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Acronyms

MH = Macular hole

OCT = Optical coherence tomography

Abstract

A full-thickness macular hole (MH) is a defect of retinal tissue involving the anatomic fovea of the eye. MH develop when the physiologic aging phenomenon of separation of the vitreous cortex from the posterior pole occurs abnormally. Optical coherence tomography (OCT) provides a noninvasive, non-contact imaging technique that, along with clinical data, allows diagnosis of MH. Fellow eyes of MH cases may show early imaging changes in the natural course of a developing MH, such as vitreomacular adhesion and vitreomacular traction. The purpose of this study was to describe these imaging features in fellow eyes of patients with unilateral MH in relation to the risk of developing a MH in a long-term follow-up.

To achieve this goal, a retrospective review of the records of 35 patients with full-thickness MH, who met the inclusion criteria, and with an average follow-up time of 30,5 months, was performed. The vitreomacular relationship in the fellow eyes was evaluated using OCT.

The main results of our study were the following: 62,9% of patients showed vitreomacular attachment at initial examination. This value decreased to 48,6% at final examination. None of the patients with complete vitreomacular separation at first observation developed a MH. Vitreomacular traction was observed in 14,3% of cases in the first visit. These patients showed presence of intraretinal fluid and retinal ellipsoid layer disruption in 20% of cases. The incidence of MH in the fellow-eye during the study period was 5,7%. Both patients who developed MH were women and initially had some degree of vitreous attachment.

We concluded that posterior vitreous detachment, evaluated with OCT, has an important role in the pathophysiology of MH and patients with vitreomacular attachment are at risk of developing this disease. Additionally, this work reinforces the notion that

complete posterior vitreous detachment after development of the MH will not necessarily eliminate disease, due to the complex pathophysiology of this condition.

Key Words

Fellow eye; Macular Hole; Optical coherence tomography; Posterior vitreous detachment; Vitreomacular interface.

Resumo

Um buraco macular de espessura completa é um defeito completo de todas as camadas retinianas envolvendo a fóvea. Os buracos maculares surgem quando a separação fisiológica do corpo vítreo em relação à retina, associada ao envelhecimento, ocorre de forma anormal. A tomografia de coerência ótica proporciona um meio imagiológico não invasivo, que, em conjunto com dados clínicos, permite estabelecer o diagnóstico de buraco macular. Os olhos adelfos de doentes com buraco macular podem mostrar alterações imagiológicas precoces durante a história natural da doença, como adesões ou trações vitreomaculares. O objetivo deste estudo foi descrever essas alterações imagiológicas nos olhos adelfos de doentes com diagnóstico de buraco macular unilateral e a sua relação com o risco de desenvolver a doença, ao longo de um follow-up de longo prazo.

Para atingir este objetivo, realizámos um estudo retrospetivo de análise dos processos clínicos de 35 doentes com diagnóstico de buraco macular e seguimento médio de 30,5 meses, e que cumpriam os critérios de inclusão. A interface vitreomacular foi avaliada através de tomografia de coerência ótica.

Os principais resultados deste estudo foram os seguintes: 62,9% dos doentes apresentavam aderência vitreomacular no momento da primeira observação. Esta percentagem reduziu para 48,6% na observação final. Nenhum dos doentes com separação vitreomacular completa na primeira análise chegou a desenvolver buraco macular. Observou-se tração vitreomacular em 14,3% dos doentes na primeira observação. Este grupo de doentes mostrou fluido intrarretiniano e deformação da camada elipsoide retiniana em 20% dos casos. A incidência de buracos maculares nos olhos adelfos de todos os doentes durante o follow-up foi de 5,7%. Todos os doentes que

desenvolveram buraco macular eram do género feminino e apresentavam algum grau de aderência vitreomacular inicialmente.

Concluímos que o descolamento posterior do corpo vítreo, avaliado através de tomografia de coerência ótica, desempenha um importante papel na fisiopatologia dos buracos maculares e que doentes com aderência vitreomacular apresentam risco de desenvolver a doença. Adicionalmente, este estudo comprova que o desenvolvimento de descolamento posterior do vítreo completo depois do surgimento do buraco macular não elimina necessariamente a doença, devido à fisiopatologia complexa que lhe está subjacente.

Palavras-chave

Buraco macular; Olho adelfo; Tomografia de coerência ótica; Descolamento posterior do vítreo; Interface vitreomacular.

Introduction

A full-thickness MH is a defect of retinal tissue involving every layer of the anatomic fovea and, primarily, the foveola of the eye. Most of these holes are idiopathic in their etiology and are relatively common, particularly in elderly women, affecting 3/1000 individuals (1,2). Imaging studies suggest that MH develop when the physiologic aging phenomenon of separation of the vitreous cortex from the posterior pole occurs abnormally due to an especially tenacious attachment to the fovea (3). Full understanding of the physiopathology of the lesions remains elusive; nonetheless, mechanisms of anteroposterior and tangential traction within these attachments, associated with the anomalous posterior vitreous detachment, as postulated by Gass et al., are considered the two major explanations (4). Despite these uncertainties, it is well known that patients with unilateral Idiopathic MH have an increased risk of 10 to 29% of developing MH in their fellow eyes (5), with a reported incidence of full-thickness MH in the fellow eyes of patients with unilateral MH of 1,5 to 13,6% (6,7). This means that the fellow eyes of MH cases may show early changes in the natural course of a developing MH, such as vitreomacular adhesion – a physiologic phenomenon in the natural vitreomacular separation, vitreomacular traction and intraretinal cysts (4,8).

