Adenoma of the retinal pigment epithelium: a report of 3 cases

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ABSTRACT • RÉSUMÉ

Objective: To report the clinical manifestations and pathologic features of adenoma of the retinal pigment epithelium (RPE).

Design: Retrospective study.

Participants: Three patients with an initial clinical diagnosis of choroidal melanoma.

Methods: Routine eye examinations, including visual acuity, intraocular pressure, slit-lamp examination, and ophthalmoscopy, were performed. Auxiliary examinations included fluorescein fundus angiography (FFA), indocyanine green angiography (ICGA), B-scan ultrasonography, colour Doppler imaging (CDI), and MRI. Endoresection of the tumours was performed, and the specimens underwent pathological examination.

Results: The tumours were of yellow-pink or brown colour and all located in the right eye. On FFA and ICGA, the tumours demonstrated hypofluorescence in the early phase and hyperfluorescence with prominent leakage in the late phase. CDI showed arterial blood signals in the tumour, and MRI showed hyperintensity in the T1-weighted image and hypointensity in the T2-weighted image. On pathological examination all the tumours were positive with periodic acid-Schiff, S-100, neurone-specific enolase, synaptophysin, epithelial membrane antigen, and vimentin staining but negative with melanoma-specific antigen HMB45, and cytokeratin. After 3 years of follow-up, there was no tumour recurrence and the retinas remained attached.

Conclusions: RPE-derived adenoma is difficult to diagnose clinically. In most cases, pathological confirmation is needed. Local resection is a favorable alternative treatment for some patients.

Objet : Compte-rendu des manifestations cliniques et des caractéristiques pathologiques de l'adénome de l'épithélium pigmentaire de la rétine (ÉPR).

Nature : Étude rétrospective.

Participants : L'étude a impliqué 3 patients ayant un diagnostic clinique initial de mélanome choroïdien.

Méthodes : On a pratiqué l'examen oculaire routinier, comprenant l'acuité visuelle, la pression intraoculaire, l'examen à la lampe à fente et l'ophtalmoscopie. Les examens auxiliaires comprirent l'angiographie à la fluorescéine du fundus (AFF), l'angiographie au vert d'indocyanine (AVIC), l'échographie mode B, l'imagerie Doppler couleur (IDC) et l'IRM. L'endorésection des tumeurs a été pratiquée et les spécimens ont fait l'objet d'un examen pathologique.

Résultats : Les tumeurs étaient de couleur jaune-rose ou brune et se trouvaient toutes dans l'œil droit. À l'AFF et à l'AVIC, les tumeurs présentaient une hypofluorescence en première phase et une hyperfluorescence avec fuite proéminente en dernière phase. L'IDC a montré des signaux de sang artériel dans la tumeur et l'IRM a fait voir une hyperintensité dans l'image pondérée T1 et une hypointensité dans l'image pondérée T2. À l'examen pathologique, toutes les tumeurs étaient positives avec l'acide périodique-Schiff, le S-100, l'énolase neurospécifique, la synaptophysine, l'antigène de la membrane épithéliale et la coloration de vimentine, mais négatives avec l'antigène HMB45 spécifique du mélanome et la cytokératine. Après 3 années de suivi, il n'y a pas eu de récurrence de la tumeur et les rétines sont demeurées attachées.

Conclusions : L'œdème dérivé de l'ÉPR est difficile à diagnostiquer cliniquement. Dans la plupart des cas, la confirmation pathologique est nécessaire. La résection locale est une bonne option de traitement pour certains patients.

