Peripheral exudative haemorrhagic chorioretinopathy (PEHCR)- A REVIEW

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ABSTRACT

Peripheral exudative haemorrhagic chorioretinopathy (PEHCR) is an underdiagnosed vascular disease of the peripheral retina. It was initially reported only in Caucasians with a benign course and conservative management. However now there are reports from across the world including Asia, of cases with hemorrhagic complications requiring active management. We have also proposed that PEHCR be added to the Pachychoroid spectrum of disorders, based on wide field OCT findings.

We present a short review and update on this intriguing entity.

Keywords: Peripheral AMD, PCV, Pachychoroid, AntiVEGF therapy.

INTRODUCTION

Peripheral exudative haemorrhagic chorioretinopathy (PEHCR) is a bilateral degenerative disease of the retina which is characterized by peripheral subretinal pigment epithelium(sub-RPE) and/or subretinal haemorrhage and exudation in the elderly. The disease remains asymptomatic unless the peripheral lesion extends into the macular area or causes breakthrough vitreous haemorrhage.

History

Historically, PEHCR has been reported mostly in Caucasian patients, but recent reports from Asian countries have narrowed down the racial disparity in the prevalence of PEHCR. On account of its peripheral location and asymptomatic nature, PEHCR principally remained unidentified and unreported as a disease entity until the advent of indirect ophthalmoscope. Since its first description by Reese and Jones in 1961 as peripheral hematomas under the retinal pigment epithelium, PEHCR has been associated with diverse terminology, diagnostic ambiguity, and equivocal treatment strategies.[1] Annesley was the first one to use the term PEHCR in a case series of 32 eyes, published in 1980.[2] He proposed a complex classification system based on the clinical presentation and evolution of PEHCR lesions. After a hiatus of almost three decades, Shields et al. published the largest case series on PEHCR including 173 eyes, all referred for management of possible choroidal melanoma.[3]

Demography

PEHCR is a disease of the elderly. The mean age various from 74-80 years.[3-7]As per the Western literature, upto 69% of those affected are female.[3-7] Goldmann et al. studied a subset of patients with PEHCR who had peripheral polyps and found that the mean age was slightly lower (70 years) in this subset, and majority of patients were men. Most of the earlier studies on PEHCR were conducted on European population and thereby show a high prevalence in Caucasian patients (99-100%).[8] However, later studies include case series and reports from Asian countries, including India as well.[9-11] PEHCR has been associated with systemic anticoagulants in 44-67% cases, and hypertension in upto 83% cases.[3,7]

Differential diagnosis

PEHCR is most commonly misdiagnosed as choroidal melanoma. Shield et al found it to be the second most

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common cause of pseudomelnoma, and delineated the features differentiating PECHR from choroidal melanoma as presence of retinal exudation, diffuse macular and peripheral RPE atrophic findings, hypofluorescence of the lesion on fluorescein angiography, lack of intrinsic vascular pulsations, presence of a clot retraction cleft on ultrasonography, and lack of sentinel vessels on slit-lamp biomicroscopy.[3]

Pathophysiology

The origin of PEHCR lesions has been hypothetically ascribed either to peripheral choroidal neovascular membrane (CNVM) or peripheral polypoidal choroidal vasculopathy (PCV). Although this hypothesis has no histopathological support but we do have the histopathological evidence of presence of peripheral choroidal neovascularization in aging eyes. 32.6% of senile eyes that Sarks studied, had choroidal neovascularization beneath the peripheral retina.[12] Interestingly, Friedman and colleagues found that essentially everyone above 60 years of age has new vessel formation near ora serrata between Bruch's membrane and the retinal pigment epithelium, especially temporally.[13] Moreover, the highly exudative and haemorrhagic characteristics of PEHCR resembling wet age-related macular degeneration (ARMD), also corroborate the hypothesis that PEHCR develops secondary to peripheral CNVM. Certain features of PEHCR also resembles those of PCV, including haemorrhagic pigment epithelium detachment (PED) and lipid exudation and dome-shaped PED on optical coherence tomography (OCT). The hypothesis is further substantiated by the presence of peripheral choroidal vascular network or peripheral polypoidal lesions on ultrawide-field fundus fluorescein angiography (UWF-FFA), indocyanine green angiography (ICGA) and OCT in eyes with PEHCR, as reported in more recent studies.[6,8,14]

