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Staphyloma-induced Serous Maculopathy

Natural Course and Treatment Effects

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Purpose: To study the natural course of staphyloma-induced serous maculopathy (SISM) and the effects of treatments.

Design: Retrospective case series.

Participants: This retrospective analysis included 26 eyes of 20 patients with SISM and at least 12 months of follow-up.

Methods: Medical records were reviewed for patient demographics, such as age, sex, spherical equivalent, best-corrected visual acuity (BCVA), type of staphyloma, and imaging characteristics. Spectralis OCT B-scans were evaluated for the presence and height of the serous retinal detachment (SRD) at each follow-up visit. An SRD episode was defined as a period with SRD in 1 patient.

Main Outcome Measures: Changes in SRD height and BCVA.

Results: Twenty-six eyes of 20 patients (70% female) were included. The mean age was 54 ± 11 years, and the mean spherical equivalent was −4.8 ± 3.3 diopters at baseline. The staphyloma was located inferior in 12 eyes (46%), inferonasal in 7 eyes (27%), and nasal in 7 eyes (27%). The mean follow-up duration was 73 ± 34 months. During follow-up, the SRD height fluctuated in all eyes, with a mean change of 125 ± 56 μm. The SRD disappeared completely during follow-up in 13 eyes (50%) and then reappeared in 7 eyes (35%). Resolution occurred spontaneous in 8 eyes (31%). The median time of an SRD episode was 25 (interquartile range 14−57) months. Treatment was performed in 20 eyes (77%) and led to resolution of SRD in 3 of the 15 photodynamic therapy treatments (21%), 2 of 5 (40%) anti-VEGF series, and 2 of 4 eyes (50%) treated with topical prednisolone. Best-corrected visual acuity at the final visit (0.42 ± 0.25) was not significantly different from BCVA at baseline (0.34 ± 0.27 logarithm of the minimum angle of resolution, $P = 0.07$), nor was BCVA change significantly different between treated eyes (n = 19) and nontreated eyes (n = 7, $P = 0.3$).

Conclusion: Serous retinal detachment in patients with SISM fluctuated over time and resolved without treatment in 31% of the eyes. Because treatment does not change the course of BCVA, a wait-and-see policy is advocated in these patients on the exclusion of treatable causes of SRD.

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Posterior staphyloma (PS) is an abnormal outpouching of the ocular wall and is the hallmark of high myopia.[1] The presence of a PS is associated with a worse visual acuity (VA) and more severe form of myopic macular degeneration.[2] In most eyes with PS, an abrupt change of the retina, choroidal thickness, and sclera can be observed with the use of OCT. The abrupt transition at the staphyloma edge makes this region susceptible to complications including retinal pigment epithelium (RPE) degeneration, myopic macular neovascularization (mMNV), or serous retinal detachment (SRD).[3−6]

The incidence of SRD in PS, or staphyloma-induced serous maculopathy (SISM), is unknown. However, in eyes with tilted disc syndrome (TDS) and inferior staphyloma, macular SRDs are a frequent complication with a prevalence of 17% to 41%.[4,7−9] One of the hypotheses is that abnormal choroidal vessels and an obstructed choroidal flow at the staphylomas edge are responsible for the SRD.[5,10,11] Several therapeutic options have been tried in small studies or case reports, including oral spironolactone, photodynamic therapy (PDT), subthreshold laser photocoagulation, and intravitreal anti-VEGF therapy.[12−15] However, the effects of treatment were limited, and, in some eyes, the SRD resolved spontaneously.[13]

Previous reports on SISM were limited by a short follow-up duration and the majority of the studies focused on TDS alone.[5,15] The purpose of this study is to investigate the presence of SRD in different types of PS, its imaging characteristics, treatment effect, and final visual outcome. The results will aid in the diagnostic process and clinical management of patients with SISM.

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Methods

Study Population

This was a retrospective, observational case series of patients demonstrating SRD and an abnormal configuration of the posterior pole, based on fundoscopy and on multimodal retinal imaging, who visited the Rotterdam Eye Hospital between January 2011 and June 2019. The inclusion criteria were defined as the presence of a PS with SRD detected on clinical examination and confirmed on radial OCT scans. A PS was defined as an abnormal circumscribed outpouching of the posterior ocular wall.[1] The exclusion criteria were the presence of SRD because of macular neovascularization (MNV), polypoidal choroidal vasculopathy, or central serous chorioretinopathy (CSC), as per multimodal imaging. Eyes with a dome-shaped macula (DSM) (a macular bulge of $>$ 50 μm of elevation) were also excluded, as well as eyes with $<$ 12 months of follow-up. The presence of SISM, in absence of the exclusion criteria, was examined by 2 retinal specialists (S.Y. and J.P.M.C.) independently. This study was approved by the scientific review board of the Rotterdam Eye Hospital and adhered to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study.

