Retinitis Pigmentosa Associated With Fuchs’ Heterochromic Uveitis

Itay Chowers, MD; Ehud Zamir, MD; Eyal Banin, MD, PhD; Saul Merin, MD

Objective: To investigate whether the combination of Fuchs’ heterochromic uveitis (FHU) and retinitis pigmentosa (RP) in the same patient is coincidental or represents a true association.

Methods: We have examined the frequency of FHU in 338 patients with RP and in 1984 patients who were seen in our primary care ophthalmic clinic because of reasons other than RP.

Results: Of 338 patients with RP, 4 (1.2%) had the typical findings of FHU. Three of them had Usher syndrome type II, and 1 had RP simplex. By contrast, only 1 patient in the control group had FHU (5%), and the difference in the frequency of FHU between the 2 groups was significant (P = .002, Fisher exact test).

Conclusions: Fuchs’ heterochromic uveitis is associated with RP. Since autoimmune phenomena have been previously described in patients with RP, it is conceivable that RP predisposes to the development of FHU.

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The etiology of Fuchs’ heterochromic uveitis (FHU) is unknown.1 Eight patients with both FHU and retinitis pigmentosa (RP) have been previously described in the literature.2–4 However, it is unclear whether the combination of RP and FHU is coincidental or represents a true association. To study the possible association between RP and FHU, we assessed the prevalence of FHU in a large cohort of patients with RP as compared with a control group.

RESULTS

Of the 338 patients with RP, 150 had RP simplex, 141 had autosomal recessive RP, 32 had autosomal dominant RP, and 15 had X-linked RP. Systemic syndromes associated with RP (such as Usher syndrome) were found in 43 patients. The study group included 158 women and 180 men, and the mean±SD patient age was 46±16.6 years (range, 6-93 years).

Four of the 338 patients with RP had the typical findings of FHU. None of them had other factors that may be associated with FHU, such as congenital toxoplasmosis, history of trauma, Horner syndrome, or positive family history for FHU.1 The RP was symmetric in all 4 cases, but patient 4 had a more severe maculopathy in the left eye. Data for these patients are summarized in the Table. All 4 had the typical findings of FHU as described here. Three patients developed posterior subcapsular cataracts that necessitated cataract extraction and 1 patient had ocular hypertension (Figure 1). Course of RP was typical for the disease (Figure 2), with extinct electroretinogram and constriction of the visual fields to less than 20° on the Goldmann V4e isopter in all 4 patients. Patient 1 and patient 4 had 1 and 3 siblings, respectively, who were affected by Usher syndrome type II but did not manifest FHU.

The control group included 1052 females and 932 males, and the mean±SD patient age was 47±23.4 years (range, 6-92 years). Fuchs’ heterochromic uveitis was diagnosed in a single patient in the control group. The difference in the occurrence of FHU between the controls and patients with RP was significant (P = .002, Fisher exact test).

COMMENT

Fuchs’ heterochromic uveitis has been previously described in 8 patients with RP. Five of those patients had RP simplex, 2 had autosomal dominant RP, and 1 had au-
tosomal recessive RP. Fuchs’ heterochromic uveitis in those patients was typical, except that the 2 autosomal dominant RP cases were a father and son. Whether the phenomenon of both FHU and RP in the same patient is coincidental or represents a true association was a matter of debate. This question could not be decided, since all previous reports included case description alone. Our data from a controlled study clearly show, for the first time, that FHU was indeed associated with RP in our cohort. Furthermore, since 3 of our 32 patients with Usher syndrome type II had FHU, it seems that FHU is even more common in patients with Usher syndrome type II than in other patients with RP.

