Cataract in Gyrate Atrophy: Clinical and Morphologic Studies

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The clinical appearance of the cataract in nine phakic patients with gyrate atrophy of the choroid and retina is described. The gross and microscopic examination of three cataractous lenses removed from patients 31 years to 47 years of age is reported. Clinically, the lens opacities appeared primarily along the confluence of the sutures posteriorly, interfering with vision because of their location in the visual axis. Histologically the region of the posterior sutures was filled with liquified and degenerated lens material typical of senile cataractous changes. By the second decade, cataract is a uniform finding in patients with gyrate atrophy and appears to be unique as compared with cataracts associated with other forms of retinal degeneration. Invest Ophthalmol Vis Sci 24:432-436, 1983

Although the most significant clinical sign of gyrate atrophy (GA) is progressive chorioretinal degeneration, a posterior sutural cataract is common, usually occurring in the second decade of life. It often requires surgical intervention by the third or fourth decade. The clinical appearance of the cataract in patients with GA at various stages is described in the present report. In addition, the light and electron microscopic findings of three patients who underwent intracapsular cataract extraction are presented.

Materials and Methods

The diagnosis of gyrate atrophy of the choroid and retina (GA) was confirmed in the present series of 14 patients on the basis of the typical chorioretinal ophthalmoscopic appearance, hyperornithinemia (Tables 1, 2) and deficiency of ornithine-δ-amino transferase (OAT) activity in cultured fibroblasts. Plasma ornithine concentrations were measured by standard amino acid analyzer techniques on samples obtained between 8:00 am and 9:00 am after an overnight fast. OAT activity was measured radioisotopically as previously published and ranged from undetectable to 3% of normal activity in this group of patients.

Clinical evaluation included postpupillary dilation photography of the lens using the Zeiss stereo photo slit lamp in nine phakic patients (Table 1). Five patients were aphakic (Table 2) at the time of initial evaluation.

Intracapsular cataract extraction under local anesthesia was performed on three eyes of three patients (cases 7, 8, 9, Table 1) whose visual acuity was reduced by lens opacities, the density of which was compatible with a visual acuity of 20/200 or less. Following alpha chymotrypsin, the lens was extracted without loss of vitreous using a lens loop and counterpressure below.

Each of the three extracted lenses was fixed in its entirety in 4% glutaraldehyde in 0.15 M phosphate buffer for 24 hr at room temperature. After gross examination of the entire lens using a dissecting microscope and photographic documentation of the appearance of the lens, the lens was divided into two halves. One half was dehydrated in ethyl alcohol and embedded in glycol methacrylate. Sections cut at 1-3 μm were stained with toluidine blue, hematoxylin-eosin, and periodic acid-Schiff reaction for light microscopy. Small pieces of the second half measuring less than 0.5 mm² were dissected from various portions of the lens and postfixed in 1% osmium tetroxide for 1 hr, dehydrated in ethanol, and embedded in an epoxy resin. Ultrathin sections were examined by transmission electron microscopy.

The remaining lens tissue from the second half was stored in a 10% formalin solution and later studied by scanning electron microscopy. Lens fibers at several locations were gently teased off while the tissue was in the storage solution, washed well in distilled water, dehydrated in a critical point dryer, coated with gold palladium, and examined by scanning electron microscopy.
Table 1. Phakic patients with gyrate atrophy

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Plasma ornithine (μM)</th>
<th>Cataract surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 LM</td>
<td>12</td>
<td>F</td>
<td>720</td>
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<td>2 TK</td>
<td>19</td>
<td>M</td>
<td>900</td>
<td>X</td>
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<td>3 SR</td>
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<td>F</td>
<td>896</td>
<td>X</td>
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<td>X</td>
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<td>F</td>
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<td>X</td>
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<td>6 PS</td>
<td>31</td>
<td>F</td>
<td>876</td>
<td>X</td>
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<tr>
<td>7 RP</td>
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<td>700</td>
<td>X</td>
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<tr>
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<td>M</td>
<td>1006</td>
<td>X</td>
</tr>
<tr>
<td>9 JO</td>
<td>47</td>
<td>F</td>
<td>656</td>
<td>X</td>
</tr>
</tbody>
</table>

* Cataract not used for histologic study.

