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Retinal pigment epithelium lesions – clinical characteristics and differential diagnosis

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Summary: Pigmented fundus lesions may represent a benign or malignant process. They can be congenital, acquired, or the result of an infectious or inflammatory process affecting the retinal pigment epithelium. This article describes examples of pigment epithelial tumours and pseudotumours, and differential diagnosis, by reviewing the literature and cases on file in the Ophthalmology and Ocular Oncology Clinic, University Hospital, Krakow.

Key words: congenital hypertrophy of retinal pigment epithelium, combined hamartoma of the retina and retinal pigment epithelium (RPE), melanocytoma.

RPE cells contain melanosomes of neuroectodermal origin that develop during the second trimester of development. RPE cells transport nutrients, ions, and water, phagocytose the outer rods and cones, maintain the blood-ocular border, metabolize vitamin A, secrete factors essential to the structural integrity of the retina, convert all-trans-retinal into 11-cis-retinal, and absorb light with protection against photooxidation [1].

Disruptions of the RPE layer may lead to hypertrophy, hyperplasia, migration, metaplasia, and atrophy of retinal pigment epithelium (RPE) cells, producing various pigmented configurations.

The following types of congenital hypertrophy of retinal pigment epithelium (CHRPE) are distinguished:

- ✓ congenital hamartomatous lesion,
- ✓ congenital hamartomatous lesion of the retina and RPE,
- ✓ adenoma or adenocarcinoma of the RPE,
- ✓ secondary RPE hyperplasia.

Based on the pigment content, the following can be distinguished:

- ✓ uniformly black focus with lacunar depigmentation and peripheral halo effect,
- ✓ non-pigmented foci of CHRPE following loss of pigment (12% of cases) [2].

Congenital hypertrophy of retinal pigment epithelium

CHRPE is a sporadic, congenital anomaly of unknown aetiology and pathogenesis. A pigmented lesion is mainly asymptomatic, solitary, flat, and well-demarcated with round, elliptical, or irregular shape. These lesions may also contain non-pigmented areas within so-called "lacunae" and non-pigmented lines at the lesional margins ("halo"). In about 50% of cases CHRPE may slowly and minimally grow. Rarely, adenomas may develop. Thickened areas may appear on the edges of RPE adenomas (Fig. 1).

CHRPE lesions should be classified as typical or atypical.

Typical lesions are often round and solitary and may even feature enlargement of the lacunae over time.

They can sometimes have a "bear track" appearance when there are multiple small lesions.

Atypical lesions include pigmented RPE lesions that are pisciform or spindle-shaped, bilateral, and multiple in number. Atypical presentations of CHRPE may show a higher predisposition for familial adenomatous polyposis (FAP), a risk factor for developing colon cancer.

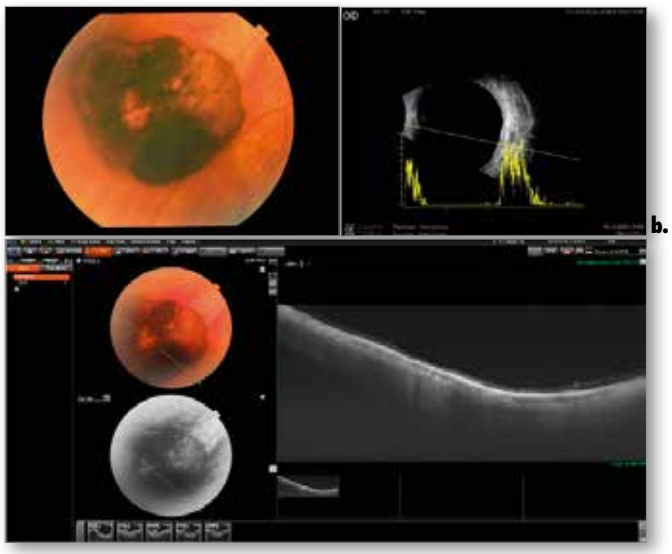

Fig. 1. Colour photograph – A, ultrasound – B, and C – OCT of CHRPE.