Diagnosis of idiopathic MH is based on clinical data along with imaging, such as OCT. The emergence of OCT more than 2 decades ago dramatically altered the understanding and management of vitreoretinal pathologies, enabling physicians to monitor vitreoretinal interface with greater consistency and accuracy (8). OCT provides a noninvasive, non-contact imaging technique with a high level of correlation between clinical assessment and OCT findings of MH (8), in a way that early detection of anatomical features such as vitreomacular adhesion, vitreomacular traction and perifoveal

posterior vitreous attachment may indicate the risk for potential development of bilateral MH.

The prognosis of patients with bilateral MH is unfavorable with severe central vision loss and marked decreased visual acuity (4). Only 5% of patients with bilateral MH achieve a visual acuity of at least 20/50 (5). The presence of the already mentioned anatomic foveal alterations carries a greater risk of disease, of about 40 to 60%. On the other hand, the identification of complete posterior vitreous detachment, indicated by a Weiss Ring or by medical ultrasound, means that the risk of progression to MH is less than 1% (3). These are the main factors to be considered in the follow-up of patients with unilateral MH.

Treatment of MH is based on eye surgery with vitrectomy, with or without internal limiting membrane peeling, to eliminate the antero-posterior and tangential traction that causes the disease. Recently, studies have been made to evaluate the role of pharmacological vitreolysis with ocriplasmin intravitreal injection in inducing detachment of the posterior vitreous interface and resolving the MH (9,10). This less invasive new treatment may be useful in the treatment of this disease, at least in some stages of disease.

The heavy burden of disease seen in bilateral MH patients and the better outcomes obtained with both early diagnosis and treatment show the importance of imaging the fellow eyes in patients with unilateral MH, and determining the relevance of early anatomical changes as a means to evaluate risk of future disease in the fellow eye. These outcomes can also help in decision about surgical therapy (8).

The purpose of this study was to describe the imaging vitreomacular structure alterations and MH formation in fellow eyes of patients with unilateral idiopathic full-thickness MH in relation to the risk of developing a MH in a long-term follow-up.

Materials and Methods

A retrospective review of the records of patients with full-thickness MH was performed at Centro Hospitalar e Universitário de Coimbra. The study was approved by the Ethics Committee and in accordance to the Declaration of Helsinki.

The fellow eyes of patients with unilateral full-thickness MH were included if they had well executed OCT imaging follow-up greater than six months. Patients with the following characteristics were excluded: bilateral MH; traumatic or secondary MH such as high-grade myopia (refractive error more than -5 spherical equivalent); history of vitreoretinal surgery; bad quality OCT imaging. Also, eyes with diabetic retinopathy, age-related macular degeneration and other retinal pathologies were excluded.

OCT scans were acquired with Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA), Topcon 3D OCT (Topcon Medical Systems, Inc., Oakland, NJ, USA), and Spectralis HRA+OCT (Heidelberg Engineering GmbH, Heidelberg, Germany). All examinations were performed by an experienced operator. OCT imaging acquired data of the posterior fundus across all quadrants centered through the fovea, for both eyes.

All exams were classified for vitreomacular interface disease and vitreomacular adhesion or traction as per the *International Vitreomacular Traction Study Group Classification System* (Table 1). Furthermore, the status of posterior vitreous detachment of the fellow eye was classified into 5 stages (Figure 1) based on the OCT images as initially proposed by Uchino et al (11): Stage 0 was defined by a complete attachment of the posterior hyaloid to the retinal surface with absence of any perifoveal vitreous detachment. Stage 1 was defined by focal perifoveal posterior vitreous detachment in a maximum of 3 quadrants with persistent attachment to the fovea and optic disc. Stage 2 was defined by perifoveal posterior vitreous detachment in all quadrants with persistent

Anatomic State	IVTS Classification System for Vitreomacular Adhesion, Traction and Macular Hole

VMA	Definition:
	• Evidence of perifoveal vitreous cortex detachment from the retinal surface
	• Macular attachment of the vitreous cortex within a 3-mm radius of the fovea
	• No detectable change in foveal contour or underlying retinal tissues
	Classification:
	• By size of attachment area:
	  ○ Focal (≤1500μm)
	  ○ Broad (≥1500μm)
	• By presence of concurrent retinal conditions:
	  ○ Isolated
	  ○ Concurrent

VMT	Definition:
	• Evidence of perifoveal vitreous cortex detachment from the retinal surface
	• Macular attachment of the vitreous cortex within a 3mm radius of the fovea
	• Association of attachment with distortion of the foveal surface, intraretinal structural changes, and/or elevation of the fovea above the retinal pigment epithelium, but no full-thickness interruption of all retinal layers
	Classification:
	• By size of attachment area:
	  ○ Focal (≤1500μm)
	  ○ Broad (≥1500μm)
	• By presence of concurrent retinal conditions:
	  ○ Isolated
	  ○ Concurrent

