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Research Article

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Retinoschisis and Narrow Anterior Chamber Angle: An Uncommon Association or Mere Coincidence?

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Abstract

Objective: *To demonstrate and analyze the epidemiological, clinical, and evolutionary data of the association between retinoschisis and primary angle closure suspect (PACS), primary angle closure (PAC), or primary angle closure glaucoma (PACG).*

Methods: *A retrospective and observational study was conducted at a single ophthalmological medical center, using records from the International Classification of Diseases (ICD-10) for closed-angle glaucoma and retinoschisis. The medical records were analyzed, and all information was recorded.*

Results: *Out of the 9,854 patients evaluated, 1,144 were classified as having PACS, PAC, or PACG, accounting for 11.6% of the total. Additionally, 123 patients were diagnosed with retinoschisis, representing 1.24% of the cohort. A total of 77 eyes from 58 patients (0.58%) were diagnosed with retinoschisis and PACS, PAC, or PACG. However, 47.1% of patients with retinoschisis had the potential for progression to closed-angle glaucoma. The majority of those patients were female, over 40 years of age, hyperopic, with unilateral involvement and asymptomatic. Regarding the location of retinoschisis, the inferior temporal quadrant was the most affected. The follow-up lasted an average of 5.4 years.*

Conclusion: *The high percentage of patients with retinoschisis who presented the condition of progression to PACG suggests an association between these pathologies.*

Keywords: Primary angle closure suspect, Primary angle closure, Primary angle closure glaucoma, Retinoschisis.

1. Introduction

Glaucoma is a group of progressive optic neuropathies that share a common characteristic: progressive degeneration of retinal ganglion cells and their axons, resulting in a distinct appearance of the optic disc and a concomitant pattern of visual loss [1]. Approximately 80 million people are affected by this disease, making it the second most common cause of blindness [2]. Characterized by iridotrabecular contact (ITC) (reversible), PACS is the initial stage of primary angle-closure diseases, which can eventually progress to PAC in the presence of high intraocular

pressure and/or peripheral anterior synechiae (PAS), and PACG, which is characterized by glaucomatous damage to the optic disc and/or loss of visual field [3]. Accounting for 25% of all glaucoma worldwide, it has a prevalence of 0.4% in individuals over 40 years of age in Europeans [4]. However, it is estimated that more than three-quarters of individuals with PACG live in Asia [5,6]. This type of glaucoma is considered more destructive than the more common variant, primary open-angle glaucoma. Thus, identifying cases of primary angle-closure suspect and implementing prevention measures can help avoid unfavorable outcomes such as blindness [3,7].

Acquired retinoschisis, also known as degenerative or senile retinoschisis, is characterized by a separation between the inner and outer layers of the retina and the appearance of a cystic elevation in the retina [8]. Although it was described in 1933 , its pathogenesis is not yet fully understood [9]. However, ischemic and tractional factors have been suggested as triggers for the disease [8,9]. The prevalence of this pathology ranges from 4.0% to 22% among individuals over 40 years of age, with a higher incidence observed in hyperopic patients and females [10,11]. It is often found incidentally during indirect binocular ophthalmoscopy or posterior biomicroscopy [10,11]. It almost always begins on the temporal side, in the ora area, appearing as a band that blends with cystoid degeneration, separated from the ora serrata [10–12]. It tends to be bilateral and symmetrical, typically growing in a circular and posterior direction (especially inferior temporal), often taking on a globular shape [10–12]. Progression, characteristically slow, occurs in about 10–18% of cases over a 15-year observation period [11,13]. It is noteworthy that even when close to the fovea, it continues to behave asymptomatically [10–13]. However, it can become symptomatic in cases of extensive schisis, with involvement of the macula, or in patients with rupture of the outer layer that slowly progresses to total thickness retinal detachment (RD) [13–14]. It is estimated that degenerative retinoschisis accounts for 1.6% of all RDs [15].

Primary angle-closure suspect, PAC, or PACG, and retinoschisis have been associated with various other ocular pathologies [10,16-17]. However, up to the time of this publication, no study has shown a possible association between retinoschisis and PACS, PAC, or PACG. Therefore, the aim of this work is to show and analyze the epidemiological, clinical, and evolutionary data of eyes that simultaneously present both alterations, retinoschisis and PACS, PAC or PACG.

