Adenoma of the Ciliary Body Pigment Epithelium

The 1998 Albert Ruedemann, Sr, Memorial Lecture, Part 1

Jerry A. Shields, MD; Carol L. Shields, MD; Kaan Gündüz, MD; Ralph C. Eagle, Jr, MD

**Background:** Adenoma of the pigment epithelium of the ciliary body (CPE) is a rare neoplasm. Most reported cases have been misdiagnosed as ciliary body melanoma.

**Objectives:** To evaluate clinical features, management, pathological features, and prognosis of adenoma of the CPE and to determine clinical features that may differentiate it from ciliary body melanoma.

**Patients and Methods:** A retrospective review was performed of medical charts, photographs, and pathological features of patients with adenoma of the CPE who were treated by the authors.

**Results:** Of the 8 patients with adenoma of the CPE, 3 were male and 5 were female. Seven were white, and 1 was Asian. The mean age at diagnosis was 51 years (range, 8-73 years). The referring diagnosis was ciliary body melanoma in 7 patients and cyst in 1 patient. The lesions were all solitary and unilateral and ranged from 3 x 3 x 3 to 13 x 13 x 8 mm. Clinically, all tumors were gray to black, had abruptly elevated margins, and were dome shaped. Associated findings included secondary cataract (6 patients) and vitreous hemorrhage (1 patient). Results of ancillary studies such as transillumination, fluorescein angiography, and ultrasonography showed patterns that were helpful in differentiation from ciliary body melanoma. Fine needle aspiration biopsy, performed in 3 patients, was an accurate diagnostic adjunct. Microscopic diagnosis was adenoma of the CPE in 7 cases in which tissue was available. A consistent histopathologic feature was the presence of typical clear vacuoles within the tumor. One tumor invaded the sensory retina. Results of immunohistochemical studies were consistent with a tumor of neuroectodermal origin.

**Conclusions:** Adenoma of the CPE has characteristic features that may help differentiate it from ciliary body melanoma. In contrast to melanoma, it is generally darker and its margins are more abruptly elevated. Although it is benign cytologically, it can exhibit growth. If the diagnosis is suspected, removal of the tumor by local resection is advisable.

PATIENTS AND METHODS

The medical records of patients with the diagnosis of adenoma of the CPE seen by the Oncology Service, Wills Eye Hospital, Philadelphia, Pa, were reviewed. General data collected included patient age, sex, race, associated ocular disease, associated systemic disease, referring diagnosis, previous management, and history of ocular trauma or inflammation. Visual acuity, intraocular pressure, and ocular symptoms were noted. Tumor data included location, size (basal diameter and thickness in millimeters), surface features, color, secondary effects on adjacent structures, transillumination features, fluorescein angiographic findings, and ultrasonographic characteristics.

We assessed the cytologic results of fine needle aspiration biopsy (FNAB) (when performed) and results of histopathologic evaluation (when available). For patients who were treated with local resection or enucleation, microscopic slides were reviewed, and growth patterns, degree of pigmentation, local invasiveness, cellular atypia, mitotic activity, vascularity, and basement membrane formation were assessed and tabulated. The method and results of treatment were reviewed. Based on our observations, we make recommendations regarding the clinical diagnosis and management of adenoma of the CPE.

None of the 8 patients had a history of ocular trauma, and only patient 6 had clinical signs of iritis. The best corrected visual acuity (given in meters) in the affected eye ranged from 6/6 to 6/120 (Table 1). The tumor was located in the right eye in 5 patients and in the left eye in 3. In the 4 patients in whom visual acuity was 6/12 or worse, the decrease was due to secondary cataract in 3 patients and retinal detachment in 1 patient. Patient 6 had a history of neovascular glaucoma, and filtering surgery was considered in the right eye in 5 patients and in the left eye in 3. Patient 6 had a history of neovascular glaucoma, and filtering surgery was considered in the right eye in 5 patients and in the left eye in 3. The decrease was due to secondary cataract in 3 patients and retinal detachment in 1 patient. Patient 6 had a history of iritis. The best corrected visual acuity in the preoperative range.

Results of diagnostic FNAB, performed in 3 patients, disclosed cells compatible with a tumor of the pigment epithelium in all instances.

