Simple Hamartoma of the Retinal Pigment Epithelium: Report of Two Cases and Review of the Literature

Retina Pigment Epitelinin Basit Hamartomu: İki Olgunun Sunumu ve Literatürün Taranması

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ABSTRACT We report two cases with simple hamartoma of the retinal pigment epithelium who were initially diagnosed as choroidal melanoma. Fundus examination revealed a round-black macular lesion temporal to the fovea in both patients. Optical coherence tomography (OCT) showed a hyperreflective lesion with abrupt margins and deep optical shadowing with minimal protrusion to the vitreous. Fluorescein angiography showed blockage of background fluorescence due to the pigmented lesion and circular overlying hyperfluorescence. Ultrasonography demonstrated an echogenic mass with moderate internal reflectivity. The ophthalmoscopic, angiographic, ultrasonographic, and OCT findings led to the final diagnosis of simple hamartoma of the retinal pigment epithelium. The authors review the reported cases of simple hamartoma of the retinal pigment epithelium in the literature and emphasize its typical clinical features in the differentiation from other pigmented lesions of the retinal pigment epithelium.

Key Words: Retinal pigment epithelium; hamartoma; tomography, optical coherence; ultrasonography; fluorescein angiography

ÖZET Başlangıçta koroid melanomu tanısı almış, retina pigment epitelinin basit hamartomu olan iki olgu bildirilmektedir. Fundus muayenesinde her iki hastada da fovea temporalinde siyah, yuvarlak makula lezyonları saptandı. Optik koherens tomografide (OKT); derin gölgelenme ile birlikte, vitreusa minimal taşma gösteren ve keskin sınırlı hiperreflektif lezyon saptandı. Flöresein anjiyografide, lezyon üzerinde sirküler hiperflöresans ve pigmente lezyona bağlı alttaki flöresansın engellenmesi görüldü. Ultrasonografide, orta derecede iç yansıma gösteren ekojenik kitle tespit edildi. Oftalmoskopik, anjiyografik, ultrasonografik ve OKT bulguları retina pigment epitelinin basit hamartomu tanısını koymada yol göstermiştir. Yazarlar literatürdeki diğer bildirilen retina pigment epitelinin basit hamartomu olgularını da değerlendirmişler ve tipik klinik bulguları ile retina pigment epitelinin diğer pigmentli lezyonlarından ayırımını vurgulamışlardır.

Anahtar Kelimeler: Retina pigment epiteli; hamartom; tomografi, optik koherens; ultrasonografi; flöresein anjiyografi

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Simple hamartoma of the retinal pigment epithelium (RPE) is a relatively uncommon pigmented lesion of the fundus.[1-9] It is believed that the lesion is congenital and is composed solely of proliferating RPE cells. It is hence termed as a congenital simple hamartoma of the RPE. In search on a PubMed basis, only 11 cases of congenital simple hamartoma of the RPE were reported in the literature (Table 1). We report herein such a rare case in two patients diagnosed as congenital simple hamartoma of the

TABLE 1: Congenital simple hamartomas of the retinal pigment epithelium based on search in PubMed.

No	Age Sex	Eye	Symptom	Location	Tumor Base&Thickness (mm)	Study
1	10M	OS	None	Macula	0.9/1.5	Shields et al.[1]
2	10F	OD	Blurred vision	Macula	1.0/1.3	Shields et al.[1]
3	45F	OD	None	Macula	1.0/1.1	Shields et al.[1]
4	66F	OD	Blurred vision	Macula	1.0/2.5	Shields et al.[1]
5	80F	OD	None	Macula	0.3/1.0	Shields et al.[1]
6	14M	OS	Blurred vision	Macula	0.8/NA	Gotoh et al.[2]
7	58F	OD	None	Macula	0.5/NA	Lopez et al.[3]
8	22M	OD	Blurred vision	Macula	1.2/NA	Shukla et al.[4]
9	55F	OD	None	Macula	0.7/NA	Shukla et al.[4]
10	15F	OS	None	Macula	0.6/NA	Souissi et al.[5]
11	56F	OD	None	Macula	NA/NA	Teke et al.[6]
12	75F	OD	None	Macula	0.5/1.6	Present case 1
13	23F	OD	None	Macula	0.6/1.8	Present case 2

M: Male; F: Female; mm: millimeter; NA: non-available; OS: Oculus sinister; OD: Oculus dextrus.

retinal pigment epithelium with its clinical, ultrasonographic, angiographic, and optical coherence tomography (OCT) findings. The authors also aimed to emphasize the important clinical landmarks that enable the ophthalmologist to differentiate this tumor from other pigmented tumors of the retinal pigment epithelium.

