Pseudovitelliform Macular Dystrophy and Pigment Dispersion Syndrome: Are They Related?

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ABSTRACT

Pseudovitelliform macular dystrophy (PVMD) and pigment dispersion syndrome (PDS) are benign diseases that can evolve to a very severe stage. It is very rare to encounter both diseases in the same patient. We report a 42-year-old patient that presented a blurry vision. The anterior and posterior segment examination found pseudovitelliform macular degeneration associated with pigment dispersion syndrome. No other case was reported in the literature.

The physiopathology and the location of the two diseases are very different. Both pathologies are frequently benign. A combination of them should be considered a risk for the patient.

More cases of the two diseases should be reported to the literature if found and it could maybe lead to a link between them.

Keywords: Genetics, Pigment dispersion syndrome, Pseudovitelliform macular dystrophy.

1. Introduction

The pigment dispersion syndrome (PDS) and pseudovitelliform macular degeneration (PVMD) are two separate entities.

PDS is an abnormal concavity of the iris which is in contact with the ciliary band [1], [2] and causes pigment dispersion in the posterior and anterior chambers.

PDS can be complicated by pigmentary glaucoma (PG): the pigment obstructs the trabecular meshwork which rises the intraocular pressure (IOP) and causes nerve damage.

We estimate that 1%–1.5% of glaucoma cases in Caucasian countries are PDS causing PD [3].

On the other hand, PVMD is a very rare genetic macular disease caused by an accumulation of lipofuscin within the subretinal space [4].

PVMD and PDS are benign diseases that can evolve to a very severe stage. It is very rare to encounter both diseases in the same patient, and no case was reported in the literature.

We report a case of pseudovitelliform macular degeneration associated with pigment dispersion syndrome.

2. Case Report

A 42-year-old male presented to the hospital for blurry vision, and headaches. The refraction was –0.25 (–0.25 at 100°) in the right eye and (–0.25 at 5°) in the left eye with a 10/10 visual acuity. Intraocular pressure was 16 for both eyes. The anterior segment exam was notable for Krukenberg spindles on both sides (iris pigments in the inner layer of the cornea) (Fig. 1).

Fig. 1. Krukenberg spindle on slit lamp examination.
Gonioscopy showed an open angle (Schaffer stage 4) very pigmented with a Sampaolesi line and a posterior concavity of the iris (Fig. 2).

The anterior segment OCT shows a posteriorly bowed iris towards the zonula and posterior chamber (Fig. 3).

Retina examination showed a normal cup/disc ratio (4/10 symmetric) with an abnormal yellow reflect of the macula region in both sides (Fig. 4).

On autofluorescence, there was a hyperfluorescent lesion of the macula region (Fig. 5).

In fluorescein angiography, we find a diffusion in the fovea during all times of the examination (Fig. 6).

On OCT there was a material accumulation under the foveal depression between the retinal layers and an irregular pigment epithelium (Fig. 7).

RNFL analysis showed suspicious temporoinferior damage to the nerve fibers of the right eye, and superotemporal damages on the left eye. Ganglion cell analysis was normal in both eyes.

With all these findings, the diagnosis of PDS and PVMD was retained.

The treatment consisted of performing a peripheral iridotomy in both irises, and monitoring.

During follow-up no progression of the disease occurred, and we found no evidence of complication or visual loss.

3. Discussion

3.1. Pigment Dispersion Syndrome

PDS occurs in patients between 20 and 40 years of age. In the literature, reports of the risk of developing PG from PDS are estimated as between 35% and 50% [3].

Interestingly, congenital abnormalities due to mesodermal migration have been suggested to have a role in the
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Fig. 6. Fovea diffusion during fluorescein angiography.

Fig. 7. OCT of the macula showing a vitelliform accumulation under the retinal layers.

Fig. 8. Peripheral iris defects during transillumination [22].

Development of PDS/PG [5], and a genetic anomaly occurring in the third trimester seems to be generally accepted as an etiological factor of PDS and PG [6].

Authors hypothesized that mutation of the LOXL1 gene could lead to defects of the stromal elastic fibers of the iris [7].

PDS has been reported as an autosomal dominant disease [8]. Familial aggregation is a characteristic of PDS.

Unspecified, multiple genes coupled with environmental influences can cause these conditions [9]. Chromosome 7q35-q36 may be related to or increases the risk for PDS [8].