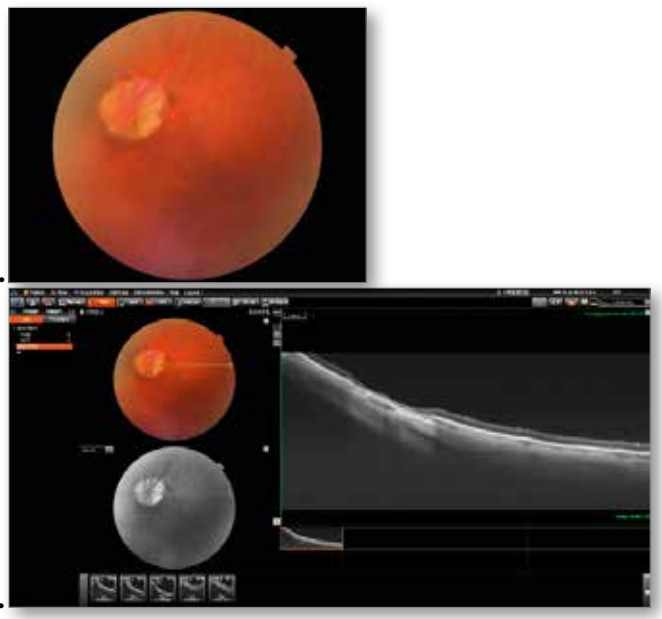

Fig. 2. Colour photograph – A, and OCT examination – B, illustrates discoloration of CHRPE.

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Discoloration and RPE cell atrophy are accompanied by reduction and loss of melanocytes, which are dependent on the anomalies in the Bruch's membrane, including thickening of the outer and inner collagen layers (Fig. 2) [2].

CHRPE are usually asymptomatic. Only lesions located in macular region can cause defects in the visual acuity and/or visual field.

No treatment is needed except in cases with neovascularisation.

Combined hamartoma of the retina and RPE (CHR)

CHR is a rare benign lesion built from glial cells, vascular tissue, and RPE cells. It is usually located in the macula or peripapillary region, or less often in the periphery. CHR is believed to be congenital – it is diagnosed in infants, but is usually recognized in children, and may occur bilaterally. The lesion most frequently occurs with neurofibromatosis type II (NF2), but it has been reported in neurofibromatosis type I and Gorlin-Goltz syndrome, Polish anomaly, and juvenile nasopharyngeal angiofibroma [3].

The lesion is slightly elevated, usually pigmented (with colouration of varying degrees), contributing to tortuosity of retinal vessels [2].

It causes vitreoretinal interface changes: gliosis, fibrosis, tractions, epiretinal membrane. Foveolar traction occurs with 100% of macular lesions. CHR can be associated with the presence of subretinal fluid, macular oedema, choroidal neovascularisation, retinal perforations, epiretinal neovascularisation, retinal detachment, and vitreous haemorrhage.

Optical coherence tomography (OCT) scans show high reflectivity of lesions located in the inner retina, and disorganisation of retinal structures (Fig. 3).

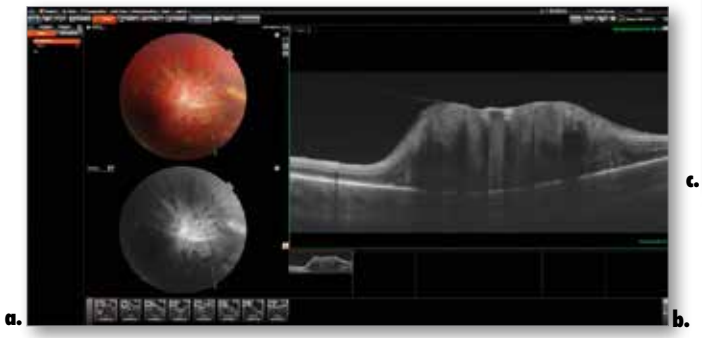

Fig. 3. Colour photographs – A, and OCT scans – B, of CHR.

CHR should be observed, and in the case of complications such as neovascularisation or vitreous haemorrhages, it should be appropriately treated: anti-VEGF injections, vitrectomy, laser photocoagulation. Systemic investigation is recommended for patients with NF 2.

Hamartoma and choristoma of RPE

This is a lesion formed by an abnormal location of RPE cells and usually affects the inner layers of the macula.

Figure 3 illustrates colour photographs and OCT scans of RPE hamartoma.

There are various forms of hamartoma: superficial, epiretinal, and epiretinal hamartoma with superficial neovascularisation.

Pigmented post-inflammatory lesions can mimic CHPRE and other RPE lesions.

RPE Hyperplasia

RPE hyperplasia occurs secondary to inflammation, trauma, vitreous traction, or therapeutic interventions. There is non-specific proliferation of RPE cells that forms an irregular-shaped pigmented retinal lesion.