Data Collection and Outcomes

Patients had undergone comprehensive ophthalmological examinations at baseline, including measurement of the refractive error, best-corrected visual acuity (BCVA) and dilated indirect ophthalmoscopy. In addition, eyes were imaged using OCT, color fundus imaging, fundus autofluorescence, fluorescein angiography (FA), and indocyanine green angiography (ICGA). Horizontal, vertical, and radial OCT B-scans were assessed, and the B-scan perpendicular to the edge of the staphyloma was selected for measurements of the SRD and choroid. The images were scaled to a 1:1 pixel ratio, and measurements of the subfoveal choroidal thickness, central macular thickness, and height of the subretinal fluid (SRF) were obtained using the calliper tool (Heidelberg Eye Explorer, version 1.10.4.0). Pachyvessels were defined as dilated outer choroidal vessels in an increased Haller layer, which correlated with areas of maximal choroidal thickness.[11] Dilation was considered present if the lumen of the vessels took up more than two-thirds of the total choroidal thickness. The type of staphyloma was assessed with the Curtin classification using multimodal imaging.[16] The edge of the staphyloma was defined as a (1) gradual thinning of the choroid from the periphery toward the edge of the staphyloma and a gradual rethickening of the choroid toward the posterior pole and (2) inward protrusion of the sclera at the edge of staphyloma, according to Shinohara et al.[17] Color fundus photographs were used to assess the presence of a tilted disc, situs inversus, peripapillary atrophy, or peripapillary crescent. An optic disc with a height to width ratio $>$ 1.3 was considered tilted. Fluorescein angiography and ICGA were assessed by 2 retinal specialists (S.Y. and J.P.M.C.). Intervortex venous anastomosis were considered to be present if $\geq$ 2 anastomotic vessels connected adjacent quadrants of vortex veins.[18] During follow-up, the BCVA, height of the SRD, and treatment performed were scored. A period with SRD is referred to as an SRD episode. The decision to treat was by the discretion of the treating retinal expert. The main outcomes were changes in VA and in SRD height from baseline.

Statistical Analysis

Data are summarized using descriptive statistics. The Δ SRF (*maximal SRF height − minimal SRF height*) and the Δ BCVA/year (*[Final BCVA − Baseline BCVA] / Follow-up in years*) was calculated for every patient. Changes in the SRF and BCVA were tested with a paired *t* test and changes per group with an independent sample *t* test. All analyses were performed in SPSS (version 25). A P value $<$ 0.05 was considered statistically significant.

Results

Clinical Presentation

This study included 26 eyes with SISM from 20 patients. At baseline, 3 patients (15%) had a symmetrical, bilateral presentation of SISM. Overall, 6 patients of this study population (30%) developed SISM in both eyes. The mean age at baseline was 54 ± 11 years, and 14 patients (70%) were female. Spherical equivalent varied between 0 and −11 diopters with a mean of −4.8 ± 3.3 diopters. The mean axial length (available in 16/27 eyes) was 25.6 ± 1.5 mm. The most prevalent type observed was the inferior staphyloma, which was found in 12 eyes, accounting for 46% of the cases. This was followed by the inferonasal staphyloma, observed in 7 eyes (27%), and the nasal staphyloma, also present in 7 eyes (27%; types are shown in Fig 1). In all eyes, the edge of the staphyloma was near or involving the fovea. Other notable retinal features were peripapillary crescent in 17 eyes (65%), peripapillary atrophy in 9 eyes (35%), situs inversus of the retinal blood vessels in 15 eyes (58%), and a tilted optic disc in 11 eyes (42%). Baseline BCVA was 0.34 ± 0.27 logarithm of the minimum angle of resolution (logMAR) in eyes with SISM and 0.12 ± 0.12 logMAR in fellow eyes without SISM (P = 0.02). A summary of the baseline characteristics is provided in Table 1.

Diagnosis by Multimodal Imaging

The FA findings were consistent in all eyes (100%), including a linear-shaped granular hyperfluorescence and hypofluorescence in the macular area in the early phase of FA. The shape of the hyperfluorescent and hypofluorescent area was found the be dependent on the specific type of the staphyloma, consistently appearing on the superior edge of the staphyloma (Fig 2A−D). In the midphase, there was a focal increase of the hyperfluorescence, with no signs of leakage in the late phase.

Early phase ICGA showed large choroidal vessels in and around the macular area in 19 of 22 eyes (86%), and 14 of the 22 eyes (64%) showed vortex venous anastomoses in the posterior pole (Fig 2E, F). In 1 eye, a delayed filling of the staphylomatous region compared with the nonstaphylomatous region was observed (Fig 2G). Late phase ICGA shows hypercyanescent spots with the absence of choroidal hyperpermeability (Fig 2H). Hypocyanescence was seen in the nonstaphylomatous area of 5 eyes (19%).

In all 26 eyes, OCT imaging showed the presence of an SRD at the edge of the staphyloma (Fig 3). The mean height of the SRF at baseline was 128 ± 53 μm, and the mean subfoveal choroidal thickness was 174 ± 54 μm. Analysis of the choroid showed an abrupt change of the choroidal thickness at the edge of the staphyloma in 17 eyes (65%), whereas the remaining eyes showed a more gradual change of the choroidal thickness at the staphyloma edge. Pachyvessels were present in 20 eyes (77%) and a pigment epithelial detachment in 3 eyes (11%). Fundus

