Adenoma of the Ciliary Body Pigment Epithelium

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

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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 $3 \times 3 \times 3$ to $13 \times 13 \times 8$ 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.


The pigment epithelia of the iris (IPE), ciliary body (CPE), and retina (RPE) can undergo reactive proliferation and migration. However, true neoplasms of the pigment epithelia are rare. We reviewed our personal experience with tumors of the pigment epithelium and have found considerable differences clinically and histopathologically among tumors that arise from the IPE, CPE, and RPE. Because of these differences, our group is reporting our series of tumors of the IPE (20 cases) and RPE (13 cases) in separate articles. Most reports of tumors of the CPE have been case descriptions or very small series. We herein report our experience with 8 cases of adenoma of the CPE and describe the clinical and histopathologic characteristics of this tumor, with emphasis on those features that help differentiate adenoma of the CPE from ciliary body melanoma.

RESULTS

There were 8 patients with adenoma of the CPE (Table 1). Patients 1 and 3 have been described previously. The mean age at diagnosis was 51 years (range, 8-73 years; median, 56 years). Three patients were male and 5 were female. Seven patients were white and 1 patient was Asian. The referring diagnosis was ciliary body melanoma in 7 patients and cyst in 1 patient. None of the patients had serious systemic disease.
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 recommended when the tumor was recognized. In patient 4, who had a retinal detachment, the tumor was noted at the time of retinal reattachment surgery, prompting referral to us.

The epicenter of the tumor was inferotemporal in 3 patients, inferior in 2 patients, inferonasal in 1 patient, nasal in 1 patient, and superotemporal in 1 patient. The tumor was dark gray to black in all patients, and it clearly originated from the ciliary body (Figure 1, A). All tumors were dome shaped and had abruptly elevated margins, but none had a mushroom-shaped configuration. The surface features of the tumors ranged from smooth to irregular with no consistent pattern. One tumor (patient 3) had prominent blood vessels near its surface that were the source of overlying vitreous hemorrhage (Figure 1, B).

A variety of ancillary procedures were used. Results of transillumination showed blockage of light by tumors. Fluorescein angiography was difficult to perform due to the peripheral location of the mass. Ultrasonography was also technically difficult to perform, but was performed in all cases. Results showed an acoustically solid, abruptly elevated, dome-shaped mass with B-scan and high internal reflectivity with A-scan (Figure 2). 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.

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<th>Patient No./</th>
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<th>Year of Diagnosis</th>
<th>Tumor Size, mm</th>
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* 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.

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

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Adenoma of the CPE usually is a tumor of adult-hood. 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 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.\(^{5-14}\) When we reviewed our personal experience with acquired neoplasms of the pigment epithelia, we intended to report all tumors of the IPE, CPE, and RPE in a single article. While collecting the data, however, we were so 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\(^3\) and 13 tumors of the RPE\(^4\) 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.\(^3,13-14\) Unfortunately, the literature is confusing because some authors included tumors of the CPE under the inaccurate rubric of medulloepithelioma of the retina,\(^3\) 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 adult-hood. The tumors in 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 cases.
CPE is ciliary body melanocytoma. It arises from the uveal stroma and often directly impinges on the vitreous. It does not have a classic mushroom or collar-button configuration that is occasionally seen with peripheral choroidal melanomas. Prominent tumor blood vessels, which are brown and somewhat less pigmented, may be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or pedunculated, it is generally dark gray or black, whereas most melanomas of the CPE can be abruptly elevated or 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tial lamellar iridocyclectomy. The 3 patients in our series who underwent local surgical removal have retention of visual acuity and no serious complications. Similar results have been achieved with adenoma of the nonpigmented ciliary epithelium. In contrast, congenital tumors of the nonpigmented ciliary epithelium (medulloepitheliomas) frequently recur after local surgical resection.

Pathologically, adenoma of the CPE has typical features that vary little from case to case. Grossly, it is a dark gray to black mass that arises abruptly from the underlying CPE and rests on the inner surface of the ciliary body without stromal involvement. 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.

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