2. Methods

This study was approved by the Medical Ethics Committee of Hospital Angelina Caron (Campina Grande do Sul/PR/Brazil). It is a retrospective and observational study conducted at the Ophthalmology Center of Curitiba (Paraná - Brazil) from December 1, 2015, to September 1, 2023, based on chart reviews using records from the International Classification of Diseases (ICD-10) for closed-angle glaucoma (H40.2) and retinoschisis (H33.1). Patients included in this study underwent at least the following examinations: a) static gonioscopy using a Goldmann 3-mirror lens, with ×25 magnification, performed with minimal ambient lighting possible and with the eye in the primary gaze position; b) indentation gonioscopy with the Volk G-4 Gonioscopy lens. These examinations allowed detection of PACS and/or PAC and/or PACG. Thus, primary angle-closure suspect was defined as the gonioscopic condition presenting reversible ITC of 180° or more, without evidence of permanent obstruction of aqueous flow, without PAS, intraocular pressure (IOP) ≤ 21 mmHg, and without glaucomatous optic neuropathy [3]. On the other hand, PAC was considered to be a narrow or closed angle, with ITC of 180° or more, with IOP ≥ 21 mmHg or PAS, resulting from long-term iridotrabecular contact [3]. Primary angle-closure glaucoma was characterized for those participants who, in addition to having closed angles, exhibited glaucomatous damage evidenced by visual field loss, nerve fiber layer damage, or optic nerve damage [3]. Once the possibility of angle closure was confirmed, peripheral iridectomy with neodymium:yttrium-aluminum-garnet (Nd:YAG) was preventively indicated. Regarding the diagnosis of retinoschisis, all participants included in this study underwent at least assessment by indirect binocular ophthalmoscopy and posterior biomicroscopy with a Goldmann 3-mirror lens. In cases of media opacification, diagnostic ultrasound was performed.

Exclusion criteria included individuals with pigmentary glaucoma, secondary glaucoma, congenital glaucoma, and a history of any eye surgery. Patients involved in this study, presenting simultaneous PACS, PAC, or PACG and retinoschisis in at least one eye, were evaluated by experienced subspecialists in the fields of glaucoma and retina/vitreous. The analysis of medical records was conducted, and data such as refraction, biomicroscopy, intraocular pressure, stereophotography of the optic disc, retinography, pachymetry, and specular microscopy of the cornea were collected. Visual field testing and optical coherence tomography (OCT) of the optic disc were crucial components of the inclusion criteria for diagnosing glaucoma in patients with intraocular pressure exceeding 21 mmHg and evidence of papillary excavation indicative of glaucoma on stereophotography of the optic nerve. When feasible, ultrasound biomicroscopy (UBM) was also utilized. All examinations conducted played a significant role in diagnosis, monitoring disease progression, and identifying other comorbidities. Procedures such as peripheral iridectomy with Nd:YAG and argon laser photocoagulation on healthy retina to demarcate retinoschisis were documented.

3. Results

Among the 9,854 patients evaluated at the ophthalmology center between December 1, 2015, and September 1, 2023, 1,144 (11.6%) patients were identified with PACS, PAC, or PACG. Additionally, 123 (1.24%) patients were diagnosed with retinoschisis, while 77 eyes from 58 (0.58%) patients exhibited an association between PACS, PAC, or PACG and retinoschisis.

Age	Results (n=58) *
Age (years)	62.3 ± 9.8 (40 - 84)
40 a 50	8.6%
51 a 60	36.2%
61 a 70	34.5%
71 a 80	19%
81 a 90	1.7%
*Described by mean ± standard deviation (minimum - maximum) or by percentage	

Table 1: Incidence of Senile Retinoschisis By Age Group

The follow-up period averaged 5.4 ± 2.8 years (ranging from 0.08 to 9 years). Bilateral retinoschisis was noted in 19 (32.8%) patients, while 39 (67.0%) patients exhibited unilateral retinoschisis. Among the participants, 38 (65.5%) were female and 20 (34.5%) were male. The age group with the highest incidence of associated changes was between 51 and 70 years, accounting for 70.7%, as detailed in Table 1. Concerning photopsia, only 10 (17.2%) patients reported this symptom, with 4 patients having predisposing lesions for retinal detachment or experiencing retinal detachment in the contralateral eye.