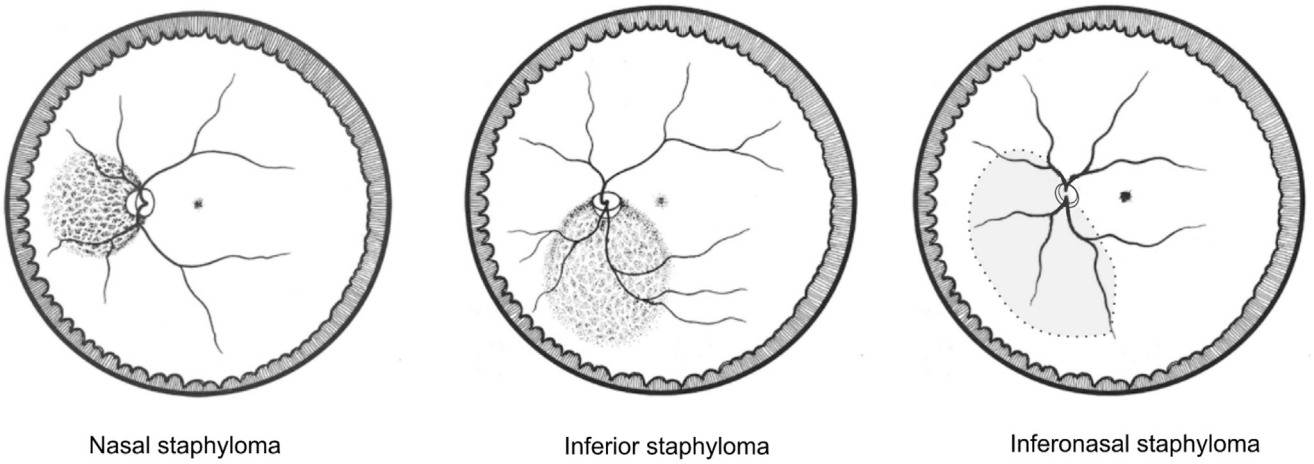

Figure 1. Types of posterior staphyloma in the studied population. Figure adjusted from Curtin et al.[16]

autofluorescence showed areas of hypoautofluorescence in all eyes corresponding to the linear-shaped granular area on FA. All RPE changes seen on color fundus photographs were located at the superior edge of the staphyloma.

Follow-up Examinations

All eyes underwent follow-up OCT examinations for a minimum period of 20 months. The mean duration of follow-up was 73 ± 34 months (range 20−123 months). During follow-up, the height of the SRF fluctuated in all eyes and the mean Δ SRF was 125 ± 56 μm. The SRD disappeared completely in 13 eyes (50%) and then reappeared in 7 eyes at some point. The mean number of SRD episodes was 1.5 ± 0.9 with a maximum of 4 episodes in 2 eyes. In total, there were 39 SRD episodes in 26 eyes during follow-up. The median time of an SRD episode was 25 (interquartile range 14−57) months. The SRD resolved over time in 21 episodes (54%) of 13 eyes, with a spontaneous resolution in 8 eyes (31%). In 18 episodes (46%) of the remaining 13 eyes, the SRD persisted until the last follow-up visit.

Table 1. Clinical Characteristics of Patients with Staphyloma-Induced Serous Maculopathy at Baseline

Variables	
Number of eyes, patients	26 (20)
Gender (female, %)	70 (n = 14)
Age, yrs, mean ± SD	54 ± 11
Spherical equivalent, diopters, mean ± SD	−4.8 ± 3.3
Axial length, mm, mean ± SD	25.6 ± 1.5
BCVA at baseline, logMAR, mean ± SD	0.34 ± 0.27
Symptoms at first presentation, n (%)	
None	8 (31)
Gradual decrease of visual acuity	6 (23)
Persistent subretinal fluid	9 (35)
Metamorphopsia	1 (4)
Acute visual symptoms	1 (4)
Nonacute visual symptoms without further specifications	1 (4)

BCVA = best-corrected visual acuity; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.

Treatment

Some eyes were left untreated, whereas other received one or multiple different treatments, as is summarized in Table 2. Of the 26 eyes with SISM, 6 eyes (23%) did not receive treatment, and spontaneous resolution occurred in 2 of these eyes (33%). The remaining 20 eyes (77%) were treated, of which 9 eyes (35%) underwent repeated or several different treatments. Treatment consisted of halve-dose PDT (15 eyes), anti-VEGF therapy (5 eyes) with 1.25 mg bevacizumab or 2 mg aflibercept, prednisolone eye drops (4 eyes), subconjunctival corticosteroid (1 eye) or systemic medication, namely oral acetazolamide (5 eyes in 4 patients), oral eplerenone (1 eye), and intramuscular octreotide injections (4 eyes in 2 patients). Of the PDT treated eyes, 13 of 15 eyes underwent PDT directly upon diagnosis, and 2 additional eyes were treated 2 years after the initial diagnosis. Six eyes (40%) received more than 1 PDT treatment (e.g., 2 treatments in 3 eyes, 3 treatments in 1 eye, and 4 treatments in 2 eyes). Regarding complete resolution of the SRD after treatment was achieved in 3 eyes after halve-dose PDT, in 2 eyes after anti-VEGF therapy, and in 2 eyes after prednisolone eye drops. After initial complete resolution of SRD, another episode occurred in 1 eye (50%) with spontaneous resolution (no treatment), in 2 eyes (67%) after halve-dose PDT, in 1 eye (50%) after anti-VEGF therapy, and in all eyes (100%) treated with prednisolone eye drops. The treatment outcomes per episode are shown in Table 2. Of the 39 episodes, 19 episodes (49%) were without treatment, and spontaneous resolution occurred in 12 of these episodes (63%). The SRD reappeared in 8 of the 12 spontaneous resolution episodes (67%).