CASE REPORTS

CASE 1

A 75-year-old female patient was referred to our hospital with a suspicion of a choroidal melanoma in her right eye that was diagnosed two months ago in an another hospital. Her past ocular history was unremarkable and past medical history was significant for a resection of a hepatic tumor 8 years ago. The ophthalmic examination showed that the visual acuities were 15/20 in both eyes. Biomicroscopy was normal except for a bilateral nuclear cataract. The fundus was normal in the left eye. The right fundus revealed a deeply pigmented, well-demarcated lesion of the retina and RPE, measuring 0.5 mm in basal dimension and 1.6 mm in thickness. The lesion was located 0.5 mm temporal to the fovea and 3.5 mm temporal to the optic disc (Figure 1a). The retina and RPE surrounding the lesion were normal except for a small island of RPE atrophy juxtanasal to the fovea. There was no retinal traction, intraretinal exudation, macular edema, or subretinal fluid. OCT showed a nodular full thickness retina and RPE involvement causing high surface reflectivity and deep optical shadowing (Figure 1b). On ultrasonography, the echogenic mass demonstrated a 1.6 mm thickness with moderate internal reflectivity and no sign of extrascleral component or foreign body (Figure 1c). No follow-up was available on this patient.

CASE 2

A 23-year-old female patient was referred to our hospital with a suspicion of a choroidal melanoma in her right eye that was diagnosed three weeks ago in an another center. In ophthalmic examination visual acuities were 20/20 and biomicroscopy were normal in both eyes. Fundus examination of the left eye showed no abnormality. Right fundoscopy revealed a pigmented, well-demarcated lesion of the retina and RPE, measuring 0.6 mm in basal dimension and 1.8 mm in thickness (Figure 2a). The lesion was located 0.5 mm temporal to the fovea and 3.5 mm temporal to the optic disc. Fluorescein angiography showed blockage of background fluorescence due to the pigmented lesion and circular overlying hyperfluorescence (Figure 2b). OCT demonstrated an increased optical reflectivity on its inner surface, deep optical shadowing, and elevated retina at the site of lesion (Figure 2c).

