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Posterior Polymorphous Corneal Dystrophy Coexisting with Central Serous Chorioretinopathy – Case Report

Dystrofia polimorficzna tylna współistniejąca z centralną chorioretinopatią surowiczą – opis przypadku

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Abstract: Posterior polymorphous corneal dystrophy is a rare, usually bilateral and asymmetric corneal genetic disorder with wide clinical manifestation. Central serous chorioretinopathy is common nonsurgical retinal disorder. Etiology, risk factors, pathomechanism of discussed diseases are not completely clear. We describe a case of unusual coexistence of these disease entities in a middle-aged woman and its potential association.

Key words: posterior polymorphous corneal dystrophy, central serous chorioretinopathy, optical coherence tomography, fundus fluorescein angiography.

Abstrakt: Dystrofia polimorficzna rogówki jest rzadkim, najczęściej obustronnym i asymetrycznym genetycznym schorzeniem rogówki o różnorodnym obrazie klinicznym. Centralna chorioretinopatia surowicza jest częstym, niewymagającym leczenia chirurgicznego schorzeniem siatkówki. Etiologia, czynniki ryzyka i patomechanizm omawianych chorób są nie do końca poznane. W poniższym opracowaniu omówiony został przypadek pacjentki, u której podczas badania okulistycznego wykryto niespotykane współistnienie powyższych jednostek chorobowych oraz ich potencjalny związek.

Słowa kluczowe: dystrofia polimorficzna tylna rogówki, centralna chorioretinopatia surowicza, optyczna koherentna tomografia, angiografia fluoresceinowa.

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Introduction

Posterior Polymorphous Corneal Dystrophy (PPCD) is a rare, bilateral, corneal endothelial disorder with autosomal dominant or recessive inheritance. The disease was first described by Koeppe in 1916. Due to the abnormal cellular metabolism, the corneal endothelium produces a defective basement membrane. PPCD is characterized by polymorphous alterations in corneal endothelium and in thickened, abnormal Descemet's membrane. The disease can be detected by slit-lamp examination, specular and confocal microscopy or anterior segment optical coherence tomography (1, 2).

Most patients are asymptomatic and the disease is stable, however some complain about photophobia, decreasing vision and dry eyes, even the corneal oedema can develop as a result of faulty endothelium. Mutations in OVOL2, COL8A2, ZEB1 gene have been identified as causing PPCD. The disease can be associated with many ocular abnormalities, including stromal and epithelial oedema, keratoconus, iridocorneal adhesions with peripheral anterior synechiae, corectopia, pupillary ectropion, increased intraocular pressure. Concomitant extraocular conditions are abdominal hernias and Alport syndrome (3).

Central serous chorioretinopathy (CSCR) has been estimated as the fourth most common retinopathy (after age-related macular degeneration, diabetic retinopathy and branch retinal vein occlusion). CSCR occurs six times more frequently in men than in women, usually in age ranges of 20 to 50 (4). The disease is defined as a serous detachment of the neurosensory retina or retinal pigment epithelium most commonly occurring in the macular region. As a consequence, the accumulated macular subretinal fluid causes the reduction of visual acuity. The presented symptoms depend on the location and amount of fluid. If the central retinal region is affected, a patient can complain of acute change in visual acuity, decreased contrast sensitivity, colour saturation, metamorphopsia, micropsia, hyperoptic shift, central scotoma (5, 6). CSCR is classified to acute, recurrent or chronic form (more than 6 months) (4). In the literature, the first description of CSCR was made by Von Graefe in 1866 (7). Since then, the understanding of the pathophysiology of this condition and its natural course has changed, thanks to the rapid development of imaging methods (4). However, the pathogenesis is still to be fully understood and no responsible pathophysiologic mechanisms have been proven. The choroidal hyperpermeability and consequent subretinal fluid accumulation with retinal pigment epithelium da-

mage could be induced by glucocorticoids, catecholamines and increased sympathetic activities. Common risk factors include steroid usage, type A personality, pregnancy, obstructive sleep apnoea, *Helicobacter pylori* infection and oxidative stress. The acute form of CSCR is usually self-limited and resolves spontaneously within 2 to 3 months. The treatment options including observation with risk factors modification, carbonic anhydrase inhibitor or anisteroidal drugs therapy, micropulse laser photocoagulation, photodynamic therapy, anti-vascular endothelial growth factor (anty-VEGF) therapy (4).