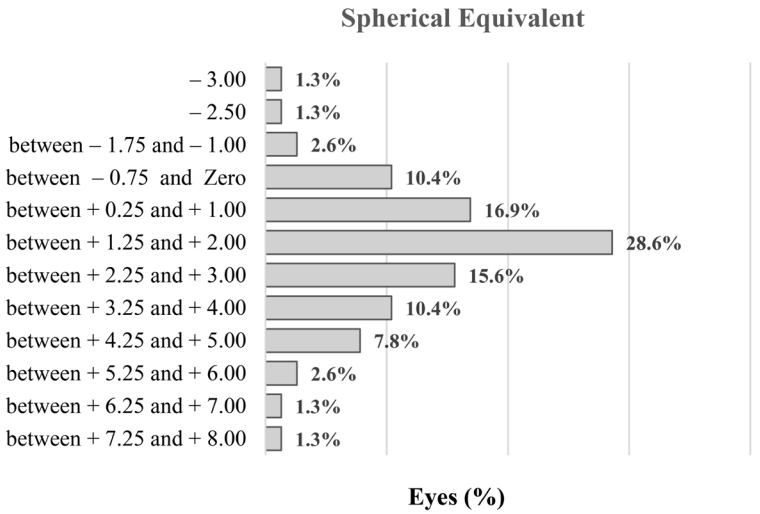

Figure 1: Relationship of The Association Between Retinoschisis And Narrow Anterior Chamber Angle with Refractive Error

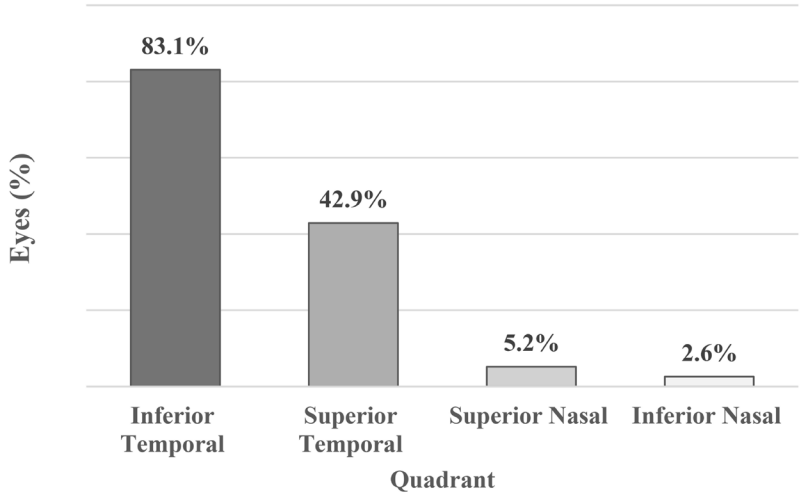

Figure 2: Location of Retinoschisis

The majority of patients were asymptomatic, seeking routine consultations or cataract surgery. Refractive data, illustrated in Figure 1, indicate that the association of these diseases primarily occurred in hyperopic patients, with a spherical equivalent ranging from +0.25 to +3.00 (61.1%). Regarding the location of retinoschisis, 26 (33.8%) eyes exhibited this alteration in more than one quadrant. A total of 64 (83.1%) eyes presented retinoschisis in the inferior temporal quadrant, making it the most affected, followed by the superior temporal quadrant in 33 (42.9%) eyes, the superior nasal quadrant in 4 (5.2%) eyes, and the inferior nasal quadrant in 2 (2.6%) eyes (Figure 2). Primary angle-closure glaucoma was diagnosed in 13 (16.8%) eyes, and tonometry, stereophotography of the optic disc, visual field testing, and OCT of the optic disc were crucial in the diagnosis. Ultrasound biomicroscopy (UBM) was performed in 42 patients, aiding in diagnostic confirmation. Additionally, B-mode ultrasound played a significant role in confirming the diagnosis of retinoschisis in 4 patients who also had cataracts. Regarding procedures, peripheral iridectomy with YAG laser was performed in 72 (93.5%) eyes. Only 5 eyes did not receive this preventive treatment. The same result was observed with laser photocoagulation on healthy retina to demarcate the retinoschisis, with only 5 eyes not undergoing this procedure.

Comorbidities	Results (n=58) *
Cataract	53.4%
Dry age-related macular degeneration	31.0%
Predisposing retinal detachment lesions	6.9%
Retinal detachment in the contralateral eye	5.2%
Retinal vein occlusion in the contralateral eye	3.4%
Guttata cornea	1.7%
*Described by percentage	

Table 2: Comorbidities Present in The Association Between Narrow Anterior Chamber Angle and Retinoschisis

Among the comorbidities listed in Table 2, cataracts were particularly prominent, affecting 31 (53.4%) patients, with 40 eyes undergoing phacoemulsification. Notably, cataract surgery in 8 eyes with primary closed-angle glaucoma was also aimed at alleviating or reducing intraocular pressure. Other comorbidities included dry AMD in 18 (31%) patients, predisposing lesions for retinal detachment, such as lattice degeneration and retinal tears, in 4 (6.9%) patients, and corneal guttata in 1 (1.7%) patient. Changes observed in the contralateral eye included retinal detachment in 3 (5.2%) patients and venous occlusion in 2 (3.4%) patients.