Results

Clinical Appearance of the Cataract

Nine phakic GA patients (18 eyes) were examined (Table 1). Varying degrees of posterior sutural opacities were noted in all lenses except the right eye of the youngest patient (case 1). Clinical photographs from selected patients in this series are representative of the different stages of the lens opacities. The earliest lens changes were noted in the left eye of case 1, age 12 years (Fig. 1A). Punctate opacities were located in the posterior cortex of the lens at the confluence of the sutures just within the posterior line of disjunction in the axial region. As the opacities increase in density at the posterior axial region as determined

Table 2. Aphakic patients with gyrate atrophy

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at cataract extraction (year)</th>
<th>Plasma ornithine (μM)</th>
<th>Current age (year)</th>
</tr>
</thead>
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<tr>
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<td>953</td>
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<td>13 WI</td>
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<tr>
<td>14 LT</td>
<td>28</td>
<td>665</td>
<td>62</td>
</tr>
</tbody>
</table>

Fig. 1. A, Case 1, age 12, left eye. Earliest lens opacities. The punctate opacities are most prominent along the posterior suture lines. B, Case 4, age 28, right eye. Increased density of lens opacity in the posterior axial region. C, Case 4, age 28, left eye. The opacities spread beneath the posterior capsule along the sutures. D, Case 9, age 48, right eye. The progression of cataract occurs with both an increase in density in the axial region posteriorly and along the sutures. Noteworthy is the rather symmetrical arrangement of the opacities.
by biomicroscopic examination, lens opacities were noted to spread beneath the posterior capsule and along the sutures with some extension more deeply into cortex. This was best seen in case 4 age 28 years in the right (Fig. 1B) and left (Fig. 1C) eyes. In a more advanced stage, the lens opacities increased in density both along the sutures as well as in the axial region posteriorly. This was clearly visualized in case 9, age 47 years (Fig. 1D). On careful biomicroscopic examination, it was felt that the visual acuity was affected primarily by increased density of the lens opacities located in the posterior axial region with little involvement of the anterior cortex or nucleus.

Gross Appearance of the Cataract in Vitro

Gross appearances of the three lenses in the present study were similar to each other. The size and shape of the lenses were considered to be within normal limits and were moderately brown in color.

All lenses had randomly distributed opaque patches of varying sizes in the superficial anterior cortex, but the most striking finding was the marked opacification in the posterior cortex primarily along the sutures that contained sharply refractile small granules and extended toward the equator of the lens and were confined to the posterior cortex. Examination of the cut surface of the lens indicated the opaque zone in the posterior pole to be a few hundred microns thick with sparing of a thin clear zone beneath the posterior capsule. The nuclear zone was translucent.

Histologic Examination

The microscopic appearance of the three lenses in the present study were strikingly similar to each other so that descriptions of any one lens applies to all three. The posterior lens opacities seen in vivo and in vitro in all three lenses were clearly identified histologically as liquified and degenerated lens material in the region of the posterior sutures (Fig. 2). The lens fibers adjacent to the posterior sutures were degenerated also, and their cell membranes were not intact. The denatured lens protein substances that were in the region of the posterior sutures formed aggregates of various size and density. The fine structure of this material as seen by transmission and scanning electron microscopy in the most dense lens opacities was not distinguishable from cataractous changes related to aging or other causes.

Of additional interest was the marked extension of the lens epithelium toward the posterior pole, well beyond the equator, and the markedly thickened capsule to which thick zonular fibers were still attached (Fig. 3). Electron microscopy revealed that the thickened capsule consisted of two layers (Fig. 4). The inner, thicker layer was located immediately adjacent to the epithelium overlying the anterior and posterior
Fig. 3. Posterior lateral zone of the lens (case 7, Table 1). The epithelium has extended beyond the equator (upper right corner), and ends without forming the bow (arrow). The capsule is markedly thickened. The lens fibers in the equatorial cortex appear normal (periodic acid = Schiff, 200X).