In this paper, we report the case of concomitant PPCD and CSCR in a middle-aged, previously untreated woman. The aim of this case is to find the probable association between PPCD and CSCR, including the review of the current literature. To the best of our knowledge, this is the first report of patient with coexisting PPCD and CRCS.

Case report

A 52-years-old, previously healthy woman was presented to the Ophthalmic Ward at the Municipal Hospital in Rzeszow due to visual impairment in the left eye persisting for three days. The patient complained of a large, dark spot in the central vision of her left eye. She described her vision as being yellowish-brown. The woman denied any ocular pain, floaters or flashes. The patient reported no trauma to the eye region. The ocular history was not significant. She denied chronic diseases, did not take any medication and was operated on uterine myomas in the past. Family history was negative for ocular diseases, however we have not examined other family members.

On admission, a complete ophthalmic examination was performed, including refraction test, applanation tonometry, slit-lamp biomicroscopy, pachymetry, specular microscopy (Tomey EM-3000), colour fundus photographs, fluorescein angiography (Zeiss FF 450 plus Fundus Camera with VISUPAC™ Digital Imaging System), anterior segment, macula and disc optical coherence tomography (Spectral Domaine Optopol Revo NX OCT), ultrasound of the both eyes (Quantel Medical Aviso S).

On ocular examination, best corrected visual acuity (BCVA) was 1.0 in the right eye and 0.6 in the left eye with a hyperopic correction (+3.75 D and +4.25 D, respectively). The corrected intraocular pressure was measured at 12.8 mmHg in the right eye and 11.7 mmHg in the left eye by applanation tonometer. Slit-lamp examination revealed bilateral corneal horizontal lesions, vesicles and polymorphous opacities located at the level of Descemet's membrane and corneal endothelium. The endothelium had a beaten metal appearance. "Surface of the moon" was observed in retro-illumination. The pupils were equal, slightly irregular and reactive to light. In the left eye, we noticed that the inner pigment layer at the pupil margin has bunched up and rotated forward through the pupil at 12 o'clock position (Fig. 1). Fundus examination showed orange-pink optic disc with sharp, flat margins. The vertical cup-to-disc ratio was symmetric and equalled 0.5. Retinal pigment epithelium degeneration was localized nasal to the fovea in the right eye. Moreover, serous macular detachment with subretinal fluid at the posterior pole was suspected in the left eye. Areas of retinal pigment epithelial hypertrophy of peripheral retina was seen mainly in the infero-nasal segment of the right eye and infero-temporal segment of the left eye (Fig. 2).

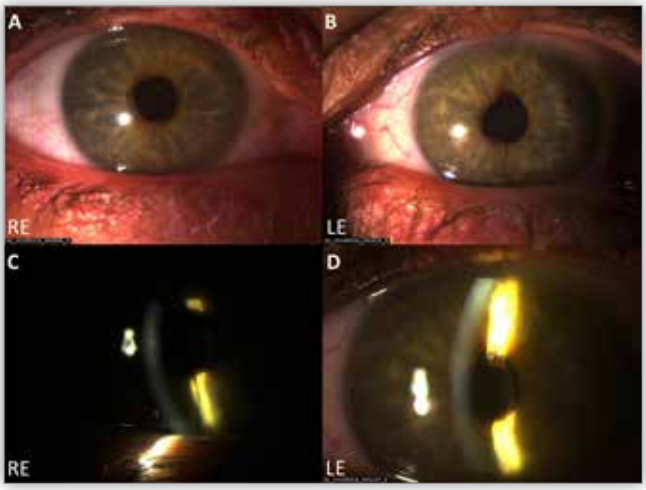

Fig. 1. Slit-lamp photos. Ectropion uveae of the right (A) and left (B) eye. Grey-white opacities, scattered vesicles and "beaten metal" appearance at the level of Descemet's membrane and corneal endothelium of the right (C) and left (D) eye.