BCVA

Best-corrected visual acuity at the last visit was 0.42 ± 0.25 logMAR and was not significantly different than BCVA at baseline (0.34 ± 0.27 logMAR; $P = 0.07$). Eyes with complete resolution of the SRD (n = 8) at the final visit had a mean Δ BCVA of 0.01 ± 0.05 logMAR/year. Eyes with SRD at the final visit (n = 18) had a mean Δ BCVA of −0.04 ± 0.09 logMAR/year, which was not significantly different from eyes with a resolution ($P = 0.1$). Eyes that were not treated during follow-up (n = 7) did not have a significant difference ($P = 0.3$) in the Δ BCVA per year compared

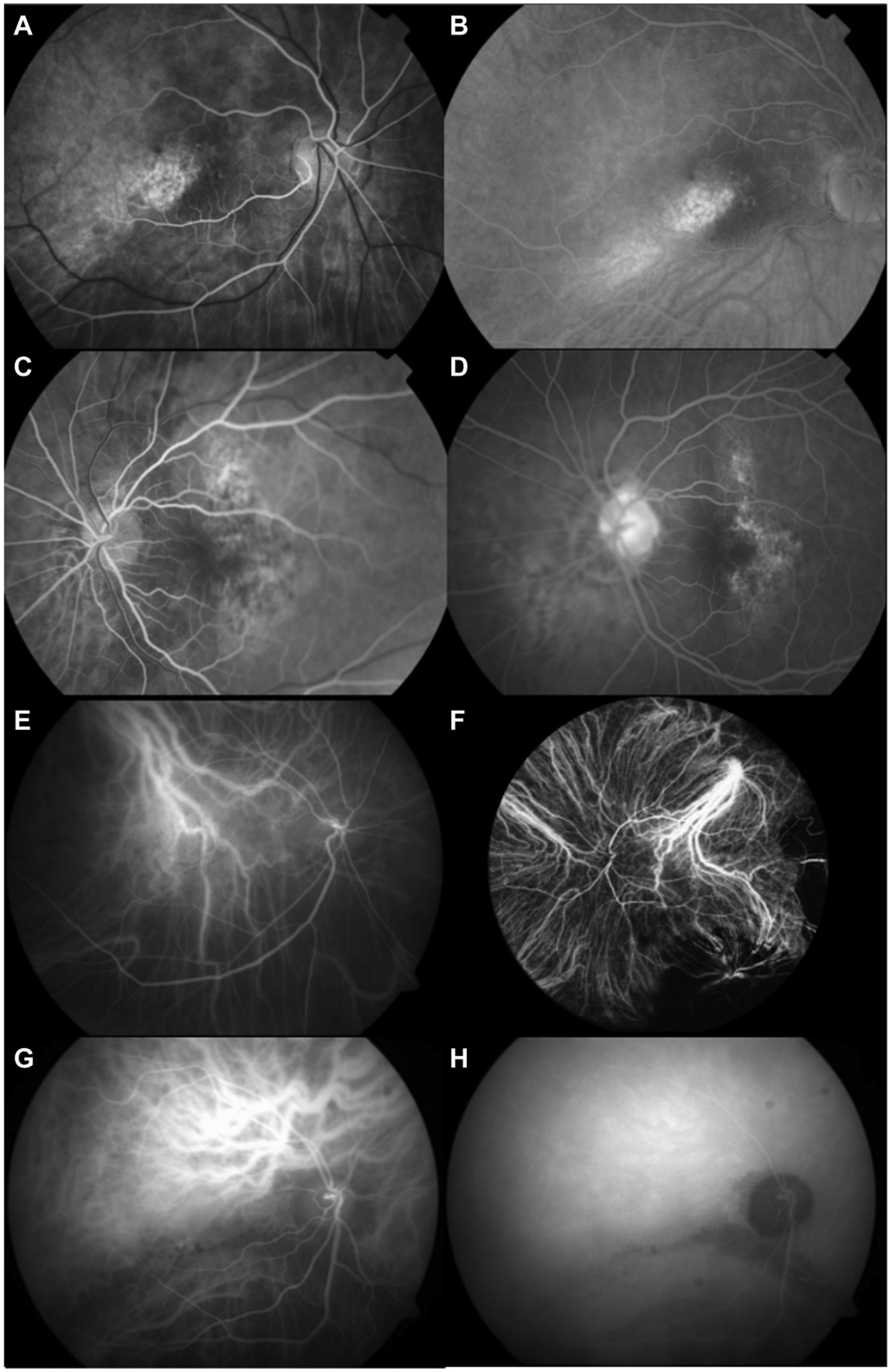

Figure 2. Fluorescein angiography (FA) and indocyanine green angiography characteristics of patients with staphyloma-induced serous maculopathy. **A,** Early phase shows a granular band-shaped hyperfluorescence and hypofluorescence with (**B**) no leakage in the late phase in an eye with inferonasal staphyloma. **C,** Fluorescein angiography shows a similar pattern of hyperfluorence and hypofluorence, but a nasal staphyloma gives another direction of the band-shaped hyperfluorescence and hypofluorescence than in panels (**A**, **B**). **D,** Also, no leakage in the late phase of this FA. **E**, **F,** Intervortex venous anastomosis in eyes with staphyloma-induced serous maculopathy and (**G**) a different distribution of choroidal vessels in the staphylomatous and non-staphylomatous area. **H,** Another characteristic was hypercyanescence without choroidal hyperpermeability with hypocyanescence on the edge of the inferior staphyloma.