Fig. 4. Posterior center zone of the lens (case 8, Table 1). The capsule consists of two layers: inner (IL) and outer (OL) layers. The inner layer is composed of multiple basal laminae and fine filaments, and the outer layer is made of homogeneous fine granular substances. Lens cells in the superficial zone are either dense or swollen and have retained their microorganelles. Cells in the deeper zone (*) have liquified (electron microscopy, 11,000X).
lens fibers and consisted of lamellar layers of basal lamina substance. Between the layers of basal laminae, which measured about 1 to 5 microns, small amounts of fine filaments measuring about 25Å in diameter were noted. The filaments were often aggregated to form small bundles. The thickness of this inner layer was variable, measuring about 20–150 microns anteriorly and about 3–10 microns posteriorly. The outer layer had the structure of normal capsule, within a uniform thickness of 10 microns anteriorly and 3 microns posteriorly.

**Discussion**

Although posterior subcapsular cataract has been associated with some forms of inherited retinal degeneration, it is not a consistent finding. By contrast, cataractous lens changes appear to occur in all GA patients. This was confirmed in our series of 14 patients, all of whom had significant lens opacities. In addition GA patients appear to develop lens opacities at a younger age than would be expected (Table 1), and although there is some variability in the rate of progression of opacification, the age at the time of cataract extraction is younger than usual (Tables 1, 2). In Usher's syndrome in which 48 patients were studied, mild lens opacities were noted primarily in the older patients with only two aphakia patients aged 50 and 69. A recent publication indicated that the overall frequency of posterior subcapsular cataract in 291 patients with various forms of hereditary retinal degeneration was only 41%. Noteworthy was the fact that many older patients with autosomal dominant, autosomal recessive, and isolated retinitis pigmentosa showed no evidence of cataract. This is in sharp contrast to the experience with GA patients.

The unique histologic characteristic in the three cataracts from patients with GA was the markedly enlarged spaces at the site of the posterior sutures. These spaces, filled with denatured lens protein material followed the pattern of the posterior sutures and corresponded to lens opacities observed in vivo and in vitro. In congenital cataract in animals, inadequate elongation of the lens cell leads to widening of the sutures. In the cataracts associated with GA, it appears as if the posterior portion of the lens cell fails to undergo a normal amount of elongation and is too short to form a normal tight suture line, thus creating a wide space in this region. The lens fibers adjacent to the widened spaces at the suture lines degenerate and denatured lens protein deposited in the spaces forms the lens opacity. Whether these lens alterations are secondary to retinal changes or are a direct result of deficiency of OAT is not clear. The extension of the epithelium posteriorly and marked thickening of the capsule suggest that these abnormal epithelial cells have been stimulated to produce excessive basal lamina substance following an initial period of normal capsule formation. The uniform thickening of the capsule in this disease is different from localized proliferation of the epithelial cells and capsule that is common in senile cataract. However, this capsule thickening appears to be similar to that described by Eshagian in a cataract from a 55-year-old patient with retinitis pigmentosa. The thin but structurally normal lens capsule in the outer zone of the thickened capsule may represent material produced normally pre partum.

Some of the nonspecific histologic changes observed in these cataractous lenses of patients with gyrate atrophy appear similar to changes of senile cataract such as sparseness and attenuation of the anterior epithelial cells, swelling, and nonspecific degeneration of the fiber cells.

Although a direct toxic effect of excessive ornithine has been demonstrated in the case of retinal pigment epithelium following intravitreal injection of ornithine solutions in experimental animals, no cataractous changes were noted in these animals except for occasional swelling of equatorial epithelial cells. The changes occurring in the patients appear to be the results of a much more chronic process.

**Key words:** gyrate atrophy, cataract, histology

**Acknowledgment**

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**References**