Unilateral Retinal Pigment Epithelium Dysgenesis: Long-Term Natural Evolution and Multimodal Imaging

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Established Facts

- Unilateral retinal pigment epithelium dysgenesis is an extremely rare, well-described retinal disease with characteristic appearance.
- Slow growth of the lesion has been described.
- Visual loss is thought to result mainly by secondary choroidal neovascularisation.

Novel Insights

- Visual loss can result from the continuous growth of the lesion and associated progressive retinal disorganisation despite lack of secondary complications.
- Optical coherence tomography angiography can delineate the retinal vascular abnormalities associated with the lesion.

Keywords

Optical coherence tomography angiography · Unilateral retinal pigment epithelium dysgenesis · Retinal pigment epithelium tumors

Abstract

Purpose: To present the natural course and describe the characteristic findings of a case of unilateral retinal pigment epithelium dysgenesis (URPED) and highlight the optical coherence tomography angiography characteristics of this

rare fundus pattern. **Methods:** Case report. **Results:** A 52-year-old male was referred 8 years ago to our clinic due to a distinctive unilateral lesion in his left fundus, of which he was aware from early adulthood. Clinical evaluation revealed an irregularly shaped patch of retinal pigment epithelium atrophy surrounding his left optic nerve, with a characteristic scalloped border and with severe distortion of the overlying retinal and vascular tissue. Retinal pigment epithelial hyperplasia was noted in the margin as well as in distinct lacunae clustered around the periphery of the lesion. Right fundus examination was normal. The patient was diagnosed with

URPED and was followed annually with multimodal imaging ever since. No choroidal neovascularization or other complication was noted. However, the lesion appeared to slowly but steadily grow to eventually affect the foveal region causing severe visual loss. Best corrected visual acuity was 20/40 at baseline and 20/200 at last follow-up 8 years after the original diagnosis. **Conclusion:** URPED is a rare retinal disease with unique clinical characteristics that can progress relentlessly even in the absence of secondary complications.

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Introduction

Unilateral retinal pigment epithelium dysgenesis (URPED) is a recently described, extremely rare condition of the posterior pole, firstly introduced by Cohen et al. [1] in 2002 under the term “unilateral, idiopathic leopard-spot lesion of the retinal pigment epithelium” [1, 2]. Very few cases have been published since, limiting our knowledge of the pathophysiology and natural history of this retinal disease. Herein, we report a case of URPED and its potentially sight-threatening natural evolution and describe its unique pattern via multiple imaging modalities including first-time description of its optical coherence tomography angiography (OCT-A) characteristics.

Case Report

A 52-year-old man was referred to the 2nd Department of Ophthalmology, Aristotle University for a peculiar lesion in the posterior pole of his left eye 8 years ago. The patient had experienced gradual visual loss and metamorphopsia from early adulthood. Past medical and ocular history were unremarkable and the patient denied any ocular trauma. Upon first examination, best corrected visual acuity (BCVA) was 20/20 in his right and 20/40 in his left eye. Slit-lamp examination, intraocular pressure, and funduscopy were normal in the right eye. Funduscopy in the left eye revealed a well-circumscribed, irregularly-shaped lesion surrounding the optic disc circumferentially, sparing only its superior border and encroaching upon the fovea. The lesion was whitish-yellowish and comprised of apparent atrophy of the retinal pigment epithelium (RPE), thickening of the above retina with epiretinal membrane formation inferotemporally, and mild tortuosity and distortion of the associated vessels (Fig. 1a). Fluorescein angiography (FA) clearly delineated the area of RPE atrophy and also revealed a peculiar, scalloped border of RPE hyperplasia surrounding the lesion as well as a few lacunae of hyperplastic RPE inside the lesion and close to its margin. It also highlighted the localized retinal vascular abnormalities (Fig. 1b). Fundus autofluorescence (FAF) showed an inverted pattern compared to FA images, comprising of hyperautofluorescence of the areas of RPE hyperplasia

(i.e., the margin and lacunae) appearing hypofluorescent on FA and hypoautofluorescence of the atrophic center which exhibited transmission hyperfluorescence on FA (Fig. 1c). During the following years, the lesion appeared to extend slowly but relentlessly, eventually evolving the central fovea and causing gradual visual loss due to progressive RPE atrophy and associated epiretinal membrane and retinal folds. Upon last evaluation, BCVA was 20/20 in the right eye and 20/200 in the left eye. The margin continued to expand, apparently creating new hyperplastic RPE lacunae, while the old ones were gradually replaced by atrophy. Continuous glial proliferation was noted to cause further retinal disorganization, retinal fold formation, and vascular distortion in the inferotemporal quadrant of the lesion (Fig. 1d, e).

Spectral domain optical coherence tomography (SD-OCT) imaging acquired 8 years after initial diagnosis revealed complete retinal disorganization with severe thickening and cystic degeneration inferotemporally and normal neurosensory retinal layers with hypertransmission due to the atrophic RPE in the rest of the lesion. The atrophic epithelium abruptly terminated to thickened, hyperplastic RPE, appearing as hyperreflective foci at the margins of the lesion (Fig. 2d–f). Synchronous OCT-A best highlighted the associated retinal vascular abnormalities, characterized by marked tortuosity and looping in the superficial layer, while exhibiting a widely anastomosed network in the deep plexus. Choroidal vasculature appeared normal with no signs of neovascularization (Fig. 2a–c).