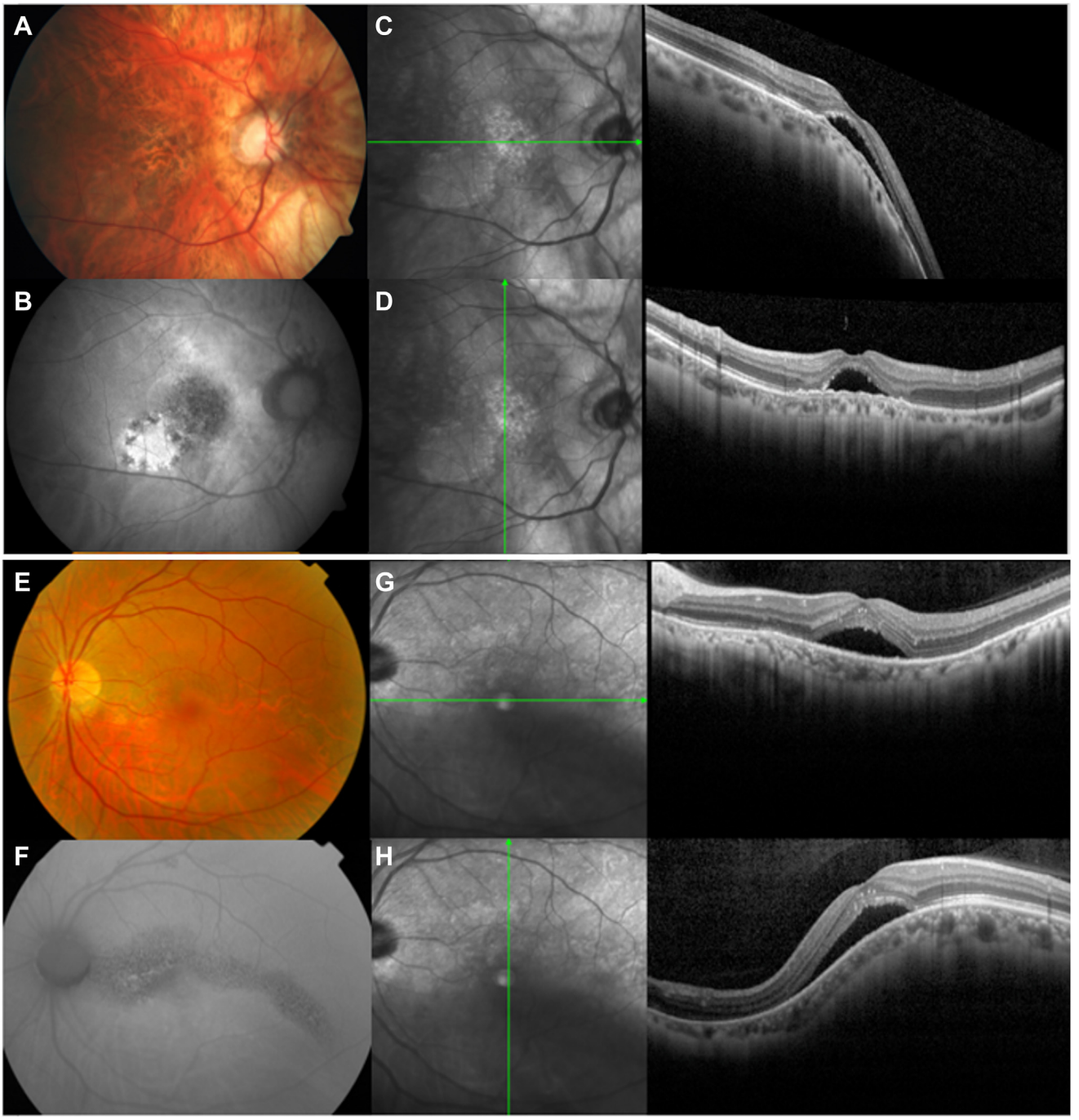

Figure 3. Multimodal imaging of eyes with staphyloma-induced serous maculopathy. **A,** Color fundus photograph of a 46-year-old female exhibiting an axial length of 26.77 mm and a nasal staphyloma. Notably, there is a distinct difference in the appearance of the nasal retina compared with the macula. **B,** Fundus autofluorescence shows hypoautofluorescence at the superior edge of the staphyloma. **C,** The horizontal OCT B-scan shows a serous retinal detachment (SRD) at the edge of the staphyloma and an abrupt change of the choroidal thickness, **(D)** whereas the vertical OCT B-scan did not show any changes in choroidal thickness. **E,** Color fundus photograph of a 58-year-old male with a refractive error of −1.25 diopters and an inferior staphyloma. The macular area shows no fundus tessellated in contrast to the staphylomatous region. **F**, Fundus autofluorescence demonstrates hypoautofluorescence at the edge of the inferior staphyloma, and the **(G)** horizontal OCT B-scan reveals an SRD with no signs of a staphyloma or change in the choroidal thickness. **H,** The vertical OCT B-scan reveals the edge of the staphyloma and a more gradual change of the choroidal thickness with an SRD over the area of the gradual decrease.