Clinical manifestations and imaging

The lesion is most commonly found in the temporal quadrant (77-100%), usually involving 1-2 quadrants, located between the equator and ora serrata in upto 89% of cases (Fig 1).[3-5,7,14] The components of peripheral lesion can include subretinal hemorrhage (64-78%), subretinal fibrosis (56%), sub-RPE hemorrhage (26-44%), serous RPE detachment (28-83%), lipid exudation (52%), vitreous hemorrhage (24%), RPE tear (10%) and RPE hyperplasia or atrophy (75%).[3-5,14] In the series by Shields et al. the lesion presented as an elevated tumor-like mass in 77% eyes.[3]

The condition can be self-limiting and asymptomatic if it is confined to the peripheral retina, but it can also lead to visual impairment due to causes which are either PEHCR-related (21%) or secondary to concomitant ARMD (upto 69%).[3,6,7] Vandefonteyne et al. reported 83% symptomatic patients in their case series.[15] PEHCR-related causes of decreased vision include vitreous haemorrhage (14%), extension of subretinal haemorrhage (5%) or subretinal fluid (2%) into the macular area, and rarely macular oedema (14%).[3,7]ARMD changes can be early, like RPE alterations and drusen; or late, like macular CNVM or geographic atrophy. Advanced age at presentation can explain the accompanying signs of ARMD in PEHCR.[3,6,7] 69% of eyes also shows RPE alterations and drusen in the periphery.[3,14]

Bilateral involvement can be seen in upto 75% cases, or higher if inactive stage of RPE sequelae is included.[3-5,7,14] RPE alterations or drusen can be seen in upto 42% of contralateral eyes.[3]

The introduction of ultrawide field imaging has changed the way PEHCR is diagnosed, classified, and managed. Earlier studies which predated the era of ICGA, used only FFA as the mainstay for diagnosing PEHCR, and failed to identify peripheral polyps associated with PEHCR in cases where they could have been present. FFA revealed either blocked fluorescence due to subretinal pigment epithelium haemorrhage or subretinal haemorrhage; or irregular hyperfluorescence in the area of RPE changes, and rarely the characteristic lacy hyperfluorescence diagnostic of CNVM.[2-4] Goldman et al published a series of 10 patients with peripheral PCV as a cause of IPCV, all confirmed by ICGA and/or FFA along with OCT.[8] In their initial series, Mantel et al could delineated a pathological vascular

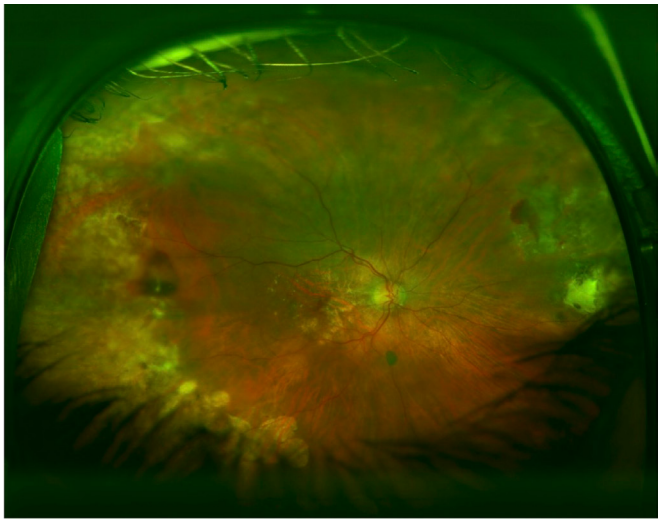

Figure 1: *PEHCR lesion including the temporal and nasal quadrant showing peripheral subretinal and sub-RPE haemorrhage along with chronic RPE changes.*