FTMH	Definition:
	• Full-thickness foveal lesion that interrupts all macular layers from the internal limiting membrane to the retinal pigment epithelium
	Classification:
	• By size:
	  ○ Small (≤250μm)
	  ○ Medium (>200μm and ≤400 μm)
	  ○ Large (≥400μm)
	• By presence or absence of vitreomacular traction
	• By cause:
	  ○ Primary (initiated by vitreomacular traction)
	  ○ Secondary

Table 1 - The IVTS Classification System for Vitreomacular Adhesion, Traction and Macular Hole. Adapted from The International VItreomacular Traction Study Group Classification of Vitreomacular Adhesion, Traction, and Macular Hole (12). Abreviations:FTMH = full-thickness macular hole; IVTS = International VItreomacular Traction Study; VMA = vitreomacular adhesion; VMT = vitreomacular traction.

attachment to the fovea and optic disc. Stage 3 was defined by posterior vitreous detachment in the fovea with persistent attachment to the optic disc. Stage 4 was defined by complete posterior vitreous detachment indicated by a Weiss Ring.

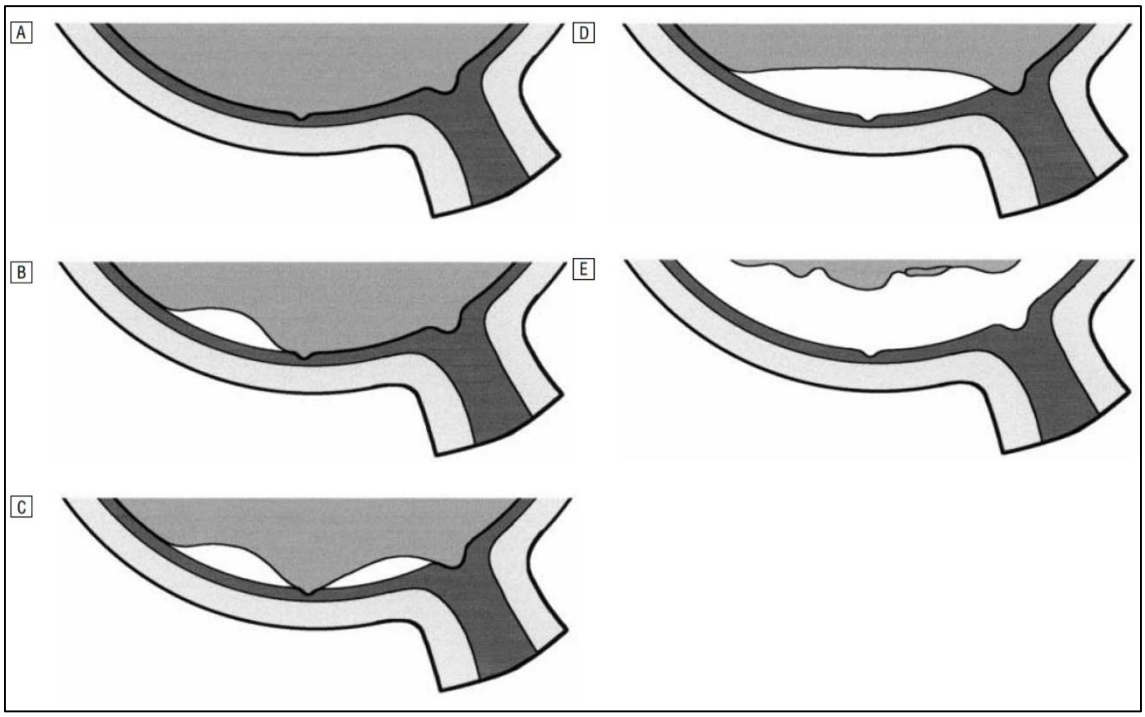

Figure 1 – Schematic illustration of the 5 stages of posterior vitreous detachment as proposed by Uchino et al. A: Stage 0 - complete attachment of the posterior hyaloid to the retinal surface with absence of any perifoveal vitreous detachment; B: Stage 1 - focal perifoveal posterior vitreous detachment in a maximum of 3 quadrants with persistent attachment to the fovea and optic disc; C: Stage 2 - perifoveal posterior vitreous detachment in all quadrants with persistent attachment to the fovea and optic disc; D: Stage 3 - posterior vitreous detachment in the fovea with persistent attachment to the optic disc; E: Stage 4 - complete posterior vitreous detachment. Adapted from Uchino et al (11).

The statistical analysis included a descriptive and inferential component. For both, STATA®, version 13.1 (StataCorp, College Station, EUA) and Microsoft Excel®, version 2016 (Microsoft Corporation, Redmond, Washington, EUA) was used. Experimental data was expressed as means ± standard deviations. Means and percentages were used for the description of quantitative data. Paired t-test and two-sample t-test were used to evaluate the statistical significance of differences between groups. A two-sided significance level (α) of 0.05 was used.

Results

Thirty-five patients who met the inclusion criteria were identified and included in this study. Approximately two-thirds were female (23/35, 66%), with a mean sample age of 66,9 years ± 5,7, ranging from 58 to 81 years. The male patients in this sample were significantly older - + 4,2 years, p=0.035 - than their female counterparts. The average length of follow-up was 30,5 ± 21,8 months, with a median length of 25 months (minimum 6 months, maximum 78 months).