Neoplasms of the retinal pigment epithelium (RPE) are rare. They mainly include 4 groups: congenital hamartoma of the RPE, congenital hypertrophy of the RPE, combined hamartoma of the retina and RPE, and adenoma or adenocarcinoma of the RPE.[1] As well, excessive hyperplasia of the RPE has an appearance similar to that of the RPE tumour. In a few conditions, when choroidal melanoma encroaches on the retina, it can also simulate the RPE tumour.[2,3] The differentiation of the various tumours is made on clinical examination by the typical ophthalmoscopic and fluorescein angiographic features. Because of the great variations in the clinical manifestations and characteristics, diagnosis of RPE adenomas and adenocarcinoma may be confirmed only on histopathological examination. We have had experience with 3 cases of RPE adenoma treated with local resection, and the

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diagnosis was confirmed by histopathology. We describe the clinical features of these 3 cases and review the relevant literature on the subject.

Methods

A retrospective study was performed of 3 patients with histopathologically confirmed adenoma of the RPE after endoresection. The clinical characteristics, differential diagnosis, treatment process, and follow-up results are presented.

This study was approved by the ethics committee of Beijing Tongren Hospital.

Results

Case 1

A 38-year-old female was referred to our eye centre with a diagnosis of choroidal melanoma in 2004. She complained of floaters and blurred vision in the right eye for more than 1 year. There was no past medical or surgical history. The visual acuity was 0.02 OD, and refractive correction proved unhelpful. The visual acuity was 0.1 OS, and the best corrected vision was 1.0. The intraocular pressure was normal in both eyes, and no extraocular abnormality was found. The anterior segment was normal in each eye on slit-lamp examination. There was only mild vitreous opacity in the right eye.

On ophthalmoscopic examination, a yellow-pink mass was seen in the inferior temporal quadrant of the right eye. The tumour was dome-shaped with distinct margins and showed a small hemorrhage on the surface. Serous retinal detachment surrounded the tumour, and some yellow exudates were present at its posterior margin (Fig. 1A). Macular edema and lattice retinal degeneration were observed. On fluorescein fundus angiography the tumour demonstrated hypofluorescence in the early phase and hyperfluorescence with prominent leakage on the surface in the late phase, but the base of the tumour remained hypofluorescent (Fig. 2A–C). Colour Doppler imaging (CDI) showed inconsistent reflectivity of moderate intensity and arterial blood signals in the tumour. The dimensions of the tumour were 9.3 × 8.0 × 6.6 mm. (Fig. 2D). On MRI the tumour showed hyperintensity in the T1-weighted image and hypointensity in the T2-weighted image (Fig. 2E, F).

Case 2

A 50-year-old female complained of blurred vision in the right eye for 2 months. She had a history of high myopia in both eyes. The visual acuity was 0.04 OD and could not be improved by refractive correction. The visual acuity was 0.2 OS, and the best corrected vision was 1.0. The intraocular pressures and anterior segments were normal. There was obvious opacity in the vitreous in the right eye. Ophthalmoscopic examination revealed a tigroid retina and a pink, solid neoplasm located at the area near the optic disc. The tumour had distinct margins and a minimal hemorrhage on its surface. There was no retinal detachment (Fig. 3A). On indocyanine green angiography (ICGA), the tumour demonstrated hypofluorescence in the early phase and hyperfluorescence with prominent leakage in the late phase. Dual circulation could be seen (Fig. 4A, B). CDI showed a solitary tumour with uniform internal reflectivity and arterial blood signals in the tumour. The dimensions were 5.7 × 5.2 × 7.1 mm (Fig. 4C).

