Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE): diagnosis and management

Hipertrofia congénita del Epitelio Pigmentario de la Retina (HCEPR): diagnóstico y manejo

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ABSTRACT

Introduction: Grouped pigmentation of the RPE has aroused the interest of ophthalmologists since it could be a manifestation of systemic diseases yet to be diagnosed.

Case Report: A 19-year-old woman visited the emergency department for ophthalmology consultation after perceiving floaters for a month. Anterior segment was normal. A flat, pigmented lesion with net edges was identified in the right eye, which had not been described previously.

Discussion: A descriptive morphological study is carried out in which the *OCT* shows a marked retinal thinning and loss of photoreceptors. *FA* shows blockage of fluorescence and the autofluorescence evidences lack of lipofuscin that helps to distinguish between other pigmented lesions as nevus and choroidal melanoma. The importance of this case lies in its relevance to identify this lesion and make the diagnosis of systemic pathology.

Key words: Congenital hypertrophy of the retinal pigment epithelium, *familial adenomatous polyposis*, Gardner.

RESUMEN

Introducción: Las pigmentaciones agrupadas en el EPR han despertado el interés de los oftalmólogos ya que pueden ser la manifestación de enfermedades sistémicas que no han sido diagnosticadas.

Caso clínico: Una joven de 19 años acude a urgencias oftalmológicas por miodesopsias desde hace un mes. El segmento anterior es normal. En el ojo derecho objetivamos una lesión plana, pigmentada y de bordes netos no descrita previamente.

Discusión: Se realiza un estudio descriptivo morfológico en el que la *OCT* de la lesión presenta un marcado adelgazamiento retiniano y una pérdida de los fotorreceptores. La *AGF* muestra un bloqueo de la fluorescencia y en la A*utofluorescencia* se evidencia un déficit de lipofucsina que ayuda a descartar otras lesiones pigmentadas como el nevus y melanoma de coroides. La importancia de este caso radica en su relevancia para identificar la lesión y hacer un apropiado despistaje de patologías sistémicas asociadas.

Palabras Clave: Hipertrofia Congénita del Epitelio Pigmentario de la Retina, Poliposis Adenomatosa Familiar, Gardner.

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INTRODUCTION

Grouped pigmentation of the Retinal Pigment Epithelium (RPE) has been known for over 100 years, but it was not until 1911 when Hoeg used CHRPE to describe clusters of pigment in the Retina. The entity has also been called *Melanosis Retinae*, bear or animal tracks (1), and naevoid pigmentation of the fundus (2). Kurz and Zimmerman (3) found on histopathology the Congenital Hypertrophy of the RPE cells (CHRPE).

Solitary CHRPE is a well-known, common fundus condition that has been the subject of considerable attention in the ophthalmic literatura because these pigmented lessions could be related with systemic diseases like Adenomatous Polyposis Coli (APC) in the context of *Gardner's disease*, but it also may be related with neurological diseases.

The aim of these report is to explain the characteristics of these pigmented lessions and their relationship with systemic diseases.

CLINICAL CASE

A 19-year-old woman comes to the Ophthalmologic emergency due to myodesopsies in right eye for a month. She denies photopsies and other systemic antecedents. In the anamnesis, she only refers headaches since one year.

The ophthalmological examination reveals that her visual acuity was the unit in both eyes. In the slit lamp examination we checked that the cornea and anterior segment were normal. At the funduscopic examination we identified in the right eye, a flat pigmented, subretinal lession, with well delimited edges in midperipheral retina.

We completed the examination with a *Fluorescein Angiography (FA), Fundus Autofluorescence (FAF)*, *OCT*, *Ultrasound* and *Visual Field* to confirm a CHRPE as diagnosis of presumption.

Due to the relationship of CHRPE with *Gardner's disease* we decided to refer the patient to the Digestologist to study possible signs of APC.

