Acquired Tumors Arising From Congenital Hypertrophy of the Retinal Pigment Epithelium

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Background: Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is widely recognized to be a flat, stationary condition. Although it can show minimal increase in diameter, it has not been known to spawn nodular tumor that is evident ophthalmoscopically.

Objectives: To report 5 cases of CHRPE that gave rise to an elevated lesion and to describe the clinical features of these unusual nodules.

Methods: Retrospective medical record review.

Results: Of 5 patients with a nodular lesion arising from CHRPE, there were 4 women and 1 man, 4 whites and 1 black. Three patients were followed up for typical CHRPE for longer than 10 years before the tumor developed; 2 patients were recognized to have CHRPE and the elevated tumor concurrently. Visual acuity was decreased in 3 patients, mainly due to cystoid macular edema. The tumor was located between the equator and ora serrata in all 5 patients. There was no predilection for quadrant of the fundus. The flat part of the lesion was black and had visible lacunae in all 5 patients. The CHRPE ranged in basal diameter from $3 \times 3$ mm to $13 \times 11$ mm. The size of the elevated lesion ranged from $2 \times 2 \times 2$ mm to $8 \times 8 \times 4$ mm. The nodular component in all cases was supplied and drained by slightly prominent, non-tortuous retinal blood vessels. Yellow retinal exudation occurred adjacent to the nodule in all 5 patients and 1 patient developed a secondary retinal detachment. Two tumors that showed progressive enlargement, increasing exudation, and progressive visual loss were treated with iodine 125-labeled plaque brachytherapy, resulting in deceased tumor size but no improvement in the visual acuity.

Conclusions: Congenital hypertrophy of the retinal pigment epithelium can spawn a nodular growth that slowly enlarges, attains a retinal blood supply, and causes exudative retinopathy and chronic cystoid macular edema. Although no histopathologic evidence is yet available, we believe that the tumor probably represents either an acquired adenoma or a reactive proliferation of the retinal pigment epithelium. The best treatment of these lesions is not yet established.
**PATIENTS AND METHODS**

We performed a review of all patients seen by the Ocular Oncology Service, Wills Eye Hospital, Philadelphia, Pa, who had been coded as having CHRPE and who developed a solid, elevated nodule that arose from the flat component of the lesion. All patients provided informed consent for inclusion in this study. We determined the age, race, sex, visual acuity, location and color of the lesion, associated macular changes, size of the CHRPE, size of the associated nodular tumor, presence of retinal feeder blood vessels and exudation, and follow-up data.

suring $2 \times 2 \times 2$ mm at ultrasonography. The patient continues to have yearly ophthalmic examinations.

**CASE 2**

A 54-year-old black woman was found in April 1995 to have a pigmented lesion at the equator superonasally in the left eye measuring $5 \times 4$ mm in diameter. Most of the lesion was flat with a well-defined border, depigmented lacunae, and marginal light halo, compatible with CHRPE. Arising from the anterior edge of the flat component of the lesion was a black nodule that measured $2 \times 2$ mm in basal dimensions and 2 mm in thickness. Minimally dilated retinal blood vessels appeared to feed and drain the nodule and circinate exudation was present around the base of the nodule (Figure 2). By April 1998, the flat component of the lesion was unchanged, but the elevated nodule had enlarged slightly and there was more yellow intraretinal exudation.

**CASE 3**

In 1984, a 47-year-old white woman was found to have a pigmented equatorial lesion inferonasally, consistent with CHRPE. In 1988, a black nodule, measuring $2 \times 2 \times 2$ mm was noted on the anterior margin of the flat lesion (Figure 3, A). The nodule had retinal feeding and draining blood vessels, yellow intraretinal exudation, and overlying vitreous inflammatory cells and erythrocytes along its anterior border. By June 1991, the elevated lesion measured $6 \times 5 \times 4$ mm (Figure 3, B). B-scan ultrasonography showed an elevated lesion with acoustic solidity, no choroidal excavation, and a secondary retinal detachment (Figure 3, C). Because of tumor enlargement, exudation, retinal detachment, and hemorrhage, the patient was treated with $^{125}$I-plaque brachytherapy in July 1992. In May 1997, her visual acuity was 3/400 OS and tumor thickness had decreased to 1.9 mm at ultrasonography. The cystoid macular edema and exudation persisted.