The fellow eyes of the patients included had their posterior vitreous detachment classified according to Uchino et al in stages from 0 to 4. The median classification stage at initial examination was stage 2 and at final examination was stage 3 (Table 2). At initial examination, 3 patients (8,6%) were classified as stage 0, 7 patients (20%) were classified as stage 1, 12 patients (34,3%) were classified as stage 2, 2 patients (5,7%) were classified as stage 3 and 11 patients (31,4%) were classified as stage 4 (Figure 2). At final examination, 3 patients (8,6%) were classified as stage 0, 3 patients (8,6%) were classified as stage 1, 11 patients (31,4%) were classified as stage 2, 1 patient (2,9%) was classified as stage 3 and 17 patients (48,6%) were classified as stage 4. The cumulative percentage of eyes with any degree of vitreomacular attachment (stages 0, 1 and 2) decreased along the follow-up period from 62,9% in the first examination to 48,6% in the final examination.

Number of patients	35
Age (Years)	66,9 (58-81)
Gender	
Male	12 (33%)
Female	23 (66%)
Follow-up Period (Months)	30,5 (6-78)
Vitreomacular relation (Initial)	
Stage 0	3 (8,6%)
Stage 1	7 (20%)
Stage 2	12 (34,3%)
Cumulative Attachment	62,9%
Stage 3	2 (5,7%)
Stage 4	11 (31,4%)
Vitreomacular relation (Final)	
Stage 0	3 (8,6%)
Stage 1	3 (8,6%)
Stage 2	11 (31,4%)
Cumulative Attachment	38,6%
Stage 3	1 (2,9%)
Stage 4	17 (48,6%)
Vitreomacular relation difference (**ignoring Stage 4**)	
Progressing 0 stages	14/24 (58,3%)
Progressing 1 stage	5/24 (20,8%)
Progressing 2 stages	5/24 (20,8%)
Macular Hole Incidence	2 (5,7%)
VMA	
Initial	19 (54,3%)
Final	14 (40%)
VMT	
Initial	5 (14,3%)
Final	3 (8,6%)
Intraretinal Fluid	
Initial	1 (2,9%)
Final	2 (5,7%)
Retinal ellipsoid layer disruption	
Initial	1 (2,9%)
Final	2 (5,7%)

Table 2 – Results. Abreviations: VMA = Vitreomacular adhesion; VMT = Vitreomacular traction.

Looking at differences between classification stage in first observation and final observation, 25 patients (71,4%) retained the same stage, 5 patients (14,3%) progressed one stage up and 5 patients (14,3%) progressed two stages up. The patients who retained the same stage had a mean follow-up time of 26,4 months. However, when patients classified as stage 4 at initial observation are excluded, the percentage of patients who retain the same stage is 58,3% (14/24), the percentage of those who progress one stage is 20,8% (5/24) and the percentage of those who progress two stages is 20,8% (5/24). A total of 10 patients (10/35) (28,6%) progressed one or more stages.

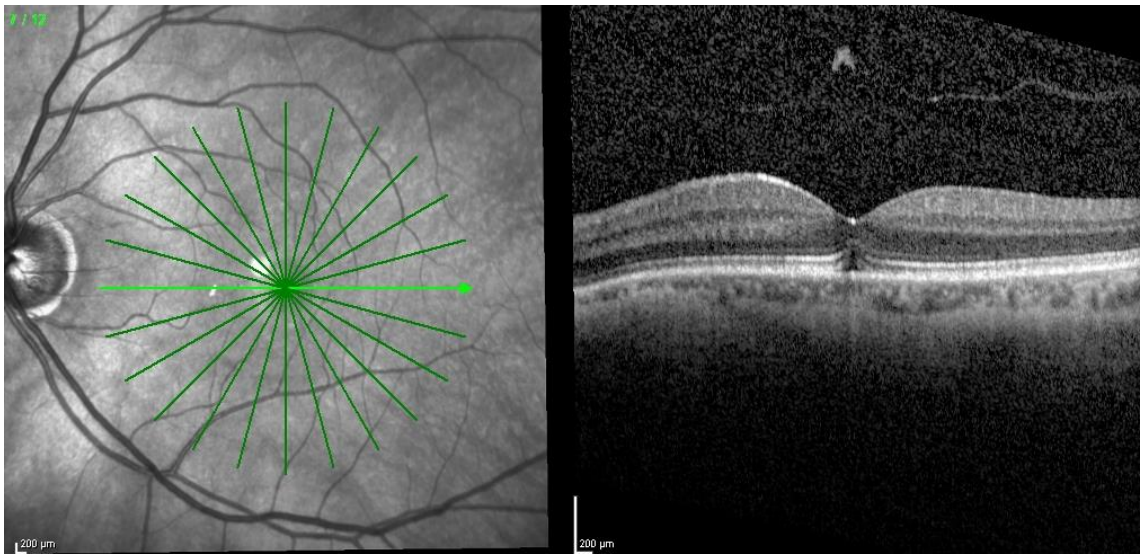

Figure 2 - OCT imaging of the fellow eye of a patient classified as stage 4 according to Uchino et al. A Weiss Ring is visible.