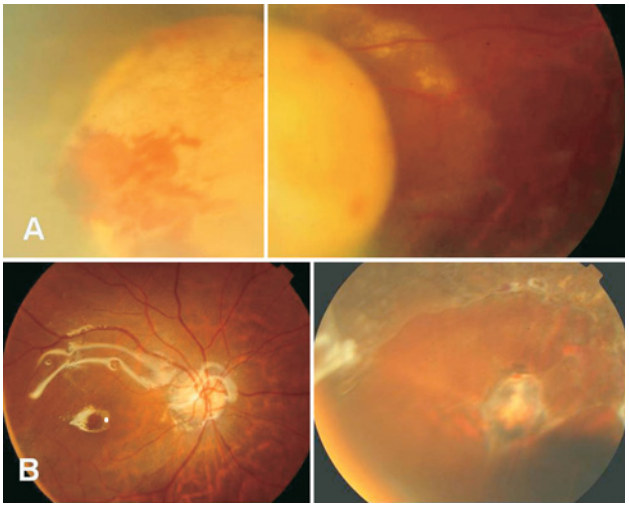

Fig. 1—Fundus photograph of the retinal pigment epithelium adenoma in patient 1 showed a yellow-pink mass in the inferior temporal quadrant (A); fundus photograph 8 weeks after the local resection surgery in patient 1 showed that the tumour was completely removed and the retina was well attached (B).

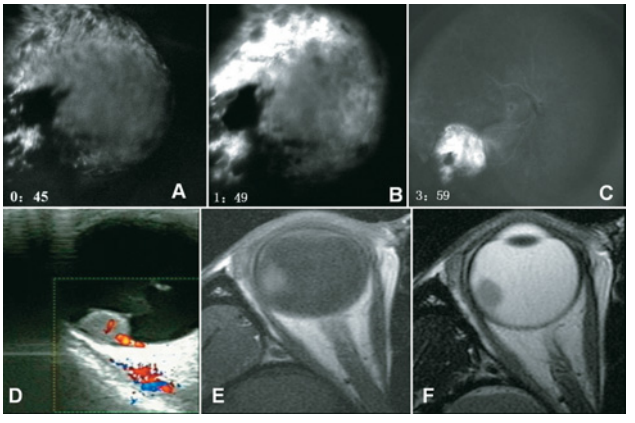

Fig. 2—Fluorescein angiography of the tumour in patient 1 showed hypofluorescence in the early stages and hyperfluorescence with prominent leakage on the surface at the late stage (A, B, C); colour Doppler imaging image of the tumour in patient 1 showed inconsistent reflectivity of moderate intensity and arterial blood signals in the tumour (D); MRI image of the tumour in patient 1 showed hyperintensity in the T1-weighted image and hypointensity in the T2-weighted image (E, F).

Case 3

A 31-year-old male complained of a dark shadow in the right eye present for 6 months. The visual acuity was 0.5 OD and refractive correction showed no improvement. The visual acuity was 1.2 OS. A brown, solid mass was located in the inferonasal quadrant of the right fundus. The surface of the tumour was smooth, and there was no retinal detachment (Fig. 5A). On ICGA, the tumour demonstrated hypofluorescence in the early phase and hyperfluorescence with prominent leakage in the late phase. Dual circulation could be seen (Fig. 6A, B). CDI demonstrated a pedunculated solitary tumour with nonuniform echo and evident arterial blood signal in the tumour. The dimensions were 11.7 × 8.3 × 5.1 mm (Fig. 6C). MRI showed the tumour protruding into the vitreous cavity with clear margins. In the T1-weighted image, the tumour showed hyperintensity compared with the vitreous, and in the T2-weighted image it showed hypointensity compared with the vitreous (Fig. 6D, E).

Treatment

Endoresection of the tumours was performed in all 3 patients by the same vitreoretinal surgeon. General hypotension anaesthesia was adopted during the surgery. Surgical procedure involved lensectomy, vitrectomy, retinal incision peripheral to the tumour, infusion of perfluorocarbon liquid, choroidal incision surrounding the tumour, separation of the whole tumour body from the eye wall, floating the tumour in the pool of perfluorocarbon liquid, and extraction of the tumour through the limbal incision. Subsequent procedures included hemostasis with endodiathermy, photocoagulation with endolaser to achieve retinal adhesion around the coloboma, fluid–air exchange to reattach the retina, and silicone oil injection with removal after 12 weeks.[4]

During the surgery, we found that the tumours were only loosely attached to the choroid, which made them easy to separate. The tumours were resected intact in all 3 cases. There were no serious complications during the surgeries. The retinas were well attached with silicone oil in place 12 weeks after surgery (Fig. 1B, 3B, 5B). After 3 years' follow-up, there were no tumour recurrences or retinal detachment (Fig. 5C). The best corrected visual acuity was 0.1 in patient 1, 0.01 in patient 2, and 0.03 in patient 3.