We treated 5 of the patients promptly with enucleation or local tumor resection without waiting to document growth, because the tumors were producing visual symptoms and because malignant melanoma was included in the differential diagnosis. In patient 8, we documented growth because treatment was refused, and the patient was followed up periodically. In patients 2 and 6, there has been no convincing growth after follow-up of 2 and 1 years, respectively. Ultimate tumor management consisted of enucleation in 2 patients, local resection in 3, and observation in 3. Our first patient (patient 1) was treated with enucleation in 1978, because ciliary melanoma was considered the most likely diagnostic possibility. She remains stable after 20 years. We subsequently began to recognize the typical features of adenoma of the CPE and recommended more conservative management. The 3 patients treated with iridocyclectomy have all maintained visual acuity in the preoperative range.

Table 1. Clinical Data on 8 Patients With Acquired Neoplasms of the Ciliary Body Pigment Epithelium*

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y/ Race</th>
<th>Year of Diagnosis</th>
<th>Visual Acuity†</th>
<th>Tumor Size, mm</th>
<th>Associated Findings</th>
<th>Management</th>
<th>FNAB cytologic Diagnosis</th>
<th>Histopathologic Diagnosis</th>
<th>Follow-up, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/27/W</td>
<td>1978</td>
<td>6/12</td>
<td>7 × 7 × 6</td>
<td>Cataract, SV</td>
<td>Enucleation</td>
<td>. . .</td>
<td>Adenoma</td>
<td>Stable, 20</td>
</tr>
<tr>
<td>2/F/54/W</td>
<td>1984</td>
<td>6/6</td>
<td>7 × 7 × 5</td>
<td>Cataract</td>
<td>FNAB, observation</td>
<td>Adenoma</td>
<td>. . .</td>
<td>Stable, 2</td>
</tr>
<tr>
<td>4/M/65/W</td>
<td>1991</td>
<td>6/60</td>
<td>5 × 5 × 5</td>
<td>Exudative RD</td>
<td>Resection</td>
<td>. . .</td>
<td>Adenoma</td>
<td>Stable, 7</td>
</tr>
<tr>
<td>5/F/73/W</td>
<td>1992</td>
<td>6/12</td>
<td>5 × 5 × 6</td>
<td>Cataract</td>
<td>Resection</td>
<td>. . .</td>
<td>Adenoma</td>
<td>Stable, 4</td>
</tr>
<tr>
<td>6/F/59/W</td>
<td>1996</td>
<td>6/120</td>
<td>10 × 10 × 5</td>
<td>Cataract, iris, glaucoma</td>
<td>FNAB, plaque, enucleation</td>
<td>Adenoma</td>
<td>Adenoma</td>
<td>Stable, 2</td>
</tr>
<tr>
<td>7/M/60/W</td>
<td>1996</td>
<td>6/6</td>
<td>5 × 5 × 3</td>
<td>Cataract</td>
<td>Observation</td>
<td>. . .</td>
<td>. . .</td>
<td>Stable, 1</td>
</tr>
<tr>
<td>8/F/8/A</td>
<td>1996</td>
<td>6/6</td>
<td>13 × 13 × 8</td>
<td>Cataract</td>
<td>FNAB, observation</td>
<td>. . .</td>
<td>Progressive cataract, tumor enlargement, visual acuity: finger counting</td>
<td></td>
</tr>
</tbody>
</table>

*FNAB indicates fine needle aspiration biopsy; F, female; M, male; W, White; A, Asian; SV, sentinel vessel; RD, retinal detachment; and ellipses, not applicable.  †In meters.
Patient 6 had a more aggressive tumor. It was diagnosed using results of FNAB, and she chose treatment with a radioactive plaque because she could not tolerate the general anesthesia required for local tumor resection. Subsequent vitreous hemorrhage prompted a vitrectomy in another institution, and the vitreous cells were interpreted by the local cytologist as compatible with melanoma. The eye was then enucleated, and the tumor proved to be an adenoma of the CPE, confirming our original diagnosis.

Pathological studies were performed after enucleation in 1 patient, FNAB in 2 patients, FNAB and enucleation in 1 patient, and local resection in 3 patients (Table 2). Grossly, the tumors usually had abruptly elevated margins and were deeply pigmented dark brown to black (Figure 1, C and D). Microscopically, they were all dome shaped or pedunculated, arising from the CPE on a small base (Figure 1, E and F). All 5 tumors that were studied histopathologically rested on the inner surface of the ciliary body and did not involve its stroma. They contained numerous characteristic round or oval clear vacuoles encompassed by cells whose cytoplasm was replete with large, spherical melanosomes (Figure 1, F and G). The vacuoles contained a hyaluronidase-resistant acid mucopolysaccharide. In some areas, the cells were less pigmented and consisted of large epithelial cells that rested on a basement membrane and contained uniform central nuclei and slightly prominent nucleoli (Figure 1, H). There was mild nuclear atypia, but mitotic figures were rare. Based on relatively bland cytologic features and only minimal local invasiveness, the 5 tumors were classified as adenoma of the CPE. The 3 tumors in which cytologic examination of FNAB specimens was performed all showed benign pigmented epithelial cells compatible with adenoma of the CPE. There were no cases of local tumor recurrence or metastasis.