In the seven patients initially classified as stage 1, four (57,1%) of them progressed to stage 2. None of them progressed to stage 4. In the twelve patients classified as stage 2, five (41,7%) of them progressed to stage 4. In the two patients initially classified as stage 3, one patient (50%) progressed to stage 4.

The incidence of MH in the fellow-eye during the study period was 5,7% (2/35). None of the fellow eyes with complete posterior vitreous detachment (classified as stage 4) developed MH. Vitreomacular adhesion was present in 19 patients (54,3%) at initial examination and lowered to 14 patients at final examination (40%). All 5 patients that

lost their initial finding of vitreomacular adhesion at final examination progressed to complete posterior vitreous detachment (stage 4). One of them developed a full-thickness MH. Vitreomacular traction (Figure 3) was observed in 5 patients (14,3%) on their first visit. During follow-up three patients of this subgroup lost any imaging sign of vitreomacular traction, as complete posterior vitreous detachment (classified as stage 4) occurred, and one patient that initially did not have vitreomacular traction developed it. This way, 3 patients (8,6%) had vitreomacular traction on their final visit. The incidence of epiretinal membrane was 11,4% (4/35) at first observation. There was one additional patient with epiretinal membrane at final observation, resulting in a percentage of 14,3% (5/35). Intraretinal fluid was detected in 2,9% (1/35) on first examination and at one additional patient on final examination, resulting in a percentage of 5,7% (2/35). The incidence of retinal ellipsoid layer disruption on OCT scan was 2,9% (1/35) on first visit and 5,7% (2/35) on final visit.

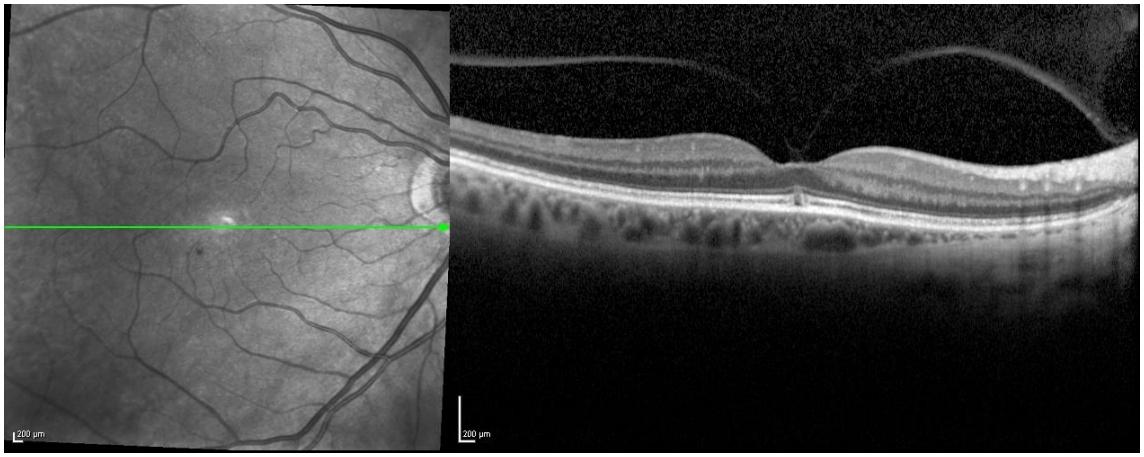

Figure 3 - OCT imaging of the fellow eye of a patient with vitreomacular traction and classified as stage 2 according to Uchino et al.

Patients presenting with vitreomacular traction on first examination (5/35) showed presence of intraretinal fluid in 20% of cases (1/5), while patients with no signs of traction (30/35) had no signs of fluid. At final examination, the same patient retained imaging signs of intraretinal fluid after 26 months of follow-up; patients without vitreomacular

traction on final examination (32/35) had intraretinal fluid in 3,1% (1/32) of cases. This patient had complete posterior vitreous detachment (stage 4) at final examination.

Retinal ellipsoid layer was disrupted in 20% (1/5) of patients with vitreomacular traction on first visit (5/35), and in 66,7% (2/3) of those with vitreomacular traction at final visit (3/35). Patients without vitreomacular traction did not show any disruption of the ellipsoid layer at any visit.

Central macular thickness had a mean value of 268,3 µm ± 52,3, ranging from 198 µm to 516 µm, at first observation. At final observation, the mean value was 271,3 µm ± 66,1, ranging from 187 µm to 513 µm. No statistically significant difference (p=0,66) was found between both observations.

Patients who developed full-thickness MH (Figure 5) in the fellow eye during the follow-up period (2/35) had the following characteristics:

One of the cases was a woman, 58 years old, with a follow-up lasting 26 months. The MH was classified as large (diameter = 600µm). At initial observation (Figure 4), imaging techniques found a partial posterior vitreous detachment, classified as stage 2, with vitreomacular traction. At final observation (Figure 5), there was still vitreomacular traction and the classification remained at stage 2.

The second case was also a woman, 69 years old, with a follow-up lasting 9 months. The MH was classified as medium (diameter = 371µm). At initial examination (Figure 6), OCT imaging identified a partial posterior vitreous detachment with

vitreomacular adhesion, classified as stage 2. At final observation (Figure 7), the vitreomacular adhesion was not present and the classification had progressed to stage 4.

