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Our experience in the diagnosis and treatment of peripheral exudative hemorrhagic chorioretinopathy

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Purpose: *To present our experience in the examination and treatment of patients with peripheral exudative hemorrhagic chorioretinopathy (PEHCR).*

Material and Methods: *We retrospectively reviewed the medical records of patients who were finally clinically diagnosed with PEHCR in the 2022-2023 period. History was collected and patients underwent ophthalmological examination including visual acuity, slit-lamp biomicroscopy, color fundus photography, fluorescein angiography and ocular ultrasound. All patients were treated with intravitreal anti-vascular endothelial growth factor (VEGF) therapy. One patient underwent vitreoretinal surgery.*

Results: *PEHCR was diagnosed in 11 patients (13 eyes), including two patients diagnosed with bilateral lesions. Clinical signs identified included a dome-shaped hemorrhagic detachment of the peripheral retinal pigment epithelium (RPE) with massive exudations. One patient underwent vitreoretinal surgery for vitreoretinal hemorrhage. On B-scan ultrasonography, the PEHCR lesion commonly presented as a dome or plateau-shaped mass with hollow or solid acoustic quality. Ten patients were treated with intravitreal aflibercept.*

Conclusion: *PEHCR is a chronic disease commonly associated with AMD. Detachment of the peripheral RPE is a major clinical manifestation of the disease, and may be complicated by sub-RPE hemorrhage in early disease. Anti-VEGF therapy is a major method of treatment whereas vitreoretinal surgery is indicated in complications accompanied by massive intravitreal hemorrhage or macula-threatening subretinal hemorrhage. Further investigation is needed to elucidate the etiology and pathogenesis of this entity and demonstrate the efficacy and safety of the aforementioned treatment modalities for PEHCR.*

Keywords:

peripheral exudative hemorrhagic chorioretinopathy, polypoidal choroidal vasculopathy, hemorrhagic detachment of the pigment epithelium

Introduction

Peripheral exudative hemorrhagic chorioretinopathy (PEHCR) is an uncommon disease of the peripheral retina. The first published description of PEHCR was by Reese and Jones [1] in 1962 in which hemorrhagic choroidal lesions were seen in the periphery of the retina in elderly patients thought to have age-related macular degeneration (AMD). There are few reports in the literature on PEHCR, although its exudative and hemorrhagic forms accounted for 8% and 5%, respectively, of all lesions that clinically simulate choroidal or ciliary body melanoma [2, 3]. The term "peripheral exudative hemorrhagic chorioretinopathy (PEHCR)" was coined by Annesley [4] in 1980. Silva and Brockhurst [5] observed findings similar to those reported by Reese and Jones [1] in six patients, and Shields and colleagues [6] reported the largest case series of 173 patients with PEHCR. Some authors believe that PEHCR may be caused by polypoidal choroidal vasculopathy (PCV). PCV is characterized by polyp-like sub-retinal pigment epithelium vascular abnormalities predominantly found in the macula and peripapillary region. Less commonly, PCV can be found peripherally [7, 8, 9].

The purpose of this study was to present our experience in examination and treatment of patients with peripheral exudative hemorrhagic chorioretinopathy.

Material and Methods

We retrospectively reviewed the medical records of patients referred to SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" for the diagnosis of choroidal neoplasm in the 2022-2023 period. Inclusion criteria were patients with the final clinical diagnosis of PEHCR based on the presence of peripheral lesions associated

with subretinal hemorrhage, hemorrhagic detachment of the retinal pigment epithelium (RPE), exudation or signs of peripheral choroidal neovascularization. Patients with history or examination evidence of eye trauma, inflammation or tumor in the eye or congenital ocular abnormalities were excluded.

History was collected and patients underwent ophthalmological examination including visual acuity, slit-lamp biomicroscopy, color fundus photography, fluorescein angiography (FA) and ocular ultrasound. FA was performed in a routine manner in the absence of contraindications and whenever the media were clear enough.

Patients were treated with 2-mg/0.05 mL intravitreal aflibercept. We used a dosing strategy with three initial 2-mg/0.05 mL intravitreal aflibercept loading doses every 4 weeks, followed by an as needed (pro re nata (PRN)) regimen.