network, not visible on FFA, in 6 eyes using ICGA; but could not visualize polyps in any patient.[6] Later, the same group, using ultrawide-field FFA, ICGA and OCT spectralis in a series of 48 patients, could visualize polyp-like structures in 33 eyes (69%) and an abnormal choroidal vascular network in 24 eyes (50%), with dome-shaped PED over the lesion on OCT. They noticed that polyps were more frequently present at the border of the lesion than under it (79% vs 27%), whereas the CNVM was located mostly under the lesion than adjacent to it (67% vs 42%). Frequent peripheral choriocapillaris closure and dilated shunting vessels was also observed.[14] PEHCR is associated with a club-shaped configuration of choroid on widefield OCT with a progressive thickening of choroid towards the periphery. This is what made our group (Shroff et al) propose that PEHCR be a new addition to the PACHYCHOROID SPECTRUM of disease (Fig 2).[16]

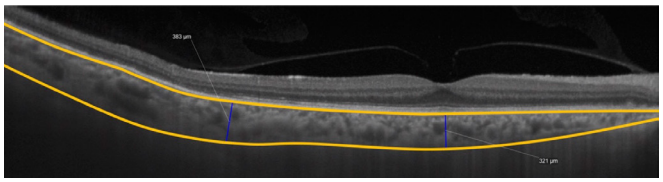

Figure 2: *SSOCT showing progressive thickening of choroid towards the temporal periphery and pachyvessels in a case of PEHCR. This is what made our group proposed addition of PEHCR to the pachychoroid spectrum of diseases. (Reference 16 of article)*

Treatment

There are no definite treatment guidelines for PEHCR in literature. Various treatment modalities include laser photocoagulation, cryotherapy, antiVEGF injection, combination therapy and vitrectomy. As the disease was thought to have a self-limiting course, treatment was traditionally indicated only if the vision was affected. Shields et al observed all the cases in their series on Caucasian patients. They noted progression only in 10 of 173 eyes. However, it's important to notice that 21 of the cases in their series had underwent treatment in the form of vitrectomy or laser photocoagulation or photodynamic therapy before presentation.[3] Rishi et al used combination therapy with antiVEGF followed by focal laser and achieved good visual outcome.[10] Kim et al used combination therapy and reported stable vision in 3 of 5 patients in their series.[9] Pinarci et al observed 11 eyes of 23 eyes (47.8%), and treated the rest with bevacizumab injections. They found that 3 eyes (13.04%), showed progression and decreased vision despite consecutive injections.[4] Goldman et al. achieved mixed results with bevacizumab in 4 of 8 eyes which were treated.[8] Cebeci et al. used bevacizumab/ranibizumab in 5 of 21 patients and found that mean VA improved from 0.81 logMAR to 0.73 logMAR.[7] Seibel et al. presented favourable anatomical outcomes in symptomatic patients with PEHCR after intravitreal injections of anti-VEGF agents.[17] Recent report by Sax et al showed resolution of vitreous haemorrhage and subretinal haemorrhage with aflibercept injection.[18] Vitrectomy is associated with favourable outcomes.[11,15,19] PEHCR was associated with more haemorrhagic complications in Asian patients.[9,11]

Our experience

We diagnose and monitor PEHCR cases using UWF-FFA, ICGA and swept-source OCT. We prefer combination therapy when possible, in cases where macula is involved or threatened. Vitrectomy is done in cases of vitreous haemorrhage along with antiVEGF injection. In view of the potentially vision threatening course, we have a low threshold for treatment in cases of PEHCR which have a history of PEHCR-related vision loss in the contralateral eye.

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