Histopathologic examination

The specimens were sent, in formalin, to the pathologist after surgery. The pathological, histochemical, and immunohistochemical findings were the same in all 3 patients. In the

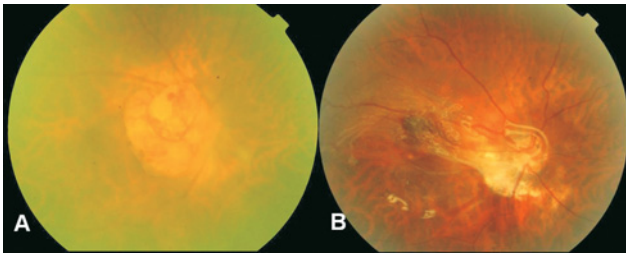

Fig. 3—Fundus photograph of the retinal pigment epithelium adenoma in patient 2 showed a tigroid retina and a pink, solid neoplasm located at the optic disc area (A); fundus photograph 10 weeks after the local resection surgery in patient 2 showed that the retina was well attached with silicone oil and there was no tumour recurrence (B).

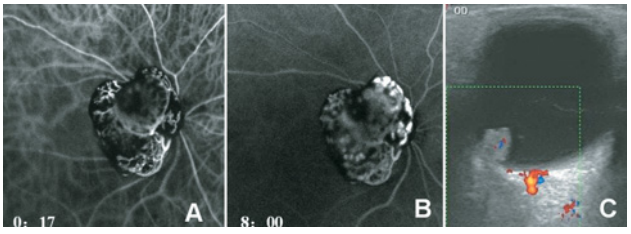

Fig. 4—Indocyanine green angiography of the tumour in patient 2 demonstrated hypofluorescence at the early stage and hyperfluorescence with prominent leakage at the late stage; dual circulation in the tumour could be seen (A, B); colour Doppler imaging in patient 2 showed a solitary tumour with uniform internal reflectivity with arterial blood signals in the tumour (C).

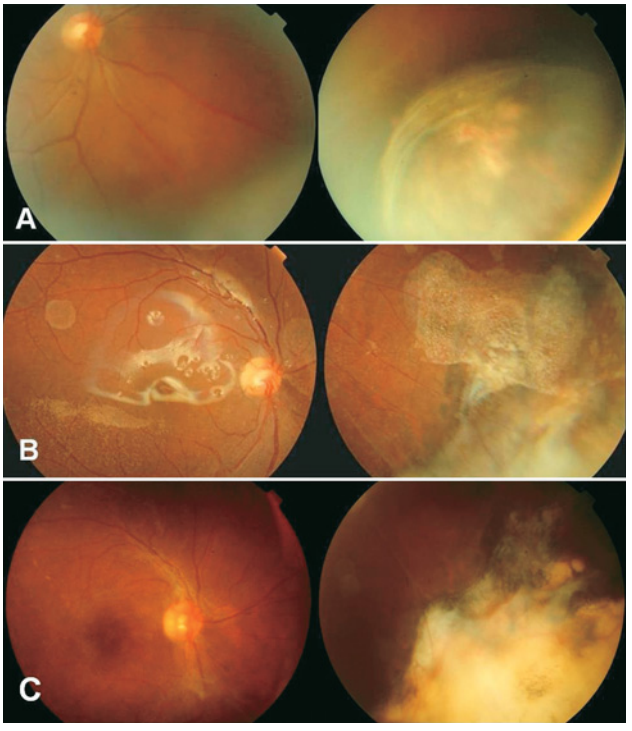

Fig. 5—Fundus photograph of the retinal pigment epithelium adenoma in patient 3 showed a brown, solid mass located in the inferonasal quadrant (A); fundus photograph 12 weeks after the local resection surgery in patient 3 showed that the retina was well attached with silicone oil (B); fundus photograph 3 years after local resection in patient 3 showed the retina to be well attached without silicone oil (C).