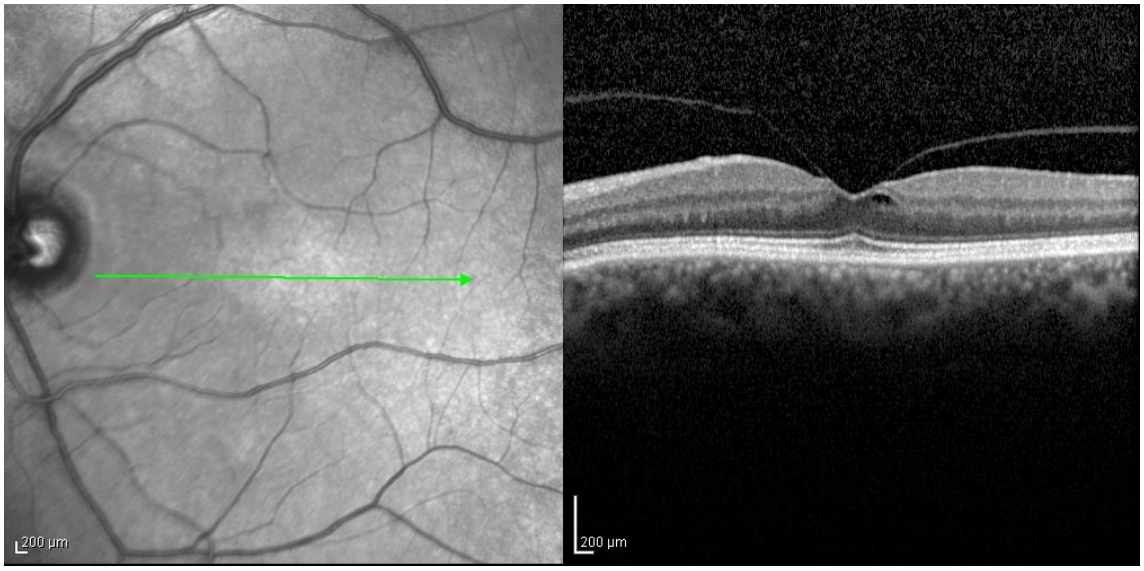

Figure 4 - Initial OCT imaging of the fellow eye of the first case previous to the development of the macular hole. Classified as stage 2 according to Uchino et al. Vitreomacular traction is visible.

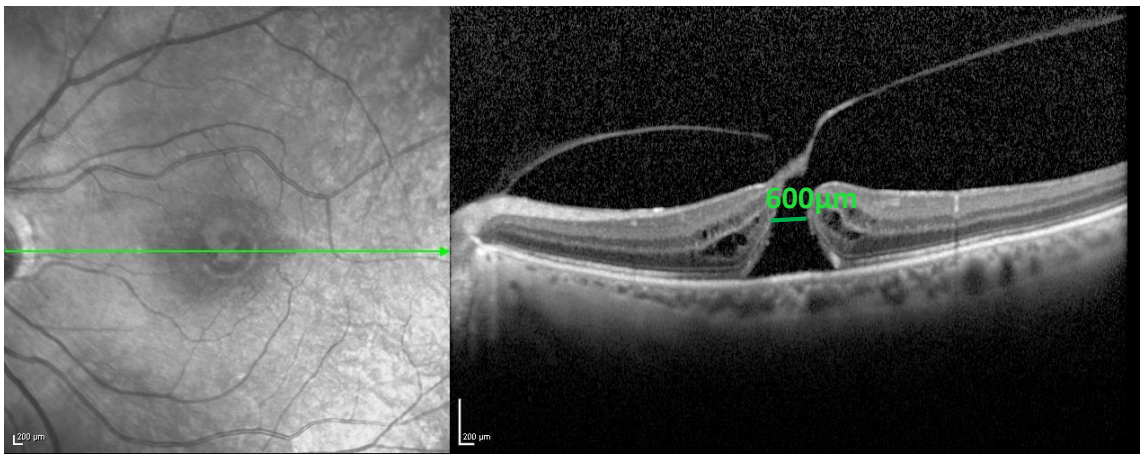

Figure 5 - Final OCT imaging of the fellow eye of the first case after development of the macular hole. Classified as stage 2 according to Uchino et al. Vitreomacular traction is visible.