Table 2. Treatment Outcomes of Staphyloma-Induced Serous Maculopathy per Eye (n = 26) and per Serous Retinal Detachment Episode (n = 39)

	Per Eye (n = 26)			Per Episode (n = 39)		
Type of Treatment	*Total No. n (%)**	*Resolved (n / Total%)*	Recurred (n / Resolved%)	*Total No. n (%)*	*Resolved (n / Total%)*	Recurred (n / Resolved%)
None	6 (23)	2 (33)	1 (50)	19 (49)	12 (63)	8 (67)
PDT	15 (58)	3 (21)	2 (67)	14 (36)	4 (29)	2 (50)
Anti-VEGF	5 (19)	2 (60)	1 (50)	5 (13)	2 (20)	1 (50)
Prednisolone	4 (15)	2 (67)	2 (100)	4 (10)	2 (50)	2 (100)
Corticosteroid s.c.	1 (4)	0	N/A	1 (3)	0	N/A
Acetazolamide†	5 (27)	0	N/A	5 (13)	0	N/A
Octreotide‡	4 (15)	0	N/A	4 (10)	0	N/A
Eplerenone	1 (4)	0	N/A	1 (3)	0	N/A

N/A = not applicable; PDT = photodynamic therapy; s.c. = subconjunctival injection.
*Nine eyes underwent repeated or different treatments; therefore, the total number of eyes is > 26.
†Four patients were systemically treated with acetazolamide, of which one patient had bilateral serous retinal detachment.
‡Two patients were systemically treated with intramuscular octreotide for bilateral staphyloma-induced serous maculopathy.

with eyes that underwent treatment (n = 19). The total duration of SRD in an eye was not significantly correlated to the change in VA ($r = 0.11$ $P = 0.6$).

Discussion

This study showed the fluctuating course of an SRD in patients with staphyloma-induced serous maculopathy and the effect on the BCVA over time. Patient with SISM rarely presented themselves with an acute onset, and most patients noticed a gradual decline of the BCVA. This study also showed that SISM can occur in many types of PS, besides the inferior staphyloma in TDS. The SRDs were always located at the superior edge of the PS with an abrupt change in the choroidal thickness in 65% of the studied eyes. The clinical and imaging characteristics of patients with TDS with an inferior staphyloma show similarities to our cases.[19] Therefore, we believe that (myopic) TDS with SRD and SISM are one and the same disease entity.

Review of Multimodal Imaging of SISM

Fluorescein angiography showed a similar pattern in every patient including early granular hypofluorescence and hyperfluorescence, suggesting RPE failure. This is supported by the hypoautofluorescent areas seen at fundus autofluorescence indicating RPE degeneration. Other retinal diseases with persistent SRF, such as chronic CSC, also show similar changes on fundus autofluorescence, which is allocated to RPE dysfunction.[20] It was notable that, also, on FA, the location of hyperfluorescence was always at the superior edge of the staphyloma, supporting the hypothesis that mechanical or hemodynamical changes at the staphylomas edge are jeopardizing RPE function, possibly leading to SRD. It is important that none of our patients showed any signs of leakage on FA, which distinguishes SISM from chronic CSC.

Almost all eyes in this study population had a striking distribution of the choroidal vessels, as seen on ICGA. Large vessels were seen that entered or crossed the macula with vortex venous anastomosis in many eyes. Abnormal patterns of choroidal vessels were also reported in previous studies including myopic eyes with and without PS.[21–23] In this study, ICGA also showed delayed filling of the choroid inside the staphyloma in 1 eye. Previous studies showed a similar pattern of delayed filling of the staphylomatous area and a change in the diameter of the choroidal vessels.[22,24] Finally, late phase ICGA showed hypercyanescent spots in eyes with SISM and no signs of choroidal hyperpermeability frequently seen in pachychoroid related diseases. Some eyes showed hypocyanescent areas on late phase ICGA outside the staphylomatous areas. A previous study suggested that this hypocyanescence is caused by the absence or severe reduction of the choriocapillaris, which could also be the case in our patients.[25]

Other characteristics of pachychoroid disease that can be detected on OCT are an increased choroidal thickness and the presence of pachyvessels. In the studied population, all eyes showed changes in the choroidal vasculature. But, although Tan et al[5] reported a significant increased choroidal thickness in patients with SRD and staphyloma compared with patients without SRD, our study did not reveal a very thick choroid, at least not underneath the foveal. Although we did not have a control group of patients with a staphyloma without SRDs, the subfoveal choroidal thickness was 174 ± 54 μm, as can be expected based on age and axial length of our study population.[26,27] However, an abrupt change of the choroidal thickness at the edge of the staphyloma was seen in 65% (Fig 3C) and a more gradual change in the remaining eyes (Fig 3H), similar to Tan et al.[5] Another striking resemblance of SISM with pachychoroid disease is the presence of pachyvessels and vortex venous anastomosis in a large proportion of the studied population, making the choroid an interesting topic to further explore in unraveling the pathophysiology of SISM.