hematoxylin-eosin staining, the tumours were seen to be composed of cords of amelanotic cells with a slightly pleomorphic round or oval nucleus; mitotic figures were rare. Some tumour cells aligned like crypts, and some aligned irregularly. Well-distributed, red-stained strip materials could be seen around the tumour cells (Fig. 7). Histochemical staining of periodic acid-Schiff was positive in the matrix of the tumour. Immunohistochemistry staining showed that the tumours were positive for epithelial membrane antigen, S-100, neurone-specific enolase, synaptophysin, and vimentin staining but negative for melanoma-specific antigen HMB45 and cytokeratin-7 staining (Fig. 8). The diagnosis of adenoma of RPE was confirmed in all 3 cases.

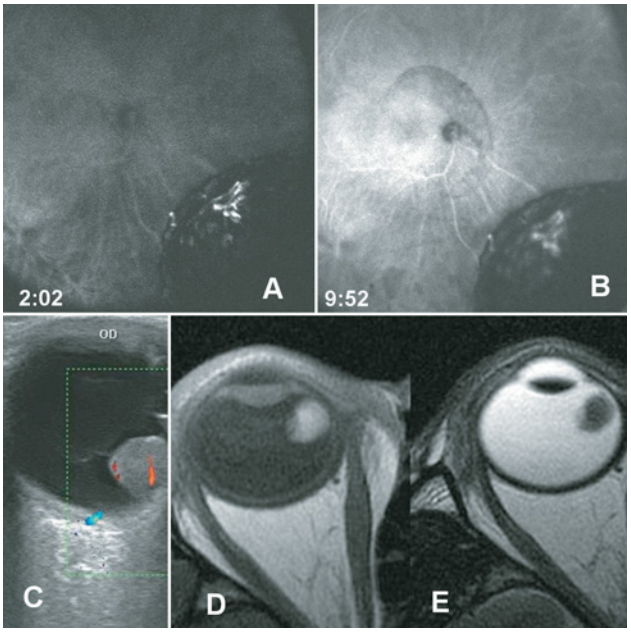

Fig. 6—Indocyanine green angiography in patient 3 demonstrated hypofluorescence of the tumour at the early stage and hyperfluorescence with prominent leakage at the late stage (A, B); colour Doppler imaging in patient 3 showed a mushroom-shaped solitary tumour with nonuniform echo and arterial blood signal in it (C); MRI of the tumour in patient 3 showed hyperintensity in the T1-weighted image and hypointensity in the T2-weighted image (D, E).

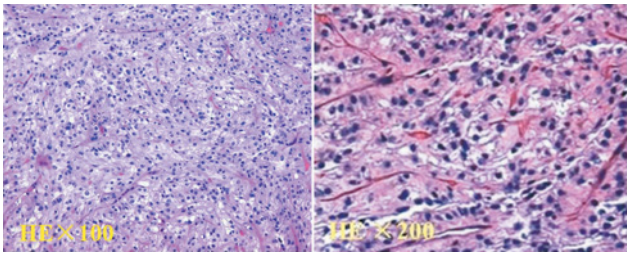

Fig. 7—In the hematoxylin-eosin staining, the tumours were seen to be composed of amelanotic cells with a slightly pleomorphic round or oval nucleus. Some tumour cells aligned like crypts, and some aligned irregularly, original magnification ×200.