DISCUSSION

Solitary CHRPE is a well-known, common fundus condition that has been the subject of attention in the Ophthalmological literature. Due to it is believed to be congenital, the median age at diagnosis is over 45 years (4). Its asymptomatic character justifies the late diagnosis despite mild visual field defects can be detected in some cases (5).

CHRPE has been related with Gardner's síndrome (35). *Multiple* or *bilateral* CHRPE may occur in *Familial Adenomatous Polyposis* (FAP), an autosomal dominant disease caused by mutations in the Adenomatous Polyposis Coli (APC) gene (6-11). This condition is autosomal dominant (12). The global prevalence of CHRPE in individuals with APC mutation is 19% (13), so CHRPE is the most common and earliest extra colonic manifestation among FAP populations which may be present at birth (80%) (14). The prevelance of CHRPE in the normal population is between 1,2% to 4,4% (15).

The Retinal Pigment Epithelium (RPE) is a single layer of cuboidal epitelial cells that constitutes the ourtermost layer of the retina. The RPE is located between the highly vascular choriocapillaris and the outer segments of photoreceptor cells. It has no photoreceptive or neural function, but also RPE is essential to the support and viability of photoreceptor cells (16).

CHRPE appears clinically as a well-demarcated flat to minimally elevated fundus plaque, usually with typical depigmented lacunae (17,18) (fig. 1) located in midperipheral or peripheral fundus. In the ***Optical Coherence Tomography* (*OCT*)** (8,35) is typical the *overlying retinal thinning*, *loss of photore-*

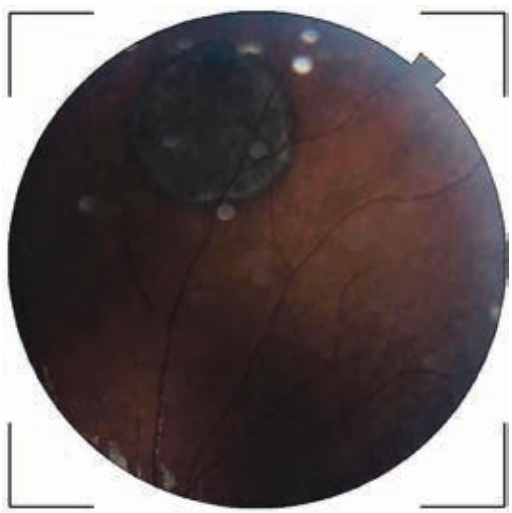

Fig. 1: Funduscopic characteristics of CHRPE. Is characteristic a well-demarcated flat to minimally elevated fundus plaque that ranges from a black homogeneous lesion, usually with depigmented lacunae.