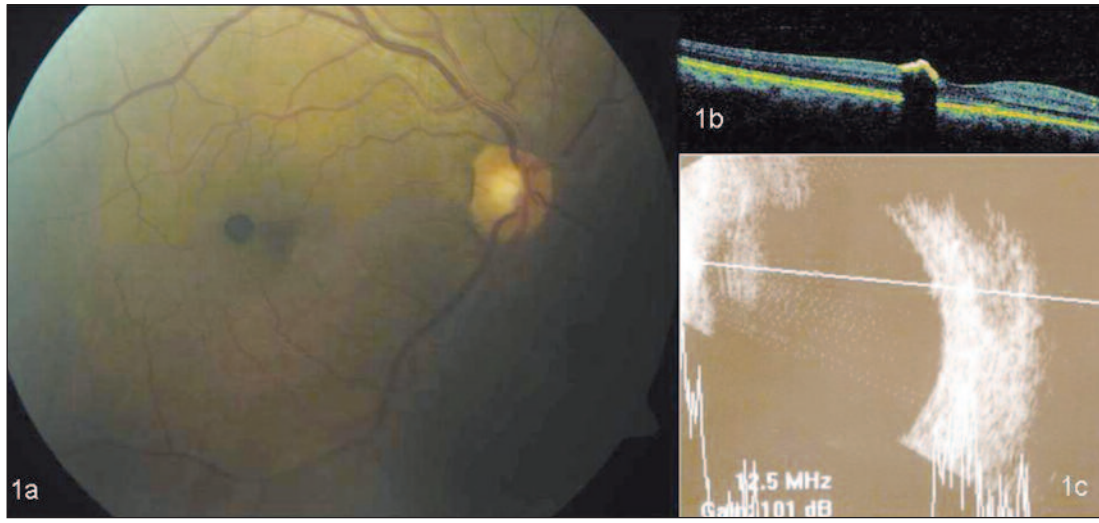

FIGURE 1a: Color fundus photograph of the right eye demonstrating a round, deeply pigmented, well demarcated, and minimally elevated lesion located just temporal to the fovea.**1b.** Optical coherence tomography of the right macula. A horizontal scan through the lesion shows highly reflective nodular elevation above the retina with sharp tumor margins and optical shadowing. **1c.** On ultrasonography, the echogenic nodular mass showing moderate internal reflectivity and no sign of extrascleral component or foreign body.
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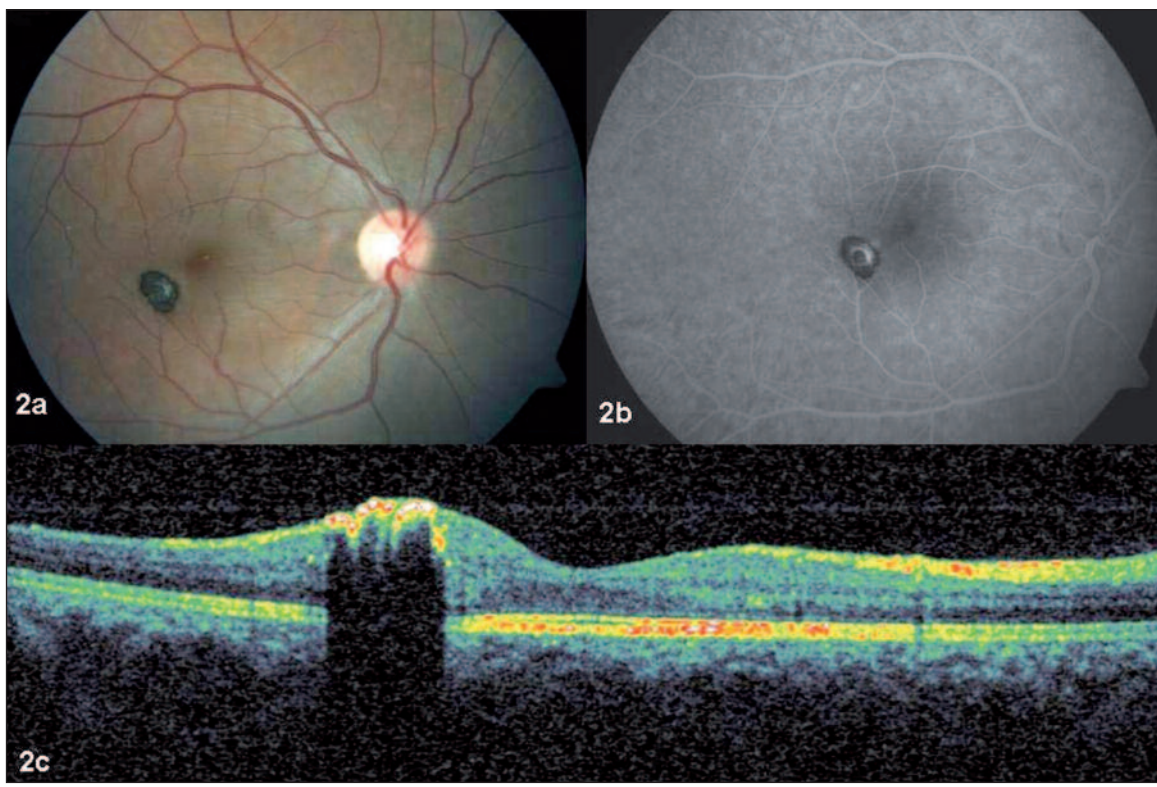

FIGURE 2a: Fundus photograph of the right eye showing a round, darkly pigmented, well demarcated located inferotemporal to the fovea. **2b.** Fundus fluorescein angiography of the right eye demonstrating blockage of background fluorescence due to the pigmented lesion and circular overlying trace hyperfluorescence.**2c.** Optical coherence tomography shows high optical reflectivity with abrupt shadowing of deeper tissues in the right macula.
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DISCUSSION