Conclusions

Adenoma of the RPE is an uncommon intraocular tumour, which can rarely be diagnosed before enucleation. The etiology is still unknown, and congenital hyperplasia of the RPE may be one mechanism for this disease; as well, some other RPE abnormalities can cause it. Neoplasms of the RPE may clinically resemble choroidal melanoma or melanocytoma, so that differentiation may be difficult without histological examination.[5,6] Generally, compared with melanoma, RPE adenoma is more likely to have retinal feeder vessels, retinal or subretinal exudates, and exudative retinal detachment. On angiography, the tumours showed hypofluorescence in the early phase and hyperfluorescence in the late phase. Dual circulation in the tumour could be detected. On ultrasonography, the tumour showed moderate or high internal reflectivity with blood signals.[7,8]

RPE neoplasms vary considerably in their clinical manifestations. They can be pigmented or nonpigmented. In several published cases, RPE adenomas were darkly pigmented, but in some, including 2 of our cases, they were clinically nonpigmented with yellow-pink colour, and only 1 tumour in our cases was brown. The tumours were located at the posterior pole, as well as anterior to the equator.[5] Microscopically, the tumour is composed of neoplastic proliferation of RPE cells, but there are also considerable histopathological variations.[9] Tumours arising from the anterior RPE tend to have a vacuolated pattern, and those located posteriorly are more likely to show a glandular or tubular configuration. Some of these tumours can be stationary for a long time, but some demonstrate progression and ocular complications such as retinal detachment, vitreous hemorrhage, and visual loss.[7]

RPE adenomas have discrete margins and are dome-shaped with steep slopes. They tend to acquire blood supply from the sensory retina and sometimes give rise to exudative retinal detachment. Small RPE adenomas can be followed up closely, but symptomatic tumours should be treated promptly. Fine-needle aspiration has been fairly accurate in the differentiation of intraocular tumours, but

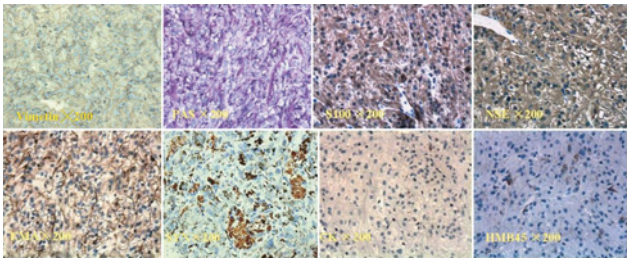

Fig. 8—Histochemistry and immunohistochemistry staining of the retinal pigment epithelium adenomas. The staining was positive for periodic acid-Schiff, epithelial membrane antigen, S-100, neurone-specific enolase, synaptophysin and vimentin but negative for melanoma-specific antigen HMB45 and CK, original magnification ×100.

we did not perform this procedure for the following reasons: (*i*) diffusion of the tumour cells along the puncture tunnel; (*ii*) intraocular complications, including bleeding and retina hole; (*iii*) the specimen was not large enough to do pathological and immunohistochemical examinations, which made the positive rate low when making the diagnosis; and (*iv*) the experience was important for the doctor and technician to perform this procedure.

There are various treatments available to ophthalmologists who care for patients with RPE tumours. In practice, these treatments are employed according to the type of tumour and conditions of the eye. In general, treatment of intraocular tumours has tended toward ocular conservation. The trends of treatment include observation, local resection, and radiation therapy. Orbital enucleation is typically reserved for large tumours or eyes with untreatable glaucoma. As new modalities of therapy have offered lower morbidity when compared with enucleation, more physicians and patients have opted for eye- and vision-sparing treatments. Brachytherapy is an effective way to treat some RPE tumours, but some severe side effects, such as radiation retinopathy and optic radiation neuropathy, which would lead to vision loss, should not be overlooked. With technological developments in ophthalmology, skilled ophthalmologists could perform surgery to remove the tumours even in some malignant cases. Our results in 3 cases showed that the retina was well attached and there was no tumour recurrence after long-term follow-up, demonstrating that local resection is a feasible alternative for RPE tumours.

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