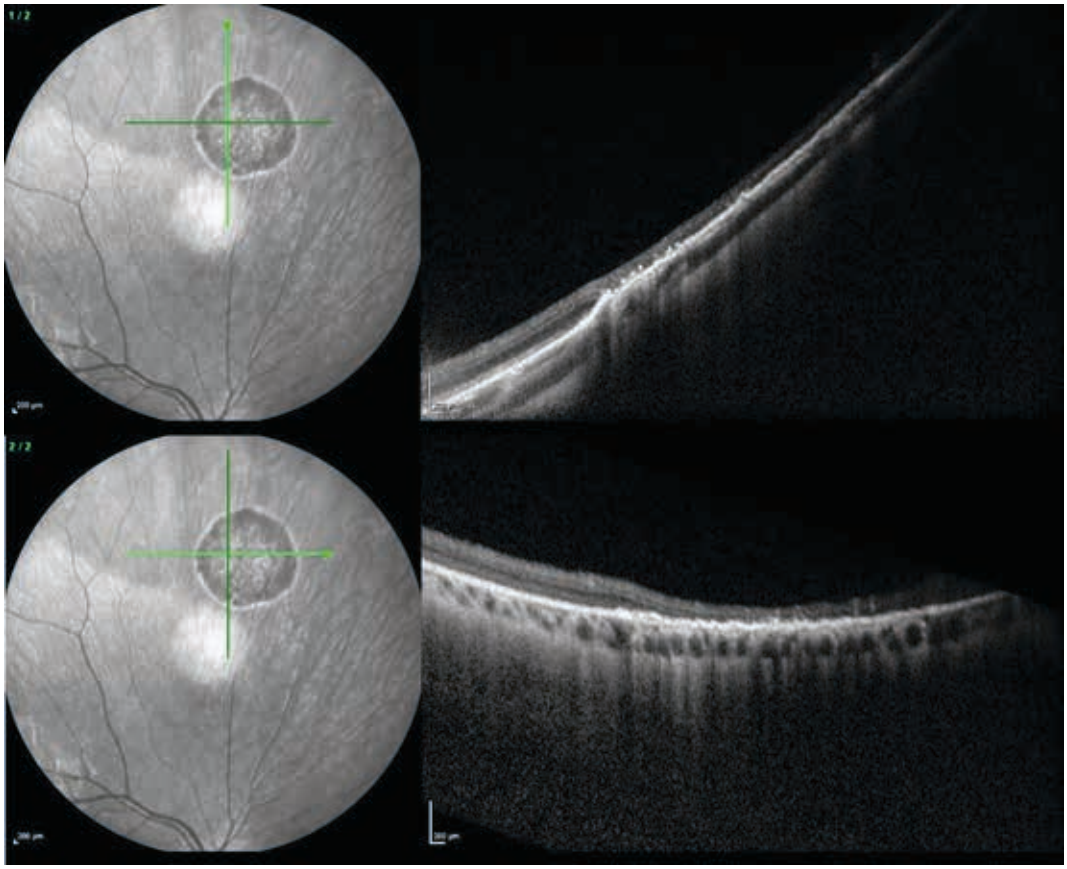

Fig. 2: OCT characteristics of CHRPE. Is very characteristic overlying retinal thinning, loss of photoreceptors and moderate relative shadowing of the underlying choroid.

ceptors, and *moderate relative shadowing* of the underlying Choroid. Orduña-Azcona *et al* (19) described the characteristics of CHRPE in HD-OCT concordant to the exposed case (fig. 2).

At CHPRE is typical that ***Fluorescein Angiography (FA)*** shows *blockage of fluorescence* throughout most of the sequences. Characteristically, there is a *persistent hypofluorescence* of the pigmented areas as

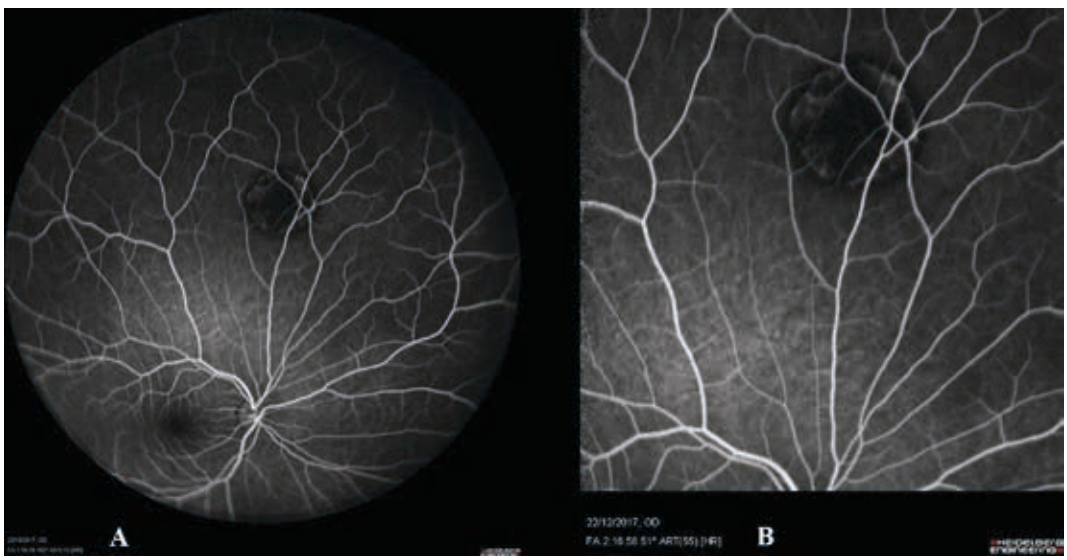

Fig. 3: FA characteristics of CHRPE. It shows a blockage of fluorescence throughtout most of the sequences.