Intavitreal aflibercept was injected in a standard sterile fashion in the operating room.

Vitreous hemorrhage was found in one eye, and was treated with a standard three-port 25-g vitrectomy for the removal of a pathologically changed vitreous with the posterior hyaloid. In addition, a 360-degree retinotomy was performed to remove massive subretinal exudates, hemorrhages and fibro-vascular tissue. Thereafter, the retina reattached correctly, and the endolaser was applied around the retinotomy site.

Results

Eleven patients (13 eyes; two patients had bilateral lesions) with the final clinical diagnosis of PEHCR were examined and treated at the institute in the 2022-2023 period. The mean patient age was 72.5 years (range, 66 to 79 years), most patients (8/11 or 72.7%) were women, and the mean age was higher in women. All patients were referred to the institute for suspected choroidal neovascularization (CNV) and were also examined at the Department of Ophthalmooncology exclude a malignancy. PEHCR was diagnosed after a comprehensive examination.

Clinical manifestations: The only common sign of PEHCR was a dome-shaped hemorrhagic detachment of the peripheral RPE. Exudative manifestations were present in all cases. Vitreous hemorrhage was present in one eye, making the visualization of the fundus difficult (signs of PEHCR were confirmed intraoperatively). Subretinal hemorrhage was the most common manifestation (100%); lipid exudation and subretinal fluid exudation were also observed (Fig. 1).

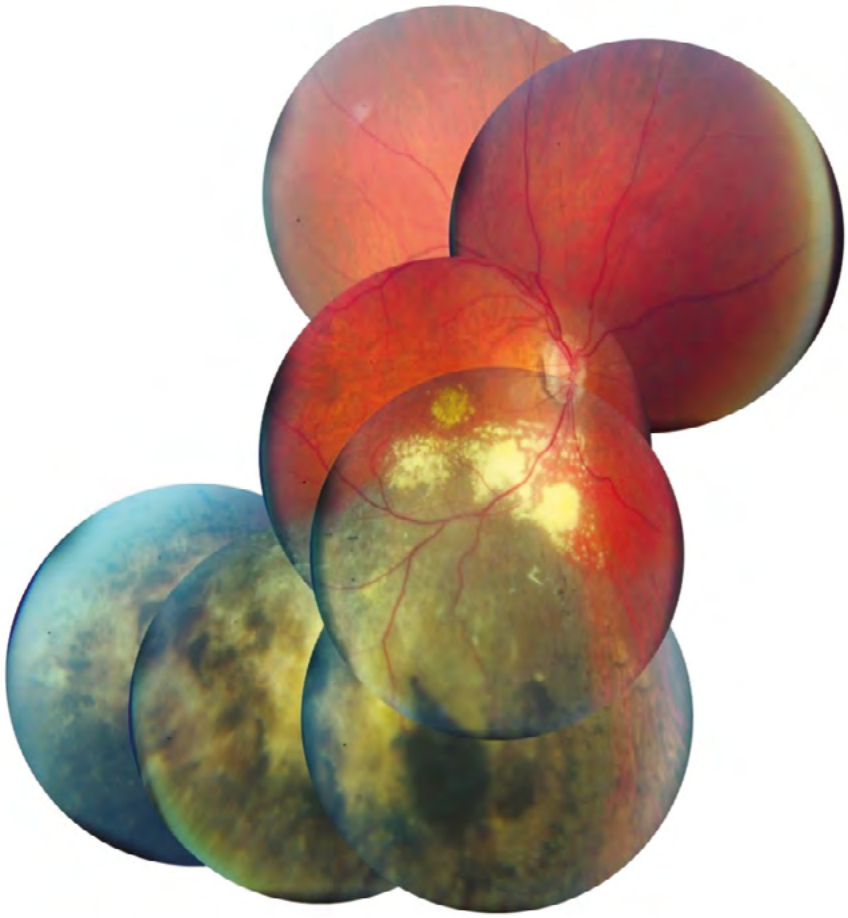

Fig. 1. Fundus photograph of a patient with peripheral exudative hemorrhagic chorioretinopathy. Note the presence of subretinal hemorrhage, lipid exudates and subretinal fluid in the inferotemporal region.