In 1970, Campbell discovered a direct correlation between the extent and position of iris transillumination defects and bundles of zonules that were inserted into the anterior surface of the lens in PDS [10]. It was proposed that frequent friction caused by iris movements led to pigment dispersion and iris transillumination [11], [12]. The typical location and proximity of the zonular bundles to the mid-peripheral iris and transillumination defects indicated that these bundles were responsible for the loss of pigment from the posterior iris [13]. Campbell also reported a characteristic backward bowing of the iris [10]. Moroi et al. [14] suggested an alternative mechanism associated with elongated anterior zonules centrally inserted on the anterior lens capsule, which could damage the iris pigment epithelium and cause pigment dispersion. A congenital posterior insertion of the iris has also been identified as a distinctive feature of PDS [15].

Pigment spreads in the anterior segment through aqueous humour and then accumulates in the trabecular meshwork on the posterior side of the cornea as Krukenberg spindles and on the anterior surface of the lens.

Pigment buildup can also be observed as a dark line on Schwalbe’s line. Detailed studies at the microscopic level have demonstrated the presence of pigmented epithelial melanosomes within the trabecular meshwork, as well as melanin inside the trabecular cells, indicating their ability to engulf and digest pigment [16], [17]. The Krukenberg spindle, a distinctive feature, is not caused by loose pigment cells sticking to the cornea. Instead, it results from pigment cells that have been engulfed by the endothelium [12], [18].

A patient with PDS may refer symptoms of headache and sporadic blurry vision, especially in the context of extreme physical activity [19].

In PDS, increases in intraocular pressure (IOP) typically range around 30 mmHg. However, occasional instances of more pronounced surges in IOP can occur, which coincide with episodes of pigment discharge and swelling of the cornea [3], [20], [21].

Slit lamp examination shows iris transillumination (Fig. 8) defects and Krukenberg spindle [22].

Increased depth both in the central and peripheral areas during anterior chamber examination [23].

In gonioscopy, the trabecular meshwork is typically very pigmented at 360° with more intense pigmentation in the inferior part caused by gravity force. The Sampaolesi line is a pigmented line located in the inferior part of the chamber angle anterior to Schwalbe’s ring. It is not exclusive to PDS but is frequently found during examination [24].

Fundus examination can find glaucomatous optic nerve neuropathy in case of evolution to PG.

OCT allows early diagnosis of glaucoma by showing a decrease in the thickness of the retinal nerve fiber layer and ganglion cells [25].

Arigfoglu and al conducted a study involving 102 patients, employing SD-OCT (Spectral Domain Optical Coherence Tomography) and visual field analysis. Their
findings revealed a reduced average thickness of the retinal nerve fiber layer in patients with PG compared to PDS. Additionally, they observed that the superior and inferior ganglion cell complex exhibited a thinner profile in PG eyes. As a result, the authors concluded that assessing the thickness of the retinal nerve fiber layer and ganglion cell complex using SD-OCT could serve as a valuable parameter for distinguishing between PG and PDS [26].

Betablockers, alpha-agonists, carbonic anhydrase inhibitors, and prostaglandins are the main treatment for IOP elevation.

Yag laser iridotomy consists in creating an orifice in the iris to balance the pressure between the anterior and posterior chambers. It helps flatten the iris and prevent contact with the zonular fibers. However, the iridotomy is still under debate as if it helps prevent the progression of PDS to PG.

3.2. Pseudovitelliform Macular Dystrophy

PVD is characterized by the deposit of a yellow material in the macular region [27]. The yellow appearance is a result of a particular amount of accumulated loose lipofuscin and photoreceptor debris [4].

It had been described for the first time in 1974 by Gass [28]. This lesion is found in a very heterogeneous family of pathologies some are known as the “pattern dystrophies” [29] and others are acquired known as “acquired vitelliform macular degeneration” (AVMD) [30].

The PVMD is an inherited autosomal dominant disease [27]. Mutations in the peripherin/RDS gene are a frequent cause of PD [31], 15 mutations of the gene have been described [32]. The gene codes for the peripherin/RDS protein which has a key role in the formation and renewal of the discs in the rod and cone photoreceptors outer segment. These structures are essential for phototransduction [33].

Considerable phenotypic variability families had been reported [34].