**COMMENT**

Acquired neoplasms of the pigment epithelium are uncommon, and most information about these tumors has been derived from case reports or very small series of cases.5-14 We were very impressed with the differences in clinical appearance, clinical course, complications, and histopathologic features that we elected to describe each group separately. Hence, our group is reporting 20 tumors of the IPE, CPE, and RPE in separate articles. We herein described 8 patients with adenoma of the CPE, with emphasis on clinical features, clinical course, complications, and management.

Our literature review disclosed only a few case reports of neoplasms of the CPE.5-14 Unfortunately, the literature is confusing because some authors included tumors of the CPE under the inaccurate rubric of medulloepithelioma of the retina,5 and others have not made a distinction between tumors of the CPE and the nonpigmented ciliary epithelium.11 Most reported cases were classified as adenomas, and only rarely have the authors identified sufficient malignant histopathologic features to warrant classification as adenocarcinoma.11 We classified all of our cases as adenoma, based on clinical, histopathologic, and cytopathologic features. Our series, combined with a literature review, has provided information to allow generalizations about adenoma of the CPE and to define features of this tumor that help differentiate it from ciliary body melanoma.

Adenoma of the CPE usually is a tumor of adulthood. There have been occasional reports of tumors of the CPE in young children, but these generally have occurred in eyes with other congenital malformations, and probably represent unusual congenital rather than acquired lesions.15-17 The tumors in adults are generally solitary and unilateral, and there is no predilection for laterality. All of these patients have been white, but there is insufficient information to determine if there is a racial predisposition. Of our 8 patients, 7 were white.

Hyperplasia of the pigment epithelium occasionally can arise from inflammatory or traumatic scars.1-2,18 Only 1 of our 8 patients (patient 6) had signs of mild intraocular inflammation, and its relationship to the intraocular tumor is uncertain. Based on our observations, we believe that most adenomas of the CPE arise in otherwise normal eyes, but it is possible that ocular trauma and inflammation could be predisposing factors in some
CPE is ciliary body melanocytoma. It arises from the uveal stroma and often directly impinges on the vitreous with adenoma because the adenoma arises internal to the vitreous cells or vitreous hemorrhage are more often seen most cases of adenoma of the CPE. In addition, pigmented monly observed in choroidal melanoma, are not seen in CPE has abruptly elevated margins that arise perpendicul-
larly from the CPE. It lacks the surrounding pigmented base that is seen with most melanomas. Although adenoma of the CPE can be abruptly elevated or pedunculated, it does not have a classic mushroom or collar-button configura
tion with B-scan (Figure 2). In contrast, a melanoma characteristically shows low to medium internal reflectivity and acoustic hollowness. During transillumination, adenoma of the CPE typically casts a dense shadow similar to that seen with pigmented ciliary body melanoma. Although magnetic resonance imaging has been reported in a case of presumed adenoma of the CPE, we do not believe that it helps differentiate this tumor from ciliary body melanoma.

Results of FNAB can assist in the diagnosis of adenoma of the CPE. The procedure generally should be reserved for cases where there is uncertainty about the diagnosis of an intraocular tumor and where microscopic diagnosis is necessary to make a therapeutic decision. It also requires close cooperation with an experienced cytopathologist. We did not recommend FNAB when we planned to remove the tumor using local resection, since FNAB would be an unnecessary step. When FNAB was performed (in patients 2, 6, and 8), the results were helpful in directing further management.

Another tumor that can be similar to adenoma of the CPE is ciliary body melanocytoma. It arises from the uveal stroma rather than the CPE, and it is a homogeneous dark brown to black lesion. It can also undergo necrosis and produce seeding into the overlying vitreous cavity. In some cases, the clinical differentiation of melanocytoma from adenoma of the CPE may be impossible.