4. Discussion

The analysis of medical records from a single ophthalmology center, conducted using the International Classification of Diseases for PACS, PAC, or PACG (ICD H40-2) and retinoschisis (H33-1), found anterior chamber angle narrowing in a large number of acquired retinoschisis cases. Initially, it is important to emphasize that ICD-10 does not include PACS or PAC. All these conditions are only involved in ICD H40-2, which exclusively corresponds to the pathology known as PACG. Thus, it became essential for this study to evaluate each patient chart with record coded of ICD H40-2 (PACG) associated with ICD H33-1 (retinoschisis). Studies show that both alterations (PACS, PAC, or PACG and retinoschisis) primarily occur in hyperopic individuals [3,10-12]. The findings of this study indicated that only 12 eyes presented emmetropia or myopia, while the others were hyperopic, mainly between +1.25 and +3 diopters (Figure 1). This is consistent with the literature. The prevalence among women was 65.5% of the patients, which aligns with existing data in the literature [10-12,18]. Additionally, all patients were over 40 years old (Table 1), a finding frequently reported in studies on closed-angle glaucoma, as well as in cases of retinoschisis [6,10-12,16,18]. This age correlation highlights the importance of monitoring older populations for the early detection of these conditions. The association of alterations occurred unilaterally in 39 (67.2%) patients, diverging from the literature, which demonstrates that both PACS, PAC, or PACG, as well as retinoschisis, typically occur bilaterally [5-6,10-12].

Regarding the suspicion of primary angle closure, PAC, or PACG, it was observed that 11.6% of the patients seen at the clinic presented ICD H40-2. When analyzing the patient charts with ICD H40-2 associated with ICD H33-1 (retinoschisis), suspicion of primary angle closure or PAC was found in 64 eyes, and PACG was identified in 13 eyes. Peripheral iridectomy with Nd:YAG laser was performed in 72 (93.5%) eyes that exhibited the association between these conditions. This procedure was carried out on an outpatient basis, as recommended by the literature [19]. Although it presents risks such as triggering cataracts, localized endothelial damage to the cornea at the surgical site, dysphotopsias or stray light symptoms, and the development of posterior synechiae [3,19], peripheral iridectomy with Nd:YAG laser is considered a safe procedure and is often used as a prophylactic measure to prevent progression to angle closure [3]. Only 5 eyes did not receive this preventive treatment. These patients chose not to undergo the procedure, completely abandoning follow-up. Coincidentally, these patients did not undergo UBM examination. It is worth noting that UBM was performed in 42 (72.4%) patients, mainly to show patients the anatomical conditions of the anterior chamber that could compromise vision. We believe that the images obtained through UBM help raise patient awareness about the importance of prevention. After iridectomy, all patients underwent pupillary

dilation for stereophotography of the optic disc and evaluation of the peripheral retina. At this time, retinoschisis was diagnosed, primarily located in the inferior temporal quadrant (Figure 2), which aligns with Byer's findings [10]. Seventy-two (93.5%) eyes underwent photocoagulation to demarcate the lesion. Only 5 (6.49%) eyes were left without this procedure. The performance of photocoagulation is considered unnecessary, as retinoschisis has a benign progression, and in few cases does it lead to retinal detachment or advancement of retinoschisis to the macular area [13,20]. However, it is important to highlight that the diagnosis of retinoschisis is difficult because the retina is transparent, and the lesion is located in the periphery of an eye that often already has media opacification which may lead to underreporting [13,14]. In our study, for example, we observed retinoschisis in approximately 1.25% of patients, while it has been reported in 4% to 22% of people over 40 years old, reinforcing the hypothesis of underreporting [10-12]. Consequently, demarcation has facilitated monitoring by clearly showing when there is progression of the lesion. It is important to emphasize that no complications related to photocoagulation occurred during the follow-up period.