Ryc. 1. Zdjęcia w lampie szczelinowej. Wywinięcie listka barwnikowego tęczówki w oku prawym (A) i lewym (B). Szaro-białe zmętnienia, rozsiane pęcherzyki i obraz „kutego metalu" na poziomie błony Descemeta i śródbłonka rogówki oka prawego (C) i lewego (D).

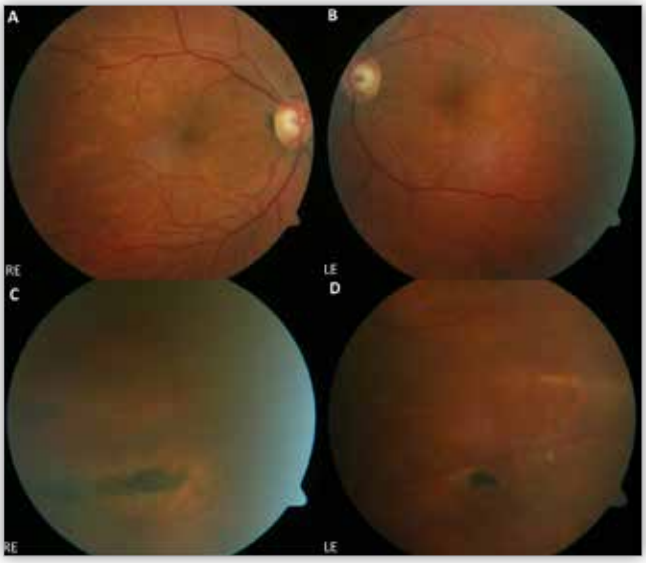

Fig. 2. Color fundus photographs. Retinal pigment epithelium degeneration nasal to the fovea in the right (A) eye. Serous macular detachment at the posterior pole in the left (B) eye. Areas of retinal pigment epithelial hypertrophy of peripheral retina in the right (C) and left (D) eye.

Ryc. 2. Kolorowe zdjęcia dna oka. Zwyrodnienie nabłonka barwnikowego siatkówki nosowo do dołka w prawym (A) oku. Surowicze odwarstwienie w plamce w tylnym biegunie lewego (B) oka. Obszary hipertrofii nabłonka barwnikowego obwodowej siatkówki w prawym (C) i lewym (D) oku.

Non-contact specular microscopy revealed bilateral variations in cell size and morphology and vesical-like changes surrounded by hexagonal cells of the right eye (Fig. 3). The endothelial densities were 2405 cells/mm^2 in the right eye and 2299 cells/mm^2 in the left eye. The endothelial cell count was slightly diminished. Endothelial polymorphism and polymegathism were noted. The central corneal thickness was 562 μm and 546 μm in the right and left eye, respectively.