One isolated PEHCR lesion was present in seven patients, at least two lesions in one eye, in two patients, and bilateral lesions were present in another two patients. Lesions were usually located in the temporal quadrants (more commonly, in the inferior temporal quadrant). Chronic RPE changes (RPE hyperpigmentation and atrophy) adjacent to the PEHCR lesion(s) were present in 10 patients (12 eyes). In addition, extensive peripheral retinal changes in the fellow eye were present in the six patients diagnosed with unilateral PEHCR lesions, supposing bilateral although asymmetric lesions.

AMD was found in seven patients. Age-related maculopathy, dry AMD or neovascular (wet) AMD was diagnosed in any patient with pathological changes in the macula.

All patients had B-scan ocular ultrasound. The mean height of the lesion was 2.8 mm (range, 1.5 to 5 mm). On B-scan ultrasonography, the PEHCR lesion commonly presented as a dome or plateau-shaped mass with hollow or solid acoustic quality. No choroidal excavation, orbital shadow or clot retraction cleft was found in any case.

FA showed irregular late hyperfluorescence and persistent areas of hypofluorescence due to blockage of choroidal hyperfluorescence by hemorrhage in peripheral temporal locations of PEHCR lesions in 10 patients.

Anti-vascular endothelial growth factor (VEGF) therapy was used as primary treatment in ten patients. Partial regression of peripheral lesions and stabilization of the process (with a reduction in exudation and lesion area, resolution of hemorrhages and formation of subretinal fibrosis) were seen in the presence of anti-VEGF therapy.

The patient with vitreous hemorrhage underwent vitreoretinal surgery, during which massive subretinal exudates, hemorrhages and fibro-vascular tissue were found inferotemporally and removed. Subsequently, the patient also received anti-VEGF therapy.

Discussion

PEHCR has been uncommonly reported in the literature, mostly because it has various synonyms, including massive spontaneous hemorrhage [10], hemorrhagic peripheral pigment epithelial disease [11], hemorrhagic detachment of the peripheral retinal pigment epithelium [5, 12, 13], extramacular disciform lesion [14] and peripheral choroidal neovascularization [15, 16].

In addition, the majority of reports have been on small case series [4, 5, 10-16].

In the current case series, the mean patient age was 72.5 years (range, 66 to 79 years), which is in agreement with the age ranges (70 to 80 years) reported in the literature [4-6, 11, 14, 16]. In a case series of PEHCR secondary to peripheral PCV [8], the mean patient age was 70 years (range, 59 to 82 years).

Female preponderance is another typical feature of PEHCR. In the present case series, the percentage of women was 72.7%, which is in agreement with the literature (55% to 79%) [4, 6, 11, 14, 16]. In a study by Goldman and colleagues [8], however, patients with PEHCR caused by peripheral PCV were most commonly men, white, asymptomatic, and had a concomitant diagnosis of AMD.

Others have reported that PEHCR lesions were found most commonly in the temporal quadrant [4, 6, 11, 16], specifically in the inferotemporal quadrant and between the equator and the ora serrata [4, 14].

Our findings are in line with reports on hemorrhagic [4-6, 10-15] and exudative [4, 6, 14, 16] nature of PEHCR lesions, commonly resulting in disciform scars. Sub-RPE hemorrhages have been reported in 76% to 94%, and solid exudates, in 21% to 37% of patients with PEHCR. Therefore, signs of exudation and hemorrhages are typical features of the disease, and may be used as diagnostic criteria [4, 6]. To the best of our knowledge, atrophic retinal changes near the major lesion have been reported only by Shields and colleagues [6].

Bilateral involvement, subretinal hemorrhage and lipid exudates are important features for differentiating PEHCR from choroidal melanoma and choroidal metastases.