**CASE 4**

A 42-year-old white man was found in October 1994 to have finger counting vision and a tumor in his right eye. Near the equator inferonasally was a black mass with a well-defined flat portion measuring $6 \times 6$ mm and a dome-shaped portion that measured $3 \times 3 \times 3$ mm arising from the anterior margin of the flat lesion (Figure 4). Our diagnosis was presumed adenoma of the RPE arising from CHRPE. Because the cystoid macular edema and visual loss were most likely secondary to the tumor, the patient was treated with $^{125}$I-plaque brachytherapy. In August 1995, visual acuity was light perception in the right eye and severe cystoid macular edema was still present.

**CASE 5**

A 63-year-old white woman with a history of branch retinal vein obstruction in the right eye was found in January 1997 to have a $13 \times 11$-mm, well-defined CHRPE lesion in the superior equatorial region of the same eye, with an $8 \times 8 \times 4$-mm light brown mass arising from its anterior aspect (Figure 5). The foveal area showed mottling of the RPE, mild preretinal vitreous fibrosis, and slight cystoid macular edema. The nodule was supplied by mini-
mally dilated retinal blood vessels. In April 1999, the lesion was slightly larger, measuring 4.3 mm in thickness.

RESULTS

A tabulation of the most pertinent information on these 5 patients is listed in the Table. There were 4 women and 1 man, 4 white and 1 black patient. The mean age at the time of diagnosis of the CHRPE was 46 years (age range, 24-63 years). The mean age at the time of diagnosis of the elevated tumor was 50 years (age range, 42-63 years). Two of the patients (cases 1 and 3) had been recognized to have typical flat solitary CHRPE before the elevated nodule (4 and 18 years, respectively). The other 3 patients (cases 2, 4, and 5) had simultaneous diagnosis of the flat CHRPE and the elevated lesion. The right eye was affected in 3 patients and the left eye in 2 patients. The meridional location of the fundus lesion was superior in 1 patient, superonasal in 1 patient, inferonasal in 2 patients, and temporal in 1 patient. The initial visual acuity in the affected eye ranged from 6/6 to finger counting. The nodular component of the lesion was black in 4 patients (cases 1 through 4) and light brown in 1 patient (case 5). The 3 patients with worse than 6/6 visual acuity all had cystoid macular edema and 2 patients had surface wrinkling retinopathy. The size of the flat CHRPE component ranged from 5 × 4 mm to 13 × 11 in basal dimensions.

There were several important associated retinal findings. As mentioned previously, 3 patients had cystoid macular edema and 2 patients had surface wrinkling retinopathy. All of these changes were remote from the main
pigmented lesion, but there were no other evident causes for the macular changes. Minimally dilated, nontortuous feeder and drainer blood vessels were identified entering and exiting the tumor in all 5 patients. Some amount of yellow intraretinal exudation was also evident adjacent to the nodule in all 5 cases. One patient (case 3) had a secondary localized exudative retinal detachment.

Ultrasonography, performed in all 5 patients, showed an abruptly elevated, round mass in all cases with high internal reflectivity with A-scan and acoustic solidity without choroidal excavation with B-scan (Figure 3, C). Spontaneous vascular pulsations were not clearly seen in any of the tumors.

Another consistent finding with this fundus condition is the development of a slightly prominent, nontortuous retinal artery and vein that supply and drain the nodular portion of the lesion, supporting the observation that the lesion has extended to involve the sensory retina. The occurrence of yellow intraretinal exudation around the nodule suggests that it contains hyperpermeable blood vessels, presumably derived from the sensory retina. Our recent study on acquired neoplasms of the RPE, which did not include the cases reported here, revealed that those RPE tumors can assume a retinal blood supply and produce exudative retinopathy. A presumed adenoma arising from CHRPE should be added to the list of lesions that can cause exudative retinopathy.

The CHRPE in these cases was located at or anterior to the equator in all 5 of our patients and the nodular growth usually occurred near the anterior margin of the CHRPE. This made it difficult to obtain clear fundus photographs of the lesions.

The microscopic features of the tumors described in this article are still unknown. Possibilities include acquired adenoma of the RPE, reactive hyperplasia of the affected RPE, secondary form of retinal vasoproliferative tumor, and choroidal melanoma.

An acquired neoplasm of the RPE (adenoma) generally occurs in otherwise normal eyes of patients who have not had prior ocular trauma or inflammation. It appears clinically as a dome-shaped pigmented mass that often assumes a retinal blood supply and induces intraretinal exudation. In that sense, reported cases of adenoma and adenocarcinoma of the RPE have been similar to the lesions described here, with the exception that they have not had typical CHRPE at their base. It is possible that some reported cases of adenoma of the RPE actually arose from CHRPE, which eventually became obscured by the overlying neoplasm.