Fluorescein angiography and ICGA were very alike in all patients with SISM. However, making the diagnosis of

Table 3. Imaging Characteristics of (Myopic) Patients with Serous Retinal Detachment or Subretinal Fluid

	Symptoms	OCT	FA	ICGA
MNV	Acute onset of blurred vision, scotoma, or distortion of vision.	Highly reflective area contiguous above the RPE, usually with minimal to no subretinal fluid.	Type 2 MNV: well-defined hyperfluorescence in the early phase with leakage in the late phase.	Type 1 MNV: hypercyanescence of neovascular network in early phase.
Simple retinal hemorrhage	Acute onset of blurred vision, scotoma, or distortion of vision.	Projection of the hemorrhage along the Henle fiber layer.	Blocked fluorescence signal at the location of the hemorrhage.	Linear hypocyanescence on late phase: lacquer cracks (±)
CSC	Acute onset of blurred vision, scotoma, or distortion of vision.	SRD and in 63% of eyes an RPE detachment, increased choroidal thickness, and pachyvessels.	Ink blot appearance, smokestack pattern and minimally enlarging spots (leakage).	Hypercyanescent spots (−) choroidal hyperpermeability (+)
DSM	Gradual onset of decreased vision or no symptoms.	SRD overlying the dome, increased choroidal thickness and focal thickening of the sclera. Dome is visible on the horizontal and/or vertical B-scan dependent on the subtype.	Window defects and pinpoint leakage.	Hypercyanescent spots (+) choroidal hyperpermeability (−)
SISM	Gradual onset of decreased vision or no symptoms.	SRD at the superior edge of posterior staphyloma, abrupt change of choroidal thickness.	Early hyperfluorescence and hypofluorescence, no leakage.	Hypercyanescent spots (+) Choroidal hyperpermeability (−)

CSC = central serous chorioretinopathy; DSM = dome-shaped macula; FA = fluorescein angiography; ICGA = indocyanine green angiography; MNV = macular neovascularization; RPE: retinal pigment epithelium; SISM = staphyloma-induced serous maculopathy; SRD = serous retinal detachment.
(+) Present, (±) sometimes present, and (−) not present.

SISM on OCT imaging alone was much more difficult. First, the OCT characteristics were dependent on the direction of the scan, which is why the B-scan perpendicular to the edge of the staphyloma was selected for the measurement of the SRD and choroidal thickness. If only the horizontal and vertical B-scan were assessed in a clinical setting, the diagnosis could possibly be missed. Secondly, not all eyes shared the exact same OCT characteristics, such as the abrupt change in choroidal thickness or SRD at the superior edge of the staphyloma. This could lead to misdiagnosis, when looking at the OCT alone in absence of multimodal imaging. This study highlights the importance of multimodal imaging, and clinicians should preferably perform FA and ICGA in every patient with SRD and PS and consider SISM as a diagnosis per exclusionem. Table 3 summarizes the differential diagnosis of SRD in the myopic eye.

Differential Diagnosis Based on Multimodal Imaging: mMNV

Myopic macular neovascularization is characterized by a sudden onset of blurred vision, scotoma, or distortion of vision. Fundoscopy usually shows a flat, small, grayish subretinal lesion.[28,29] On OCT, mMNV appears as a highly reflective area contiguous above the RPE, usually with minimal SRF. Most mMNV lesions are small, located in or in proximity of the fovea, and with hemorrhage.[30] FA usually confirms the diagnosis of mMNV and shows a well-defined hyperfluorescence in the early phase with leakage in the late phase in a classic MNV pattern. In myopic eyes, the majority of MNVs is a type 2 (classic) lesions.[31] Previous studies suggested that the area of the staphyloma edge could present anatomical characteristics that promote the occurrence of MNV.[7,24,32] However, these studies were all small retrospective studies unable to indicate whether the incidence of mMNV is truly higher in the area around the staphyloma edge. Myopic MNV should be treated as soon as possible to avoid irreversible vision loss. The standard of care is anti-VEGF injections with a single loading dose followed by a pro ne rata regime, which was shown to significantly improve the VA for 5 to 6 years.[31,33–37] To conclude, mMNV can be distinguished from SISM based on the acute visual symptoms and the leakage in the late phase of the FA.

CSC

Acute CSC also causes an acute onset of blurred vision or distorted vision. Fundoscopy shows a round or oval SRD without hemorrhage, and occasionally small, yellow subretinal deposits in and around the neurosensory detachment may be present.[38] OCT shows a SRD and frequently a pigment epithelium detachment. Central serous chorioretinopathy is caused by abnormalities in the choroidal vasculature, which results in an increased choroidal thickness and the presence of pachyvessels on OCT imaging. Myopic eyes with CSC also have an increased choroidal thickness compared with healthy myopic eyes, but this choroidal thickness would be considered normal for emmetropic eyes.[26,39] Interestingly, Tan et al[5] showed that eyes with SRD and a PS, DSM, or TDS had an increased choroidal thickness compared with similar eyes without SRD. Typical CSC FA includes ink

blot appearance, smokestack pattern, and minimally enlarging spots, whereas ICGA shows choroidal hyperpermeability. Acute CSC is considered a self-limiting disease with resolution of the pigment epithelium detachment and SRD and recovery of the VA. In chronic CSC cases, half-dose PDT is the treatment of first choice.[38] To distinguish CSC from SISM, FA an ICGA are essential. Although in CSC there is leakage on FA and choroidal hyperpermeability on ICGA, these features are not seen in eyes with SISM.