we could prove in this clinical case (figs. 3a and 3b).

Touriño *et al* (20) developed a study to determine which were the changes in the FA in patients with CHRPE. Hypofluorescence throughout the angiography was constant in all cases. Certain authors (21) suggest that these vascular changes are secondary to an excessive concentration of oxygen in the inner layers of the retina which would result in vascular damage.

What is more the ***Fundus Autofluorescence (FAF)*** shows *hypoautofluorescence* due to the decrease of lipofuscin within the enlarged heavily and uniformily pigmented RPE cells (22,23) (fig. 4). The ***Ultrasonography*** (fig. 5) does not provide a clear diagnosis, but it shows the dimensions of the lession, about 1,04 mm thickness. In the ***visual field*** results range from a mild relative scotoma to an absolute field defect, usually depending on the size of the lesion. In this case, there are no findings suggestive of any campimetric alteration.

CHRPE is a benign lesion of the optic fundus, which typically has no visual repercussion. For this reason, the management consist of *periodic observation.* This case shows, a follow up of 14 months that objectives stability of the visual acuity and the lesion. The patient is awating for a colonoscopy in spite of the probability of FAP is very low, due to she only has one lesion.

In spite of CHRPE is a benign lesion, the recent development of *multiple* or *bilateral* CHRPE lesion are often associated with FAP. At a minimum, these patients should be referred for colonoscopy (24). Colorectal examination is crucial for early intervention and treatment, colon because polyps progress to malignancy in nearly 100% of cases. *Multiple* and *bilateral* CHRPE in FAP is considered a *clinical disease marker*. CHRPE, has also been related with isolated cases of *microcephaly* and *hyperreflexia* (25).

CHRPE has no malignant potential (26). Recent reports have provided further information about the potential of solitary CHRPE to spawn a nodular growth pattern (1,27). The nodule gradually acquires a retinal feeding artery and draining vein and produces yellow intraretinal exudation and exudative retinal detachment (5).

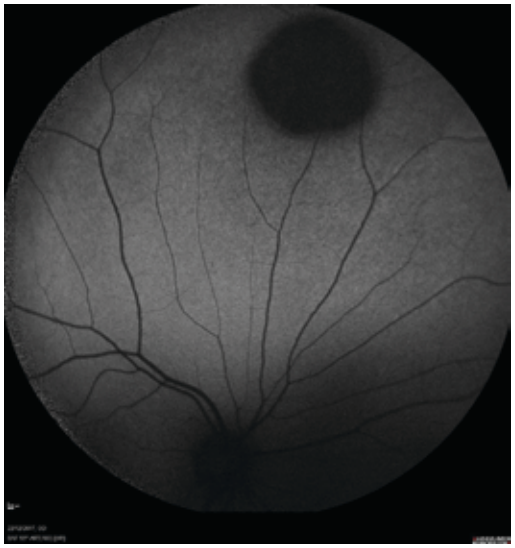

Fig. 4: Autofluorescence of CHRPE. Is typical the absence of autofluorescence of CHRPE due to de absence of lipofuscin.

The recommended management of solitary CHRPE is *periodic observation*. If a small nodular growth is dectected, it should be observed for a period of time. Due to the slow progression rate and extramacular location, patients remains asymptomatic. The prognosis for CHRPE is generally excellent.