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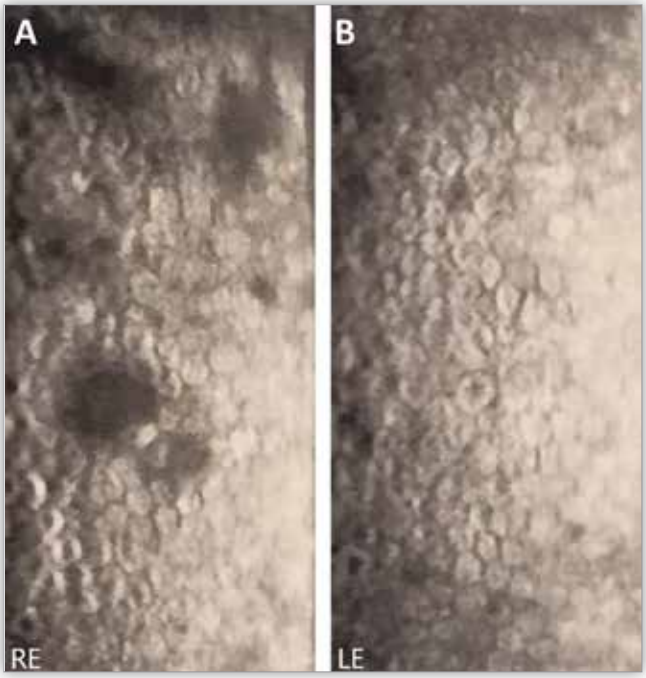

Fig. 3. Specular microscopy. Variations in size and shape of the endothelial cells in the right (A) and left (B) eye and vesical-like changes in the right (A) eye.

Ryc. 3. Mikroskopia lustrzana. Różnice w rozmiarze i kształcie komórek śródbłonka w prawym (A) i lewym (B) oku oraz zmiany pęcherzykowate w prawym (A) oku.

Anterior segment optical coherence tomography (OCT) revealed some hyperreflective irregular bands on posterior endothelial surface in both eyes (Fig. 4). Macula OCT scans showed bullous elevation of neurosensory retina with mild retinal pigment degeneration, hyporeflective space between neurosensory retina and retinal pigment epithelium and small cyst in nerve fibre layer of the left eye. The OCT scan revealed some irregularities of photoreceptors and pigment epithelium layer in the right eye (Fig. 5).

Fluorescein angiography showed two adjacent ink points of leak with a slight increase in intensity in mid- and late phase in the macular region and similar leakage point under arteriola temporalis retinae superior in the left eye. The examination of the right eye revealed a window defect where retinal pigment epithelium is missing in the macular region and single hyperfluorescence temporal between the temporal arterioles. The margins and the intensity of the fluorescence fades remained distinct (Fig. 6).

No other ocular abnormalities were observed in either eye.

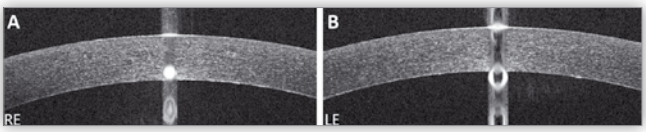

Fig. 4. Anterior segment optical coherence tomography. Raised hyperreflective lesions on the irregular posterior endothelial surface of the right (A) and left eye (B).

Ryc. 4. Optyczna koherentna tomografia przedniego odcinka. Uniesione hiperrefleksyjne zmiany na nierównej tylnej powierzchni śródbłonka prawego (A) i lewego (B) oka.

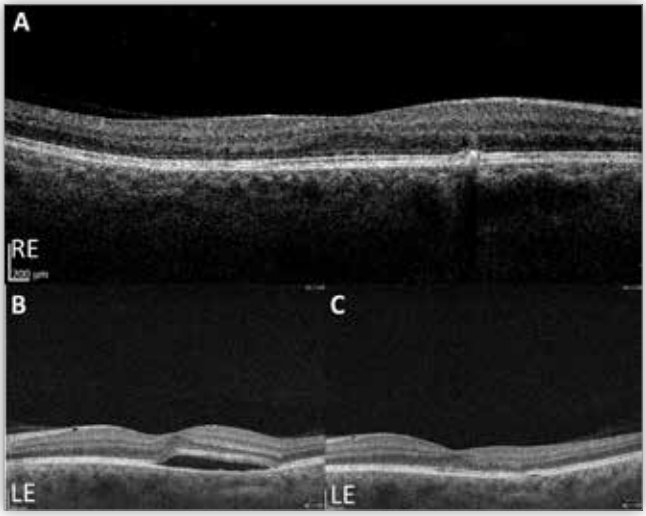

Fig. 5. Optical Coherence Tomography. Irregularities of photoreceptors and pigment epithelium layer at posterior pole of the right (A) eye and elevation of neurosensory retina with hyporeflective subretinal space and elongated photoreceptor outer segments at posterior pole of the left (B) eye. Shallow subretinal fluid with photorecetor discontinuity after one month in the left (C) eye.