Tumors of the RPE are uncommon. They can be classified in five groups, including congenital simple hamartoma of the RPE, congenital hypertrophy of the RPE, combined hamartoma of the retina and RPE, reactive hyperplasia of the RPE, and adenoma or adenocarcinoma of the RPE.[9]

Simple hamartoma of the RPE was described by Lacqua in 1981.[10] He described two cases of a small, deeply pigmented, parafoveal macular lesion that projected through full-thickness retina into the vitreous cavity. He pointed out that these lesions had distinctive features compared to the classic congenital hypertrophy of the RPE and other pigmented RPE tumors. Later, in 1989, Gass reviewed focal congenital anomalies of the RPE.[8] He illustrated similar cases and termed these lesions as RPE hamartomas. Since then, various terms have been used to describe these lesions including congenital (or primary) RPE hyperplasia or congenital RPE adenoma. They are described as focal, nodular, black lesions that appear to involve the full thickness of the retina with no changes in the surrounding sensory retina, RPE, and choroid, or no exudation and hemorrhage.[8] Most recently, Shields and coauthor preferred the term congenital simple hamartoma of the RPE to specify clearly the tissue involved (RPE), its presumed congenital origin, and to differentiate this tumor from the combined hamartoma of the retina and RPE.[1] They believed that this condition is congenital because it is detected often in children and the features are nonprogressive. Moreover, many patients are asymptomatic, explaining why adults may first be diagnosed in later life.

Differential diagnosis of simple hamartoma of the RPE includes RPE adenoma or adenocarcinoma, congenital hypertrophy of the RPE, reactive RPE hyperplasia, intraretinal foreign body, choroidal nevus, and retinal invasion by a choroidal melanoma. RPE adenoma / adenocarcinoma is relatively high and abruptly elevated, large black nodular lesion, and is typically located in the periphery of the fundus. It can gradually cause intraretinal exudation and exudative retinal detachment. Its peripheral location and surrounding retinal exudation hence help us to clearly differentiate between these two rare entities.[9] Congenital hypertrophy of the RPE are usually solitary, well-demarcated, flat to minimally elevated fundus plaques that can range from black to completely depigmented lesions. Most of them are located in the midperipheral or peripheral fundus, but occasionally at the macular area.[9,11] They typically demonstrate depigmented lacuna(e) and marginal light halo. Reactive RPE hyperplasia is usually a flat, full-thickness retinal lesion that forms as a result of previous ocular insult, such as inflammation or trauma. Generally, there is also disturbance of the surrounding RPE.[9] Intraretinal foreign body is almost always associated with ocular trauma and usually displays vitreous traction and fibrosis, surrounding RPE atrophy, and ultrasonographic echodensity with shadowing. Choroidal nevus rarely involves the retina, usually has less prominent borders, and the color is usually dark brown - not pitch black. Choroidal melanoma can develop retinal invasion, but this usually occurs with large, mushroom-shaped tumors that show echolucency on ultrasound.[9] Simple hamartoma of the RPE has typical features that differentiate it from aforementioned RPE lesions. It typically occurs immediately adjacent to the fovea (macular location) and generally is 1.5 mm and less in base. The patient is usually asymptomatic and there is usually lack of retinal traction, intraretinal exudation, macular edema, or subretinal fluid. The characteristic ophthalmoscopic features in conjunction with ancillary tests such as OCT (nodular full thickness retina and RPE involvement causing high surface reflectivity and deep optical shadowing), ultrasonography (echogenic mass with medium internal reflectivity), and fundus fluorescein angiography (early blockage of the deeper retinal layers with trace overlying hyperfluorescence in the late frames) help us directly to diagnose this typical lesion.

In summary, simple RPE hamartomas are infrequent, benign pigmented lesions of the fundus. Since these lesions are usually asymptomatic, they are generally diagnosed during routine ophthalmic examination and do not require any treatment. The

distinction from other pigmented fundus lesions is straightforward with its typical ophthalmoscopic appearance (macular location, black color with sharp margins, and small retinal mass with minimal protrusion into the vitreous cavity), ultrasonographic features (slightly protuberant echogenic mass with moderate internal reflectivity), angiography findings (blockage of fluorescence due to pigmented tumour with minimal overlying hyperfluorescence), and OCT findings (nodular full thickness retina and RPE involvement causing high surface reflectivity and deep optical shadowing).

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