Fluorescein angiography and ultrasonography are difficult to perform on adenoma of the CPE because of its peripheral location. It is our impression, however, that the results of these studies differ from those seen with melanoma. Since the adenoma arises from the CPE rather than the choroid, it lacks the double circulation that typifies pedunculated melanoma. Results of ultrasonography generally show high reflectivity with A-scan and acoustic solidity with an abruptly elevated, domed configuration with B-scan (Figure 2). In contrast, a melanoma characteristically shows low to medium internal reflectivity and acoustic hollowness. During transillumination, adenoma of the CPE typically casts a dense shadow similar to that seen with pigmented ciliary body melanoma. Although magnetic resonance imaging has been reported in a case of presumed adenoma of the CPE, we do not believe that it helps differentiate this tumor from ciliary body melanoma.

Table 2. Data on 7 Patients With Microscopic Diagnosis of Adenoma of Ciliary Body Pigment Epithelium*

<table>
<thead>
<tr>
<th>Patient No.†</th>
<th>Procedure</th>
<th>Pattern</th>
<th>Pigment‡</th>
<th>Local Invasion</th>
<th>Nuclear Atypia‡</th>
<th>Basement Membrane§</th>
<th>Prominent Vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Enucleation</td>
<td>Vacuolated</td>
<td>4</td>
<td>None</td>
<td>4</td>
<td>0</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>FNAB</td>
<td>. . . . . .</td>
<td>. . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
</tr>
<tr>
<td>3</td>
<td>Resection</td>
<td>Vacuolated</td>
<td>4</td>
<td>Retina</td>
<td>1</td>
<td>0</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>Resection</td>
<td>Vacuolated</td>
<td>3</td>
<td>None</td>
<td>1</td>
<td>1</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Resection</td>
<td>Vacuolated</td>
<td>4</td>
<td>None</td>
<td>2</td>
<td>0</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Enucleation</td>
<td>Vacuolated</td>
<td>3</td>
<td>. . . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
</tr>
<tr>
<td>7</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
</tr>
<tr>
<td>8</td>
<td>FNAB</td>
<td>. . . . . .</td>
<td>. . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
<td>. . . . . .</td>
</tr>
</tbody>
</table>

* FNAB indicates fine needle aspiration biopsy; ellipses, not done because of type of biopsy or limited information.
† Numbers are given in Table 1.
‡ Described on a scale of 1 to 4, in which 1 indicates minor involvement; 4, major involvement.
§ Described on a scale of 0 to 2, in which 0 indicates none identified; 1, mild involvement; and 2, marked involvement.

©1999 American Medical Association. All rights reserved.
Posterior RPE. However, tumors of the more peripheral CPE (medulloepitheliomas) frequently recur after local surgical resection. In contrast, congenital tumors of the nonpigmented ciliary epithelium (medulloepithelioma associated with persistent hyperplastic primary vitreous) are small, extremely rare tumors with similar clinical and pathological features that vary little from case to case. Microscopically, it consists of a solid proliferation of bland pigment epithelial cells that can display mild nuclear atypia, but contain few mitotic figures. A characteristic feature consistently seen in our patients was the presence of myriad small, clear microcysts that contained a hyaluronidase-resistant acid mucopolysaccharide. Such cysts usually are not found in tumors of the IPE or the posterior RPE. However, tumors of the more peripheral RPE may have such microcysts, similar to those seen in our patients.

Finally, we should comment on the differences that we have observed among tumors of the IPE, CPE, and RPE. Tumors of the IPE generally are small, tend to be stable, and rarely require treatment. Tumors of the RPE tend to be considerably more aggressive and can demonstrate growth, invasion of the sensory retina, dilated retinal feeder blood vessels, exudative retinal detachment, hemorrhage, phthisis, and occasional orbital extension.

This study has provided information about the clinical features and clinical course of adenoma of the CPE. This tumor can demonstrate slow progression and can produce progressive cataract and other complications. We believe that the diagnostic guidelines set forth herein will assist the clinician in the diagnosis and management of this unusual neoplasm.

Accepted for publication January 6, 1999.

This study was supported by the Eye Tumor Research Foundation, Philadelphia, Pa; the Award of Merit in Retina Research, Houston Tex (Dr J. A. Shields); the Macula Foundation, New York, NY (Drs C. L. Shields and Gündüz); and the Noel and Sarah Simmonds Endowment for Ophthalmic Pathology, Wills Eye Hospital, Philadelphia (Dr Eagle).


Reprints: Jerry A. Shields, MD, Oncology Service, Wills Eye Hospital, 900 Walnut St, Philadelphia, PA 19107.

REFERENCES