To explain the relatively high incidence of FHU in patients with RP, the pathogenesis of FHU and the inflammatory features of RP should be considered. Histological sections from eyes with FHU show inflammatory reaction that is predominated by lymphocyte and plasma-cell infiltration. In addition, several immune abnormalities have been described in FHU, among them the existence of autoantibodies to a corneal antigen, oligoclonal immunoglobulin G (IgG) in the anterior chamber, circulating immune complexes, and reduced activity of suppressor T-cell lymphocytes. Therefore, activation of both T-cell and B-cell lymphocytes seems to play a role in FHU. However, anterior chamber antigens that are the target of the immune response, other than the aforementioned corneal antigen, have not been identified so far.

Patients with RP and patients with uveitis show several common clinical and laboratory inflammatory features. Among these are vitreal cellular infiltrations, cataract, leakage from retinal blood vessels with retinal edema, and, rarely, retinal neovascularization. Both cell-mediated and humoral autoimmune responses to retinal antigens were found in patients with RP. For example, it was demonstrated that some patients with RP have circulating B cells reactive with retinal antigens; it was speculated that these cells represent immature plasma cells. It is unclear whether such autoimmune reactions

### Patient Data

<table>
<thead>
<tr>
<th>Patient No./Age, y/Sex</th>
<th>RP Type</th>
<th>Age at Diagnosis, y</th>
<th>Eye Affected by FHU</th>
<th>Complications</th>
<th>Treatment</th>
<th>Best-Corrected Visual Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RP</td>
<td>FHU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/33/F</td>
<td>Usher type II</td>
<td>15</td>
<td>Left</td>
<td>PSC cataract</td>
<td>Cataract extraction</td>
<td>6/6</td>
</tr>
<tr>
<td>2/31/F</td>
<td>Usher type II</td>
<td>21</td>
<td>Right</td>
<td>PSC cataract</td>
<td>Cataract extraction</td>
<td>6/12</td>
</tr>
<tr>
<td>3/42/M</td>
<td>RP simplex</td>
<td>20</td>
<td>Right</td>
<td>HTN</td>
<td>0.5% Timolol</td>
<td>6/9</td>
</tr>
<tr>
<td>4/36/F</td>
<td>Usher type II</td>
<td>18</td>
<td>Left</td>
<td>PSC cataract</td>
<td>Cataract extraction</td>
<td>6/36</td>
</tr>
</tbody>
</table>

*RP indicates retinitis pigmentosa; FHU, Fuchs’ heterochromic uveitis; PSC, posterior subcapsular; HTN, ocular hypertension; and HM, hand movements.

Figure 1. Right (left) and left (right) iris of patient 2. Marked hypochromia and posterior subcapsular cataract are evident in the right eye.
are primary or secondary to the dystrophic process. However, it is interesting to note that inflammatory activity, when present in patients with RP, is similar to that in FHU in being low-grade and chronic. It is possible that autoimmunity against ocular antigens in patients with RP may lead to an increased risk for ocular inflammation. Although phenotypically similar to other patients with RP, it is possible that certain RP subtypes, such as Usher type II, are more susceptible to FHU because of a higher inflammatory tendency.

We speculate that the tendency for autoimmune reactions in patients with RP could be the cause for their increased susceptibility to develop FHU. Patients with RP may develop autoimmune reactions to anterior chamber antigens that are similar to retinal antigens, leading to the clinical manifestation of FHU. However, since most patients with RP do not suffer from FHU, and since FHU in patients with RP is unilateral, additional and yet unknown factors are possibly required to evoke FHU in patients with RP.

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Corresponding author: Itay Chowers, MD, Department of Ophthalmology, Hadassah University Hospital, PO Box 12000, Jerusalem 91120, Israel (e-mail: chowers@md2.huji.ac.il).

REFERENCES

A look at the past . . .

Loss of Vitreous — This is the most important complication. Much has been written minimizing loss of vitreous in the intracapsular operation, but it cannot be sufficiently stressed that any disturbance of vitreous is serious and should be avoided. It is not the amount that is so important; it is the presence of the hyaloid membrane in the incision, which interferes with the normal healing of the incision and leads to inflammatory changes in the eyeball. The more experience one gathers in cataract surgery, the greater respect one acquires for the vitreous.