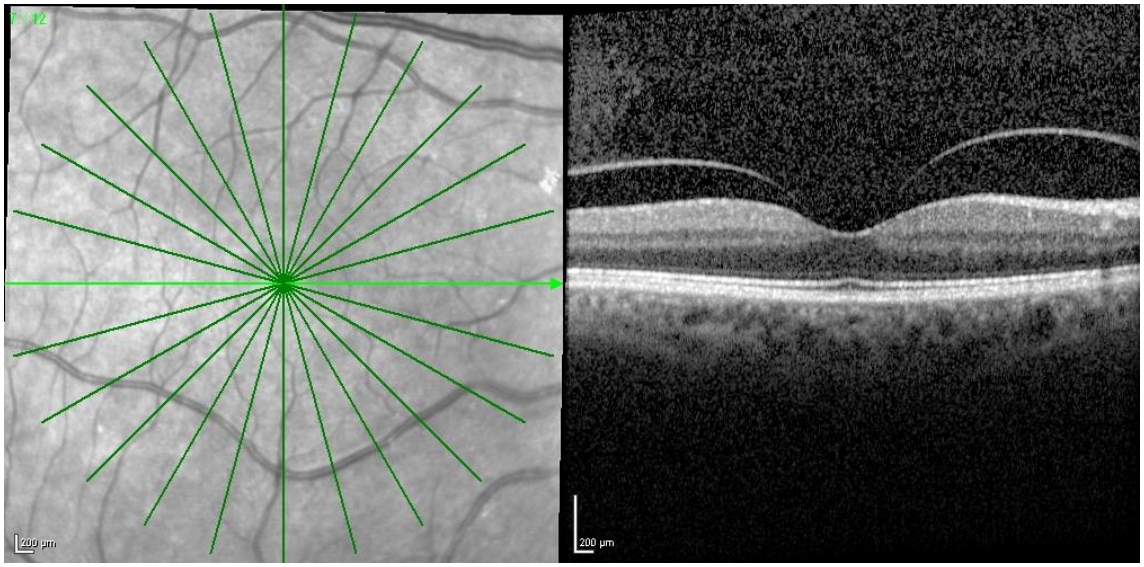

Figure 6 - Initial OCT imaging of the fellow eye of the second case previous to the development of the macular hole. Classified as stage 2 according to Uchino et al.

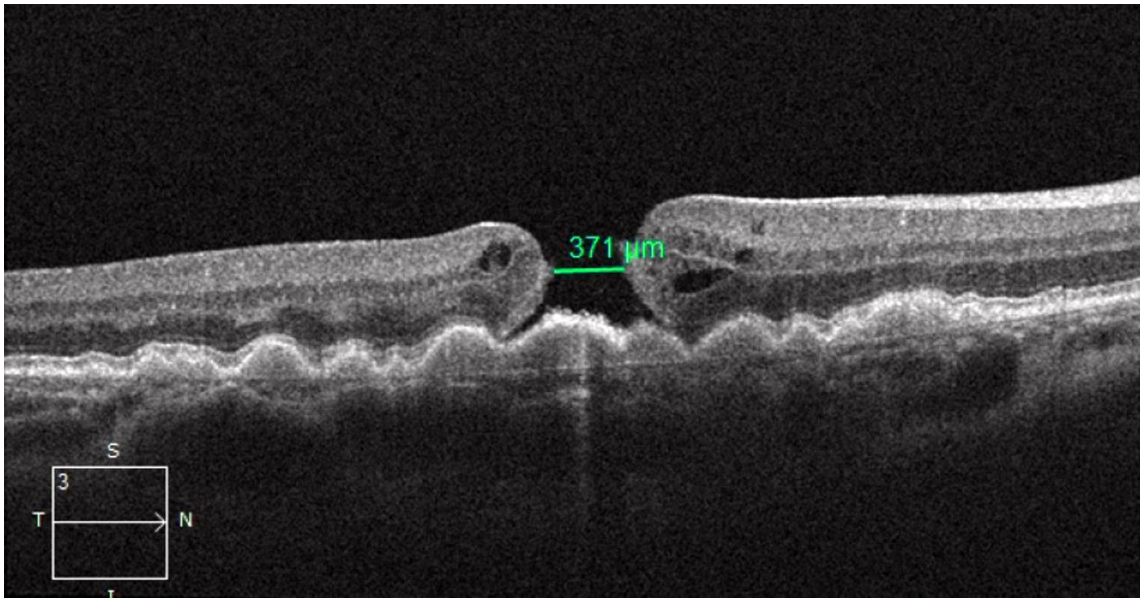

Figure 7 – Final OCT imaging of the fellow eye the second case after the development of the macular hole. Classified as stage 4 according to Uchino et al.

Discussion

A MH is a condition that carries a great risk over visual acuity of the affected eye. This means that development of the same condition in the fellow eye is an important consideration for any clinician when evaluating treatment and prognosis. Also, evaluating the risk of development of MH in the fellow eye is a challenge of the utmost importance since presence of bilateral MH will have a heavy impact on quality of life of patients (12). Careful analysis of the vitreomacular interface status through OCT can provide valuable information and expand knowledge about prognostic factors on the fellow eye allowing improved management of this condition.

It has been shown that there is a higher incidence of foveal deformations in the asymptomatic fellow eyes of patients with unilateral MHs when compared with fellow eyes of patients with other retinal diseases and with healthy eyes (13). Some foveal deformations are seen as predisposing lesions and are well established as prognostic factors, for example, the presence of an impending hole indicates an higher risk (40-60%) of progression to full thickness MH (1). However, many other foveal deformations can be seen in the fellow eyes of patients with unilateral MH and their prognostic relevance needs to be ascertained (13).

Focus on the vitreomacular interface of the fellow eyes in our sample shows that, as expected, vitreomacular detachment increases over time, with 31,4% of patients initially classified as stage 4 evolving to 48,6% at final observation. This finding fits the proposed pathophysiology of separation of the vitreous cortex from the posterior pole as time passes and the relation of MH and aging.