DSM

Dome-shaped macula can also be complicated with a SRD and leads to a gradual onset decrease of the VA or distorted vision.[40] On OCT, the macula is protruded with a shallow SRD, disruption of the photoreceptors, and/or a flat irregular pigment epithelium detachment overlying the dome. The exact pathophysiology of DSM remains unclear, but focal thickening of the subfoveal sclera has been shown to be a likely mechanism.[40,41] Angiograms show window defects and pinpoint leakage on FA and hypercyanescent spots on late phase ICGA, which is not seen in patients with SISM. The natural course of SRD in patients with DSM is also fluctuating. Various treatment modalities have been tried including PDT, laser photocoagulation, anti-VEGF therapy, mineralocorticoid receptor antagonists, and intravitreal steroid injections. However, none of these treatments had an overwhelming positive outcome of the SRD in DSM eyes.

Treatment

Many treatments have been tried in these clinical patients to reduce the SRD. The increased choroidal thickness and the presence of pachyvessels previously reported in SISM are similar to cases with CSC.[5] Therefore, treatments like PDT, oral eplerenone, and oral acetazolamide, as tried in CSC, were a plausible choice.[38] PDT was successful in some cases but did not result in the resolution or reduction of the SRD in 79% of the eyes. Another study was also unable to find a beneficial effect of PDT, with verteporfin in 2 patients with TDS and SRD.[42] In contrast to our study, one of these patient showed a hyperfluorescent pinpoint with minimal of leakage on FA. Recently, the use of prednisone eye drops was proven useful in a retrospective study in eyes with peripapillary pachychoroid syndrome. Topical prednisolone reduced the intraretinal fluid after 4 weeks of treatment in all 17 eyes treated.[43] Because our cases show some similarities to other entities in the pachychoroid disease spectrum, we applied this treatment in 4 eyes. Two of the 4 eyes treated benefited from topical prednisolone treatment, and none of them showed an elevated intraocular pressure. In one case, 4 weeks of topical prednisolone was the only period in 112 months of follow-up in which the SRD disappeared. Prednisolone is a minimal invasive, affordable treatment that could be interesting to investigate in the future.

A previous case report also stated to have successfully treated a case with SISM after 4 monthly bevacizumab injections.[15] It should be noted that the SRD did not disappear in this patient but was relocated at the superior edge of the PS. In this study, we also treated 5 eyes with SISM with multiple anti-VEGF injections. Bevacizumab (1.25 mg) was used in 2 eyes and aflibercept (2 mg) in 3 eyes, which led to a resolution of the SRD in both eyes treated with bevacizumab. The SRD resolved in 1 eye after 4 monthly bevacizumab injections, but the recurrence of SRD 1 year later in the same eye resolved spontaneously. In the other eye, the first episode of SRD resolved spontaneously, and the second episode resolved after 3 monthly bevacizumab injections. In both eyes of different patients that responded to anti-VEGF therapy, we reevaluated multimodal imaging for the presence of myopic MNV, but none of the eyes showed any signs of myopic MNV in retrospect. Therefore, we consider the change of SRD height or even disappearance of the SRD after treatment the natural course of the disease, rather than a true effect of treatment. Furthermore, eyes that were treated did not show significant change in BCVA, compared with eyes that were not treated.

This study has strengths and limitations. One of the strengths is that this case series describes the natural course of SISM with the longest follow-up currently available. Whereas other studies focused on TDS alone, we included all types of PS. This allowed us to compare the multimodal imaging of different types of staphylomas and conclude that all staphyloma edges can be complicated with SRDs. Another strength is our long-term follow-up on treated eyes, allowing us to investigate the effect of the treatment on the change in SRD and BCVA. The limitations of this study lie in the retrospective design and the relatively small numbers, which limited our statistical power to compare different treatment groups. Nonetheless, this is one of the largest case series on SISM, with the longest follow-up.

In conclusion, serous macular detachment is a complication of PS with a nonacute clinical presentation and is mostly observed as an incidental finding on OCT. Patients experience a suboptimal VA, which remains relatively stable, despite the presence of a SRD over time. However, it is important to distinguish SISM from other complications that may benefit from treatment including mMNV and chronic CSC. Patients with SISM have a very typical FA and ICGA pattern, but OCT is less discriminating. Therefore, FA and ICGA at baseline are essential in all eyes with PS and SRF to exclude other diagnoses. The SRD fluctuated and resolved without treatment in 31% of the SRD episodes. Many treatments were tried in these patients, but none of these appeared overwhelmingly successful. Because SRD can resolve spontaneously and treatment does not change the visual prognosis, a wait-and-see policy is advocated in these patients.

Footnotes and Disclosures

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Abbreviations and Acronyms:
BCVA = best-corrected visual acuity; **CSC** = central serous chorioretinopathy; **DSM** = dome-shaped macula; **FA** = fluorescein angiography; **ICGA** = indocyanine green angiography; **logMAR** = logarithm of the minimum angle of resolution; **mMNV** = myopic macular neovascularization; **MNV** = macular neovascularization; **PDT** = photodynamic therapy; **PS** = posterior staphyloma; **RPE** = retinal pigment epithelium; **SISM** = staphyloma-induced serous maculopathy; **SRD** = serous retinal detachment; **SRF** = subretinal fluid; **TDS** = tilted disc syndrome; **VA** = visual acuity.

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