Reactive hyperplasia of the RPE is best known to develop in traumatized or inflamed eyes. Usually there is a history or clinical findings of such prior insults. None of our patients had a history or ocular findings to suggest inflammation or trauma. It is possible that CHRPE, which was clearly evident in our patients, could spawn reactive hyperplasia of the RPE. In a histopathologic study of a case of flat CHRPE, Wirz et al noted a small focus of associated hyperplasia of the RPE. However, it had not assumed tumorous proportions.

The presumed acquired retinal hemangioma, more recently called “vasoproliferative tumor of the fundus,” is a recently described entity that can occur as a primary or sec-

### Data on Patients With Nodular Lesions Arising From Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE)*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age of Patient at Diagnosis, y</th>
<th>Visual Acuity</th>
<th>Status of Macula</th>
<th>Size, mm</th>
<th>Presence of RFV/Exudation</th>
<th>Duration of Follow-up, y</th>
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<td>63</td>
<td>6/15 6/18</td>
<td>13 × 11</td>
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*RFV indicates retinal feed vessels; CF, counting fingers; LP, light perception; CME, cystoid macular edema; and SWR, surface wrinkling retinopathy.
The secondary form develops in association with intermediate uveitis, retinitis pigmentosa, Coats’ disease, chronic retinal detachment, and a variety of other ocular insults. It is feasible that such a vasoproliferative process could occur secondary to solitary CHRPE. The vasoproliferative tumor typically is a fleshy red-pink, whereas lesions in our patient were deeply pigmented. The only exception was our patient 5 in whom the nodule was a light brown. However, the tumor in that case clearly arose from solitary CHRPE. The light color of the lesion in that patient does not exclude adenoma of the RPE, since we have observed cases of histologically documented neoplasms of the RPE in which the tumor had a fleshy color clinically.11,15

We speculate that the tumors observed in these patients probably are examples of acquired adenoma of the RPE that arose from solitary CHRPE. However, it is possible that they represent a reactive proliferation of the RPE. Attempting to differentiate acquired adenoma from reactive hyperplasia may be superfluous because both are benign conditions that have similar clinical courses.1,2

There have been several reports of CHRPE in which histopathologic studies have been done,3,5,12,16-18 but none have shown a solid nodule similar to the ones observed clinically in our patients. The case of Reese and Jones16 showed reduplication of the RPE, but no distinct nodule was observed clinically or histopathologically. The case of Duke and Maumenee17 was reported as a flat lesion but histopathologically it showed irregular pigment in the overlying sensory retina. However, the pigment epithelial component of their lesion was flat, whereas in our patients there was a distinct nodule, confirmed clinically and ultrasonographically. Likewise, the case reported by Kurz and Zimmerman18 was flat, with no nodular component. Kasner et al19 reported histopathologic studies of the multiple pigment epithelial lesions that occurred in a patient with familial adenomatous polyposis. Although their patient had been examined clinically, none of the lesions formed a distinct nodule as seen in our patients. The RPE lesions seen in familial adenomatous polyposis are different clinically from the solitary lesions described in this article, although it is possible that the lesions in our patients could have a similar histopathologic pattern.

Concerning management of these lesions, it seems advisable to observe them periodically if the patient is asymptomatic and there is no apparent visual threat from cystoid macular edema or progressive exudation. Four of our 5 patients experienced visual loss secondary to macular changes, presumably related to the peripheral mass. Management options for those causing visual loss include treating the macular edema medically or with grid laser photocoagulation or cataract surgery. The 2 tumors that were treated with 125I-plaque brachytherapy showed a moderately favorable response but the cystoid macular edema and exudation persisted.

CONCLUSION

We have described 5 patients who developed an elevated nodule that arose from solitary CHRPE. This tumor, which we believe has not been previously described, is characteristically slowly progressive, assumes a blood supply from the sensory retina, causes localized exudative retinopathy, cystoid macular edema, and surface wrinkling retinopathy. Although histopathologic evidence is yet unavailable, we speculate that the mass is either an acquired adenoma of the RPE or a reactive proliferation of the RPE. Clinicians should be aware of this lesion and periodically follow up patients with solitary CHRPE for its development. Asymptomatic patients can be observed without treatment. The best management for those that produce visual loss is not clearly established.

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REFERENCES