Following pupillary dilation, pilocarpine was administered to prevent angle-closure glaucoma in cases of plateau iris, where there remained a risk of pupillary block despite having undergone peripheral iridectomy [3]. It is worth noting that pilocarpine was used for preventing and treating primary angle-closure glaucoma and other types of glaucoma [21]. The use of this eye drop is controversial, as it has been associated with triggering retinal detachment [22]. In cases of retinoschisis, which may be linked to tractional factors the administration of pilocarpine is even more questionable [12]. This raises an important reflection: prior to the advent of peripheral iridectomy with argon laser photocoagulation, and later the more effective and safer application of YAG laser, pilocarpine was routinely and chronically used to treat and prevent glaucoma, particularly angle-closure glaucoma [23]. During that time, several cases of retinal detachment related to pilocarpine were reported [22]. This leads to the question: did some of those cases of angle-closure glaucoma have retinoschisis, and did the chronic use of pilocarpine contribute to triggering retinal detachment? This question remains highly relevant today, as this type of eye drop has once again been used chronically for the correction of presbyopia, with scientific articles emerging that link it to retinal detachment [22]. Another important consideration regarding pilocarpine is that, while the resulting miosis can effectively pull the peripheral iris away from the anterior chamber angle, alleviating pupillary block and enhancing aqueous outflow, it paradoxically may also lead to a dose-dependent narrowing of the anterior chamber by anteriorization of the ciliary processes. This narrowing has the potential to precipitate angle closure in affected eyes [23-24]. In the present study, no cases of retinal detachment and angle closure were observed following the instillation of pilocarpine; however, it is important to note that it was used only once to mitigate pupillary dilation and prevent acute angle-closure glaucoma.

Among the comorbidities observed in Table 2, cataracts stand out, occurring in 53,4 % of cases, and 40 eyes underwent phacoemulsification. It is important to highlight that cataract surgery performed on 8 eyes with primary closed-angle glaucoma also aimed to alleviate or reduce intraocular pressure. Phacoemulsification has been considered by some authors as a first-line treatment option for PACG [25]. The second most frequent comorbidity was dry AMD, observed in 31% of patients. It is worth noting that these are elderly patients, and similar to cataracts, AMD occurs more frequently in this age group [17]. Predisposing lesions for retinal detachment were also part of the comorbidities found in this study. Lattice degeneration was observed in 1 (1,29%) eye and retinal tears in 3 (3,89%) eyes. On the other hand, a study of the natural history of 218 eyes with senile retinoschisis demonstrated the association of this disease with lattice degeneration (9.7%) and unrelated retinal tears (8.1%), among other changes observed in the retinal periphery [10]. The presence of these peripheral lesions may be underreported in cases of narrow angles due to the fear of inducing acute glaucoma caused by pupillary dilation [17]. It is important to emphasize that such predisposing lesions for retinal detachment have also been associated with glaucoma [17]. Another comorbidity found was retinal detachment, which was present in the contralateral eye of 3 patients. In these cases, the decrease in visual acuity was the main reason for seeking ophthalmological consultation, and both angular narrowing and retinoschisis were findings from the ophthalmological evaluation. The association of retinal detachment with glaucoma or retinoschisis has been the subject of several publications [15,26]. Four of the 10 patients who reported photopsia had predisposing lesions for retinal detachment or retinal detachment, demonstrating the asymptomatic nature of the retinoschisis [13,14]. Central retinal vein occlusion was another comorbidity observed in the contralateral eyes of two patients.

A strong point of this study was to demonstrate the possibility of the association between PACS, PAC, or PACG and retinoschisis. Although this association was theoretically expected, as both are more frequently found in hyperopic eyes and people over 40 years of age, it has never been cited so clearly. Several factors may contribute to the limited number of publications on this subject. Initially, it is important to emphasize the technical difficulty in diagnosing retinoschisis, which usually requires the support of a retinal specialist for this purpose. However, when this patient is initially evaluated by a retinal specialist, the analysis of the anterior chamber angle often becomes secondary due to the focus on the retinal problem. From the perspective of the retinal specialist, this responsibility increases, as 47.1% of patients with retinoschisis presented the possibility of progression to angle closure glaucoma. Thus, this study alerts glaucoma specialists and retinal specialists to this association and the necessity of diagnosing both diseases simultaneously to avoid a poor prognosis. Among the weaknesses of the present study, we highlight the retrospective design. Due to this fact, important information such as anterior chamber depth and biometry were not performed or recorded.

5. Conclusion

The analysis of medical records from an ophthalmology clinic demonstrated a similarity to the literature regarding the epidemiological and evolutionary data of the simultaneously

involved pathologies: retinoschisis and PACS, PAC, or PACG. The high percentage of patients with retinoschisis who presented the possibility of progression to PACG demonstrates a potential association between these pathologies.

Research Data and other Materials Availability: The contents are already available Institute where the work has been carried out: Centro Oftalmológico de Curitiba Rua Emiliano Perneta, 390, Conjunto 1407 Curitiba- Paraná- Brazil 80420 080

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