AMD was more common in our series (63.6%) than reported in the literature (4.5% to 39%) [4, 6, 14, 16]. Although PEHCR and AMD are similar in terms of mean age and some clinical manifestations, there are some differences between these diseases. Not every patient with PEHCR exhibits features of AMD. Drusen are a feature of AMD, but they have been not observed around the lesion in PEHCR. In the current study, B-scan echogenicity was mostly solid or hollow (48.2% and 39.3%, respectively), which is in agreement with clinical and FA evidence of hemorrhagic or serous detachment of the RPE. FA is useful in the disgnosis of PEHCR despite some technical limitations associated with the peripheral location of lesions. Bardenstein and colleagues [14] reported that FA showed late leakage or blockage of choroidal fluorescence in 83% of eyes with PEHCR. This is consistent with the current study, in which FA demonstrated late irregular leakage in eyes with PEHCR. Optical coherence tomography (OCT) and indocyanine green angiography (ICGA) are other useful techniques for detecting peripheral choroidal polyps and subretinal neovascularization in patients with peripheral PCV [8, 9].

An OCT study by Shroff and colleagues [17] found that the choroid was significantly thicker in temporal periphery in PEHCR eyes as compared to controls. They concluded that thicker choroid and pachyvessels favor inclusion of PEHCR into a pachychoroid disease spectrum, which includes e.g. PCV [18].

We found a report on the histological examination of the PEHCR eye with finding of the hemorrhagic rupture of the RPE in the periphery and total hemorrhagic retinal detachment, but without signs of neovascularization, accumulation of drusen or basal lamina accumulation in the peripheral retina [19, 20]. This is in agreement with the hypothesis by Goldman and colleagues [8] who suggested peripheral PCV to be a cause of PEHCR. Goldman and colleagues [8] used ICGA to find type 1 subretinal neovascularization in all PEHCR eyes of the study.

In general, there is no standard of care for this uncommon disease entity. Asymptomatic patients should be observed because the majority of PEHCR lesions (89% of cases in a series by Shields [6]) stabilize or regress. In the current cases series, anti-VEGF therapy (intravitreal aflibercept) was employed as a method of treatment in most cases, and partial regression of peripheral lesions was seen in the presence of this treatment, which is in agreement with previous reports by others [21-23].

Takkar and colleagues [24] reported on a case of PEHCR with extramcular choroidal neovascular membrane (CNVM). The patient was treated successfully with a single dose of intravitreal bevacizumab followed by laser photocoagulation of the CNVM. Others have reported on successful treatment with (1) intravitreal bevacizumab and indocyanine green angiography-guided laser photocoagulation for PEHCR caused by peripheral PCV [7] and (2) a combination of transscleral cryotherapy and intravitreal anti-VEGF ingections for PEHCR and peripheral PCV [9].

Although most eyes with PEHCR from peripheral PCV experience a benign course with spontaneous resolution, a subset of eyes may experience macula-threatening hemorrhage, requiring treatment with laser-based therapies, anti-vascular endothelial growth factor injections, or surgical intervention [8]. Vitreoretinal surgery may be used for vitreous hemorrhage [9]. In the current study, vitreous hemorrhage was present in one eye, making the visualization of the fundus difficult, and vitreoretinal surgery was performed to remove vitreous hemorrhage and subretinal subretinal exudates, hemorrhages and fibro-vascular tissue.

Conclusion

PEHCR is a chronic disease commonly associated with AMD. Detachment of the peripheral RPE is a major clinical manifestation of the disease, and may be complicated by sub-RPE hemorrhage in early disease. Anti-VEGF therapy is a major method of treatment whereas vitreoretinal surgery is indicated in complications accompanied by massive intravitreal hemorrhage or macula-threatening subretinal hemorrhage. Further investigation is needed to elucidate the etiology and pathogenesis of this entity and demonstrate the efficacy and safety of the aforementioned treatment modalities for PEHCR.

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Disclosures

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Ethical considerations: *Informed consent was not applicable due to the retrospective nature of the study.*

The study was approved by the local Institutional Review Board (IRB) and followed the Declaration of Helsinki, the European Convention on Human Rights and Biomedicine, and relevant laws of Ukraine. Animals were not used in this study.

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Abbreviations: *AMD, age-related macular degeneration; Anti-VEGF, anti-vascular endothelial growth factor; PEHCR, peripheral exudative hemorrhagic chorioretinopathy; PRN, ProReNata; RPE, retinal pigment epithelium*