Ryc. 5. Optyczna koherentna tomografia. Nieregularności fotoreceptorów i nabłonka barwnikowego siatkówki w tylnym biegunie prawego (A) oka oraz uniesienie siatkówki neurosensorycznej z hiporefleksyjną podsiatkówkową przestrzenią i wydłużonymi zewnętrznymi segmentami fotoreceptorów w tylnym biegunie lewego (B) oka. Powierzchowna warstwa płynu podsiatkówkowego z utrata ciągłości fotoreceptorów po pierwszym miesiącu w lewym (C) oku.

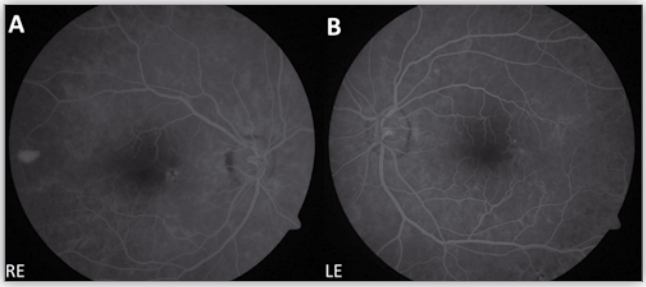

Fig. 6. Fluorescein angiography – late phase. Window defect in the macular region and single hyperfluorescence temporal between the arterioles temporalis in the right (A) eye. Two adjacent ink points of leak in the macular region and similar leakage point under arteriola temporalis retinae superior in the left (B) eye.

Ryc. 6. Angiografia fluoresceinowa – faza późna. Okienkowy ubytek w rejonie plamkowym i ognisko hiperfluorescencji skroniowo między arkadami skroniowymi w prawym (A) oku. Dwa sąsiadujące ogniska przecieku typu plamy atramentu w rejonie plamkowym i podobne ognisko przecieku pod naczyniem skroniowym górnym w lewym (B) oku.

Discussion

PPCD is a rare genetic disorder, that can be asymptomatic for decades. In most cases it does not require any treatment (8). Due to its natural history, the disease could be detected incidentally during the ordinary ocular examination. The awareness of PPCD is crucial for the patient, because he/she requires frequent check-up eye exams. The ophthalmologist should pay attention to secondary glaucoma screening and detailed anterior segment examination. Glaucoma associated with PPCD is caused by the growth of the abnormal endothelium

over the angle inhibiting the drainage of aqueous humour (3). Another risk factor for optic nerve damage is hyperopia, which can contribute to primary angle-closure glaucoma. The vertical cup-to-disc ratio was symmetric and increased (0.5), however cupping is not one and only indicative of glaucoma. Retinal nerve fiber layer (RNFL) thinning was not found and the adjusted intraocular pressure values were within normal limits. At that moment, based on the performed exam, we did not diagnose glaucoma and we recommended regular and complex examinations.

Liskova et al. (9) reported the highest prevalence worldwide of PPCD in Czech Republic (at least 1 in 100,000 inhabitants). Collected data suggested that, as of yet, undiscovered mutation could be inherited from a common ancestor. Due to the fact that Poland shares the boarder with Czech Republic on the south, further studies on larger series with genetic investigations are recommended to find a possible correlation between PPCD morbidity in Poland and Czech Republic.

To the best of our knowledge, a case report of a patient with concurrent PPCD and CSCR has not been published yet. Pathogenic mechanisms of both diseases remain unclear, which leads to the conclusion that there might be a common pathogenic factor contributing to concomitance of PPCD and CSCR, with regard to contemporary literature.