PVMD is distinguished by the existence of horizontally oval macular lesions that are about one-third the size of a disc, displaying a clearly defined border and appearing grayish yellow in color. While smaller than the vitelliform lesions observed in Best’s disease (BD), they exhibit a remarkable similarity in their coloration [27].

The classical appearance of BD is the single, bilateral symmetrical yolk yolk-like (vitelliform) lesion at the fovea [35] (Fig. 9).

BD is the principal differential diagnosis of pseudovitelliform dystrophy, but it most commonly affecting a juvenile population.

The diagnosis of PVMD can be challenging there is not a single diagnostic test or imaging modality that can provide a definitive diagnosis [30].

Macular OCT, fluorescein angiography and autofluorescence can help to orientate and assess the diagnosis.

Fluorescein angiography shows generally a leakage during the late phases of the exam.

It was believed that the presence of autofluorescence in the ocular fundus was solely due to lipofuscin in the retinal pigment epithelium (RPE). However, it has now been recognized that the autofluorescent material in the RPE comes from indigestible components of photoreceptor outer segments that have been phagocytized [36]. Additionally, autofluorescence also occurs within photoreceptor outer segments themselves [36].

In the OCT image, one can observe that the lesion is typically found within the subretinal space, situated between the retinal pigment epithelium (RPE) and the neurosensory retina. [37].

Till today, there is no proven and efficient treatment of this disease. Some authors suggest anti-VEGF injections however, the effect of anti-VEGF on these lesions remains uncertain, and the existing body of literature does not present a unanimous agreement regarding their advantages in this disease [30].

The other option is to monitor closely the patient and is the most privileged choice.

PVMD is identified by mild visual impairments affecting both eyes, with a noticeable lack of significant deterioration in vision or extremely slow progression of visual loss [27].

However, there is a range of perspectives regarding the impact of PD on visual disability. Some authors argue that PD primarily leads to mild visual impairment [38], [39]. But there are also reports of families where visual loss appears to be more pronounced [40], [41]. The prognosis is not necessarily benign, and progression often results in significant impairment and legal blindness in its advanced stages [29].

3.3. Synthesis

Certainly, the two diseases have a genetic origin but the genes responsible are not the same and no evident connection has been found. Loxl1 which is muted in the PDS is located on the 15th chromosome, meanwhile, the peripherin/RDS also known as the PRPH2 gene is located on the 6th chromosome.

The peripherin/RDS gene mutation is found in a minority of patients diagnosed with pattern dystrophies [31]. The
mutation has also been identified in other retinal diseases such as retinitis pigmentosa, cone-rod dystrophy, areolar choroidal dystrophy, and punctata albescens [3]. The gene mutation is not specific to pseudovitelliform dystrophy.

We can assess that PVMD has a multi genetic mutation origin, not only peripherin/RDS gene is involved. Other genes can certainly be found causing this disease. Maybe there is a common gene between PVMD and PDS that is not identified yet.

More genetic studies are needed for these two pathologies, and the Lox11 gene should also be studied in PVMD disease, it can be linked to it.

4. Conclusion

The physiopathology of the two diseases has not yet been fully elucidated and the location of the two diseases are very different.

PDS is an anterior segment disease with findings on the cornea, the irido-corneal angle, and the lens meanwhile PVMD touches the outer layer of the retina specifically in the macular region. Both pathologies are frequently benign, but in some cases, they can become severe, moreover, a combination of them should be considered a risk for the patient, and close monitoring should be started.

Until today there is no relation found between them and no other case has been reported in the literature.

A very careful fundus exam of patients with PDS can maybe reveal a pseudovitelliform lesion, and an anterior segment exam with gonioscopy could reveal PDS in patients known to have PVMD. This is why a complete anterior segment exam with gonioscopy could reveal PDS in a patient with pigmentary dispersion syndrome. This is why a complete anterior segment exam with gonioscopy could reveal PDS in a patient with pigmentary dispersion syndrome. This is why a complete anterior segment exam with gonioscopy could reveal PDS in a patient with pigmentary dispersion syndrome.

More cases of the two diseases should be reported to the literature if found and it could maybe lead to a link between them.

Other genetic studies should be done for the two diseases than can lead to a common gene mutation.

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Conflict of Interest

Authors declare that they do not have any conflict of interest.

References


