; cholesterol, 151 mg/dL; triglycerides, 161 mg/dL</td>
<td>Treated for vernal disease at age 22 y</td>
</tr>
<tr>
<td>Fine et al4</td>
<td>M/63</td>
<td>Iran</td>
<td>Bilateral</td>
<td>Idiopathic, no vessels; bulging toward anterior chamber; cholesterol, neutral fats, phospholipids; extracellular and intracellular</td>
<td>Normal; cholesterol, 295 mg/dL</td>
<td>None</td>
</tr>
<tr>
<td>Friedlaender et al5</td>
<td>F/55</td>
<td>Probably white</td>
<td>Bilateral</td>
<td>Episodes of pain; changes mostly anterior; phospholipids</td>
<td>Normal; cholesterol, 217 mg/dL; triglycerides, 72 mg/dL</td>
<td>Concurrent episodes of skin rash on face and chest; myocardial infarct at age 52 y</td>
</tr>
<tr>
<td>Baum6</td>
<td>F/72</td>
<td>China</td>
<td>Unilateral</td>
<td>Idiopathic; bulging toward anterior chamber; cholesterol (esters)</td>
<td>Normal; cholesterol, 125 mg/dL; neutral fats, 207 µEq/L</td>
<td>None</td>
</tr>
<tr>
<td>Barishak and Stein7</td>
<td>F/31</td>
<td>White</td>
<td>Unilateral</td>
<td>Idiopathic; bulging toward anterior chamber; cholesterol, neutral fats (extracellular)</td>
<td>Normal; cholesterol, 274 mg/dL</td>
<td>None</td>
</tr>
<tr>
<td>Szasz8</td>
<td>F/34</td>
<td>White</td>
<td>Unilateral</td>
<td>Recurrence after inflammation; intracellular lipid</td>
<td>Normal; cholesterol, 176 mg/dL</td>
<td>None</td>
</tr>
<tr>
<td>Present case</td>
<td>M/35</td>
<td>Saudi Arabia</td>
<td>Bilateral</td>
<td>Idiopathic; bulging toward anterior chamber; lipids intracellular and extracellular</td>
<td>Normal; mild hypertriglyceridemia</td>
<td>Tumor in the pituitary region</td>
</tr>
</tbody>
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