Concerning *differential diagnosis*, solitary CHRPE can appears similar to *choroidal melanoma* (8) and nevus (table 1). Choroidal melanomas have diffuse FAF pattern (28) in contrast, CHRPE is hypoautofluorescence. FA of choroidal melanomas, shows hypofluorescence during the arterial phase and *progressive hyperfluorescence* during the subsequent phases (29). However, FA in CHRPE shows *blockage* of fluorescence throughout most of the sequences. In choroidal nevus, FA shows *hyporeflective* mass with no significant deformity of choroidal vasculature and an intact retinal pigment epithelium-Bruch's membrane complex (30).

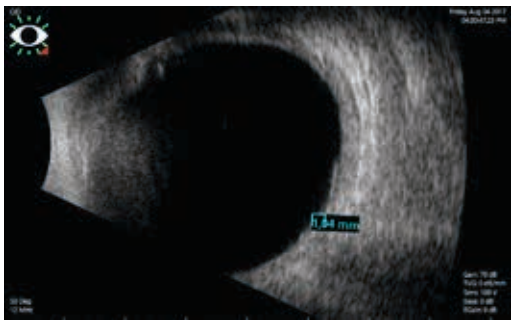

Fig. 5: Ultrasonography. It shows the lession to be about 1,04 mm thickness.

Table 1. Differential diagnosis. The table shows the characteristics of CHRPE, Choroidal Nevus and Choroidal Melanoma in the different complementary test carried out on the patient of the clinical case

Imaging technique	CHRPE	Choroidal nevus	Choroidal melanoma
Fundus imaging	Well-demarcated flat that ranges from a black homogeneous lesion, usually with depigmented lacunae	Round/oblong brown or coloured mass undermeath the retina with overlaying drusen.	Larger and thicker than nevus with orange pigmented and subretinal fluid and in advanced cases mushroom-shaped configuration.
SD-OCT EDI	Overlying retinal thinning, loss of photoreceptors, and moderate relative shadowing of the underlying Choroid	Slightly elevated dome-shaped mass with posterior shadowing related to the degree of pigmentation. RPE alterations photoreceptor loss subretinal cleft.	Similar appearance to nevus with homogenous optical reflectivity anteriorly with shadowing posteriorly thinned choriocapillaris and shaggy photoreceptors in 49% versus 0% in nevus.
Fluorescein angiography	Blockage of fluorescence throughtout most of the sequence.	Hyperfluorescent lesion in the nevus.	Blockage of background choroidal fluorescence with late staining
Ultrasonography	Flat lesion about 0.5mm to 1.5 mm thickness	It cannot depict small nevus	Hypo echoic round mass with smooth anterior surface and choroidal excavation.
Fundus Autofluorescence	Absence of autofluorescence due to lack of lipofuscin.	Hipo-FAF due to chronic RPE atrophy	Hyper-FAF due to overlaying lipofuscin within the RPE.

CONCLUSIONS

Grouped pigmentation of the RPE has aroused the interest of ophthalmologists due to it could be a manifestation of systemic diseases. In fact, it could be the first manifestation of a pathology which has not been diagnosed.

The most frequently related pathology to CHRPE is *Gardner's disease*, but it also may be related with neurological diseases. Furthermore, concerning *differential diagnosis*, solitary CHRPE can appear similar to *choroidal melanoma* and nevus.

A meticulous anamnesis is convenient to determine if CHRPE is related with congenital or familiar diseases. Furthermore, all the complementary tests should be done to determine the characteristics of the lesion and stablish future tracking. In this patient, during the follow up time of 14 months we did not find signs of spread of the lesion and no new ones were observed. The VA has remained at 1.

CHRPE has no malignant potencial, but there are cases in which CHRPE spawn a nodular growth pattern (1,31) that could produce an intraretinal exudation and exudative retinal detachment (5). The recommended management of solitary CHRPE is periodic observation through diagnostics tests described and the appropiate referral to the digestologist.

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