Discussion

Cohen et al. [1] first reported in 2002 four cases of a unilateral condition they called unilateral, idiopathic leopard-spot lesions of the retinal pigment epithelium. They added another 5 cases and described the unique characteristics of the fundus pattern they renamed unilateral pigment epithelium dysgenesis [2]. Among the most significant features of URPED are the scalloped margin of RPE hyperplasia and central atrophy of the RPE and the inverted pattern of FAF as compared to FA. Other distinctive features are the fibroglial proliferation in the above retina, vascular tortuosity, and retinal folds, while OCT characteristics may vary including transmission defects due to the atrophic changes of the RPE, epiretinal membranes, cystic thickening of the neurosensory retina, and serous retinal detachment. It has been recently postulated that URPED may be a forme fruste of combined hamartoma of the retina and RPE (CHRRPE) [3]. However, CHRRPE, probably a congenital lesion, tends to be diagnosed at a younger age and though it bears similarities to URPED, i.e., retinal thickening and disorganization with tortuous, leaking vessels, it lacks the characteristic pattern of extending RPE atrophy and hyperplastic RPE borders, while it tends to progress little or not at all, in contrast to the observed continuous growth of URPED

Fig. 1. **a** Color photograph of the left eye at presentation shows a whitish-yellowish irregularly shaped lesion surrounding the optic disc and comprising of central RPE atrophy and thickening of the overlying retina with epiretinal membrane formation inferotemporally. **b** Fluorescein angiography (FA) exhibits hypofluorescence of the scalloped border and of a few lacunae of hyperplastic RPE surrounding the hyperfluorescent atrophic lesion. It also highlights the localized retinal vascular abnormalities. **c** Fundus

autofluorescence image reveals an inverse pattern of hyperautofluorescence of the margin and lacunae and hypoautofluorescence of the atrophic center compared with FA. **d** Continuous fibroglial proliferation and expansion of the lesion eventually evolving the central fovea 8 years after initial diagnosis. **e1, e2** FA images acquired after 3 and 8 years after initial diagnosis, respectively, delineating the newly formed lacunae and expanding borders of the lesion.

lesions. Moreover, CHRRPE tumors tend to appear mostly homogenous on OCT, whereas URPED-related retinal disorganization appears heterogenous and cystic, as illustrated in this case. A few case reports have been published since. Renz et al. [4] described RPE abnormalities in the fellow eye of a patient diagnosed with URPED detected with FAF, while Yamasaki et al. [5] detected electroretinographic abnormalities in the 30-Hz flicker test and photopic electroretinography in their case. Shimoyama et al. [6] presented a case of CNV associated with URPED, which was resistant to treatment (triamcinolone acetate and bevacizumab), and Gal-Or et al. [7] described a patient with a presumed RPE tumor originating from URPED. Our case adds to our knowledge of the natural history of this rare condition, showing its relentlessly progressive, vision-threatening nature despite the lack of secondary complications such as CNV and retinal detachment. Our patient has been followed up for several years with multimodal imaging and recently imaged with OCT-A, which demonstrates the retinal vascular abnor-

malities that seem to coexist with the rest of retinal disorganization associated with the presumed primary feature of RPE dysgenesis. To our knowledge, this is the first report of imaging with OCT-A in an eye with URPED without any secondary complications.

In conclusion, we described a rare retinal disease thought to arise from RPE dysgenesis leading to hyperplasia and subsequent atrophy and added to our knowledge of its potentially vision-threatening natural evolution. Raised clinical awareness is warranted in order to recognize this unique entity, while more research and especially histopathologic findings will add to our knowledge of the disease etiology and pathophysiology.

Statement of Ethics

Our institutional review board does not require approval for data from a single patient.

Fig. 2. **a** En face OCT-A image of the retinal vascular plexuses (superficial and deep) shows vessel tortuosity and anastomoses. **b** En face OCT-A image at the level of the choriocapillaris slab, with no signs of neovascularization. **c** Vessel density map of the superficial retinal plexus report, showing severe capillary dropout. **d** En face OCT image highlights the associated epiretinal membrane and retinal folds located inferotemporally. **e** Scanning laser ophthalmoscopy image clearly delineates the margin of the lesion. Arrow in-

dicates location and direction of structural OCT scan with flow overlay through the foveal region (**f**), which depicts the severe thickening and cystic disorganization of the neurosensory retina, hypertransmission defect due to the atrophic retinal pigment epithelium (RPE), and a thickened, hyperreflective focus of hyperplastic RPE corresponding to the lesion border (asterisk). OCT-A imaging was performed at last follow-up, 8 years after initial diagnosis.

Disclosure Statement

The authors declare that there is no conflict of interest.

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Author Contributions

Paraskevi Riga: conception, design, acquisition/interpretation of data, drafting of manuscript. Anna Dastiridou: design, interpretation of data, review of manuscript. Despoina Tzetzis: design, interpretation of data, review of manuscript. Sofia Androudi: design, interpretation of data, review of manuscript, final approval. Periklis Brazitikos: interpretation of data, overall supervision.

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