Choroidal naevi are **located in the uveal tract** and can affect the retina lying above them. Typically, naevi are without subretinal fluid or orange pigment, they include overlying drusen, and are no thicker than 1.0 mm. Atypical naevi may have ill-defined borders and appear less uniform. Naevi should be serially documented and objectively photographed and measured with B-scan ultrasound to monitor features such as size (i.e. diameter and depth) and internal reflectivity over tim [2].

Progression in size and development of subretinal fluid or orange pigment should prompt a re-evaluation of the diagnosis. Malignant transformation of choroidal naevi to malignant melanoma is rare, with estimates as low as 1 out of every 8000. OCT is a helpful tool in differentiating a benign naevus from a malignant melanoma.

Melanocytoma (Magnocellular nevus)

Melanocytomas are typically unilateral black lesions that commonly occur over the optic nerve and may extend into the choroid or neurosensory retina (Fig. 4).

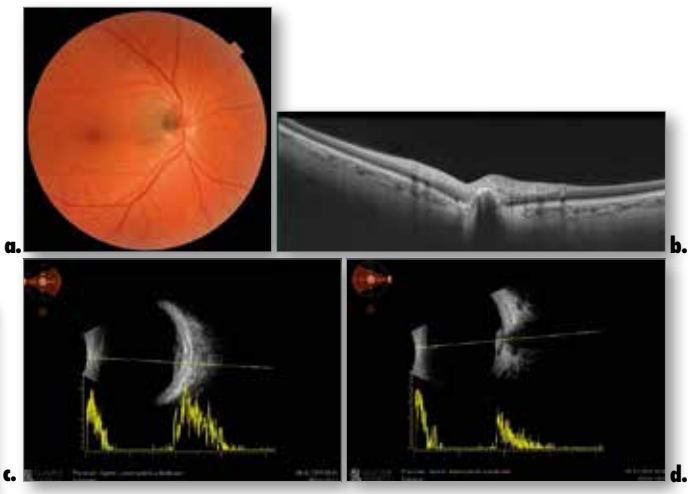

Fig. 3. Colour photographs – A, and OCT scans – B, of CHR.

Their growth does not necessarily indicate malignant transformation, as up to 15% of melanocytomas demonstrate enlargement over the years.

Due to the risk of malignant transformation in 1–2% of cases, observation is recommended with serial fundus photography.

Toxoplasmosis classically presents as focal retinitis with overlying vitreous inflammation, described as "headlights in a fog", with a nearby pigmented chorioretinal scar.

The inflammation and scars can be caused by other infectious processes, including tuberculosis, toxocariasis, syphilis, cytomegalovirus, herpes simplex virus, varicella-zoster virus, autoimmune processes, Behcet's disease, and retinal vasculitis.

Metastatic carcinoma

Metastatic processes can occur in the eye, conjunctiva, eyelid, or orbit. Metastatic carcinomas are the most common intraocular tumours. Any lesion suspected to be ocular metastasis should be referred to an ocular oncologist. The majority of patients with breast cancer metastasis have a known diagnosis of cancer; however, this rate is not as high as other cancers such as lung metastasis, where only around 66% of patients have a cancer diagnosis. Intraocular metastases most often arise in the choroid, in the posterior pole, and are mostly light and cream in colour. Pigmented tumours are metastases of cutaneous melanoma, which are very

rare. When there is sufficient concern for metastasis to the eye without a known history of malignancy, further investigation should be done.

Age-related macular degeneration (AMD) should be considered in the differential diagnosis of macular changes.

Age-related macular degeneration

AMD changes the appearance of the macula in various ways. Signs include drusen, RPE changes, subretinal fibrosis, geographic atrophy, and subretinal fluid. The exudative form (wet AMD) with haemorrhages and pigmentation may mimic a tumour [4, 5].

The differential diagnosis for wet AMD includes other choroidal neovascularisation causes, including pathologic myopia, angioid streaks, choroidal rupture, and ocular histoplasmosis. Other foveal pathologies such as pigment epithelial detachments or vitelliform lesions will not typically leak on fluorescein angiography. Pachychoroid spectrum disorders such as polypoidal choroidal vasculopathy may develop pigment epithelial detachments, which are not associated with drusen.

Summary

There is a wide variety of benign retinal lesions. It is important to characterise critical aspects of the lesion, such as the anatomical level of the lesion, colour, size, thickness, tumour base, shape, surface features, and location. Imaging modalities such as colour fundus photographs, OCT imaging, B-scan ultrasound, and additional methods (autofluorescence and fluorescein angiography) may be helpful in the diagnosis.

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