As in other studies (5), the present work sample shows a higher prevalence of MH in the female population as two-thirds of patients were women and the two patients that progressed to MH in their fellow eye were both women. The mean patient sample age

was around 67 years, a finding that matches the known epidemiology of this condition (5). On the other hand, the male patients were considerably older than female patients, which corroborates the greater prevalence among women, as aging plays a central role in the pathophysiology of disease.

The process of posterior vitreous detachment seems to be a slow one, since along the mean follow up period of 30,5 months, there was only a 14,3% (62,9% to 48,6%) decrease in the cumulative percentage of fellow eyes with some sort of vitreomacular attachment. Furthermore, when patients with stage 4 were excluded, 58,3% of patients retained the same stage during the study time, a finding that corroborates this disease's slow natural history concept. However, the mean follow-up of patients who retained the same stage was considerably smaller (26,4 months) than that of the total samples (30,5 months), which could bias this finding. Studies suggest a similar value of 50% of eyes with vitreomacular attachment at initial examination that show no apparent change in either the posterior vitreous detachment grade or macular status over the follow-up period (6). Also, other studies indicate that the early stages of posterior vitreous detachment are chronic and slowly progressive (11). This means that the follow-up of patients with unilateral disease must necessarily be one of long term, as with short term observation many new MH of the fellow eye will probably go undiagnosed at initial stages. On the other hand, this finding suggests that even at the end of follow-up, almost half of the sample was still at risk of developing a MH on the fellow eye as some degree of attachment was still present. These values generally coincide with other studies on this matter which indicate that 30-40% of fellow eyes have various stages of perifoveal vitreous detachments with persistent attachment to the foveal center and are at risk of developing MH (6).

Also, 40% of patients showed vitreomacular adhesion and 8,6% showed vitreomacular traction on the fellow eye at final examination, values which enhance the

latent risk of MH development. We found no statistically significant difference between central macular thickness at first and final observation, which might suggest that this anatomic parameter isn't a useful tool in risk assessment for the fellow eye.

The combination of smoldering disease progression with the ever present risk of MH development shows the importance of carefully watching of these patients over time, namely until they develop complete posterior detachment. In this study, despite the exclusion criteria considering pre-MH conditions, the overall incidence of full-thickness MH in the fellow eye was 5,7%. Another study by Otsuji et al. indicates similar values (6). During the follow-up period one of these patients had progressed to stage 4. At initial observation, both patients that eventually developed MH had partial posterior vitreous detachment, but not all at final observation. These findings confirm the importance of separation of the vitreous cortex from the retina in the pathophysiology of MH. On the other hand, the pathophysiology of MH is rather complex and does not rely only on vitreomacular adhesion and traction, as the event of complete posterior vitreous detachment on eyes that have developed MH will not necessarily mean MH closure and elimination of disease, as confirmed in other studies (10).

There are some limitations to this study, namely attributable to its retrospective nature, uneven follow-up time and relatively small sample size. Additionally, a complete evaluation of the posterior vitreous detachment status would require submitting all patients to ocular ultrasonography, in order to better distinguish between stage 0 and stage 4, which was not performed. Also, this work focuses only on structural and anatomical alterations and ignores functional variables, such as visual acuity. Finally, since age related changes in the vitreomacular interface occur slowly, it is hard to determine the "real" incidence of MH formation in the fellow eye (6), which is by itself a relatively rare event. Additional prospective studies with longer follow-up periods and very large sample sizes are needed to address this issue. Nevertheless, our retrospective study design

allowed us to have some insight on this phenomenon and represent a necessary exploratory stepping stone into larger prospective studies.

Conclusion

In conclusion, this study showed that 5,7% of patients developed MH in their fellow eye, along an average follow-up period of 30,5 months. This study shows that, even though approximately half of patients are free of risk of developing fellow eye MH due to complete posterior vitreous detachment, the other half still carries some degree of interface adhesion and therefore is at risk of developing MH in the fellow eye. These findings show the importance of posterior vitreous detachment on the pathophysiology of MH. On the other hand, complete posterior vitreous detachment of the affected eye will not necessarily eliminate the disease. This evidence confirms previous works.

Also, this work shows that vitreomacular traction is associated with other vitreomacular interface abnormalities, such as intraretinal fluid and retinal ellipsoid layer disruption.

Additionally, this study shows that OCT scanning is an excellent tool for aiding in patient workup, treatment decision and follow-up. At the time of this study, this non-invasive imaging technique is the only means to simultaneously evaluate the macular structure and the vitreoretinal interface, allowing it to assume a prominent role in the assessment of risk factors for MH development.

Development of bilateral disease can represent dramatic outcome for patients as the disease carries an ominous decrease in quality of life. Estimating the risk for bilateral disease and its burden on patient day-to-day life may be important concerns for future studies. The heavy decrease in quality of life together with the insidious character of this

disease and the importance of early diagnosis and treatment of these patients gives great relevance to the follow-up of patients with unilateral MH. Innovation on tools for assessment of risk of disease in these patients is of the utmost importance.

This work puts in evidence some of the factors that may have prognostic value. Further studies of prospective nature and larger samples will be needed to fully assess some of the findings of the present work.

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