PPCD is usually asymmetric, bilateral and is characterized by heterogeneity of clinical manifestation from asymptomatic course to photophobia, decreased vision, corneal oedema and glaucoma. The suspicion of corneal dystrophy was made through asymmetric granular and horizontal band-like lesions centrally and ectropion uveae on slit lamp examination of the right and left eye. Abnormal endothelial cells transform and migrate in Descemet's membrane causing secondary alterations. As a consequence, the hexagonal endothelial cells are replaced by the epithelial-like cells (3). These disorders are visible in specular microscopy as round cystic or vesicular areas and band-like dark areas with some lighter smaller cells called "snail track " lesions among the normal hexagonal cells.

To confirm the diagnosis, we performed additional imaging studies: specular microscopy and anterior segment OCT that identified the typical described features. This case shows that anterior and posterior corneal surfaces imaging can be very useful in PPCD diagnosis.

Detailed fundus examination revealed abnormalities in posterior pole of the both eyes. Various retinal pigment epithelium disorders were manifested: central degeneration with microrip in the right eye, serous macular detachment in the left eye and bilateral unifocal lesions of hipertrophy in the peripheral retina. The oldest and classic imaging technique Fundus Fluoresceine Angiography and first-line modern technique OCT showed the presence of subretinal fluid.

The pathophysiology of CSCR has not been cleared so far. It has been suggested that the combination of the complex Bruch's membrane – RPE dysfunction and choroidal hypermeability may result in the increase of fluid leakage to the subretinal space (10, 11).

Del Turco et al. (12) reported collagen disorder in basement membrane layer in PPCD and large colloid drusen. According to him, collagen deposition abnormalities in the endothelium are presented in PPCD. Moreover, colloid drusen are related to Bruch's membrane (which mainly consists of collagen) dysfunction. Detailed study and genetic tests are needed to confirm his hypothesis.

Alport syndrome is an inherited disease with mutations in COL4A5 (85% cases), COL4A3 or COL4A4 genes which results in disorders in the collagen biosynthesis ($\alpha 3 \alpha 4 \alpha 5$ type IV collagen chains). Type IV collagen is an important part of basement membranes, mainly in the kidney, cochlea and eye. Alport disease is characterized by kidney disease, hearing loss and ocular abnormalities like PPCD, keratoconus, posterior lenticonus, dot-and-fleck retinopathy that are caused by collagen network dysfunction (12, 13).

According to Norouzpour et al. (14), high level of endogenous or exogenous glucocorticosteroids is associated with the accumulation of subretinal fluid in CRCS. One of the mechanism of glucocorticoid effects is suppression of collagen synthesis in Bruch's membrane that may inhibit any reparative process and lead to the focal leakage.

There is much to be discovered about the pathophysiology of PPCD and CSCR, however abnormalities in collagen deposits in basement membrane in cornea and Bruch's membrane can be found in these conditions as well.

On follow-up examination one month after the onset of CRCS, subfoveal fluid has been almost completely absorbed. The residual amount of subretinal fluid persisted temporally to the fovea. OCT showed slight discontinuity of photoreceptors of intact region (Fig. 5). The patient denied dark spot in the central vision, but BCVA was 0.8 in the left eye that suggests irreversible damage of retinal pigment epithelium. The patient has been treated with oral acetazolamide (carbonic anhydrase inhibitor) for 10 days and nepafenac eye drops for 30 days. The natural course of CSCR is in general self-limited and standards of the treatment are not clearly defined (7), therefore establishing of the therapy, especially of recurrent or persistent CSCR, can be demanding.

Conclusion

In conclusion, we consider described case report a unique and valuable contribution to medical knowledgebase. The unexpected association between PPCD and CSCR indicates the potential dysfunction of collagen structure, as per detailed description of this article. Additional genetic investigations and further research on larger scale are needed to confirm the common contributing factor.

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