Retina Atlas

Series Editors: Sandeep Saxena · Richard F. Spaide · Eric H. Souied · Timothy Y.Y. Lai

Surgical Retina

Masahito Ohji
Editor

Springer

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Series Editors

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Epiretinal Membranes and Macular Pseudoholes

1

Jen-Hsiang Shen, Wei-Chi Wu, and Chi-Chun Lai

1.1 Introduction

1.1.1 Epiretinal Membrane (ERM)

Epiretinal membrane usually occurs in patients over 50 years old and could be seen in 10–30% of the general population over 70 years old. Bilateral involvement is present in 20% of these patients. Eighty percent of these membranes are idiopathic, while about 20% are secondary to previous retinal detachment, vascular, or inflammatory retinal diseases [1–5].

The initial presenting visual acuity is usually fair, and the progression is usually slow [6, 7].

Epiretinal membrane and its pathogenesis had first been reported by Iwanoff in 1865 [8]. However, most of the advances on etiopathogenesis and management took place from the 1980s.

Historically, epiretinal membrane had also been called as primary retinal folds, cellophane maculopathy, surface wrinkling retinopathy, preretinal macular fibrosis, macular pucker, wrinkling of the internal retinal surface, internoretinal fibrosis, and vitreoretinal interface changes [9].

The pathogenesis of ERM was believed to be discontinuity of the internal limiting membrane (ILM). Glial cells may proliferate onto the inner retinal surface. The collagen fibrils of the cortical vitreous may tangle with the proliferation and together form firm vitreoretinal attachment [9–11]. Epiretinal membrane in case with prior retinal break or detachment often had retinal pigmented epithelium (RPE) component and sometimes had pigmented appearance [12–14].

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In 1977, Gass proposed a classification as follows: (1) grade 0 (cellophane maculopathy), in which a translucent epiretinal membrane is not associated with distortion of the inner retina; (2) grade I (crinkled cellophane maculopathy), in which the inner retinal surface is distorted by a thin membrane; and (3) grade II, in which the membrane is thicker, with a distinct grayish appearance, and in which it obscures underlying vessels and causes marked distortion of the retina (Table 1.1) [15].

The management of ERM includes observation and vitreoretinal surgery. Most ERMs are with stable clinical course, but VA deterioration and intolerable metamorphopsia may still occur. Surgery is advised to patients: VA deteriorates under 20/100–20/50 or worse and/or intolerable metamorphopsia [9, 16].

1.1.2 Macular Pseudohole (MPH)

Macular pseudohole (MPH) originates from contraction of epiretinal membrane (ERM), and it is typically round and reddish under biomicroscopy (Fig. 1.1a, b). Patients' initial visual acuity (VA) is often fair, but metamorphopsia may still exist in some patients. MPH could be seen in 8–20% of eyes with ERM [17].

MPH was first described by Arthur W. Allen, Jr., an American ophthalmologist, and John Donald MacIntyre Gass, a Canadian-American ophthalmologist in 1976. They reported four patients having a hole in an epiretinal membrane overlying

Table 1.1 Epiretinal membrane grading proposed by Gass [15]

Grade	Description
0; cellophane maculopathy	Translucent epiretinal membrane is not associated with distortion of the inner retina
I; crinkled cellophane maculopathy	Inner retinal surface is distorted by thin membrane
II	Thicker membrane with a distinct grayish appearance, and in which it obscures underlying vessels and causes marked distortion of the retina

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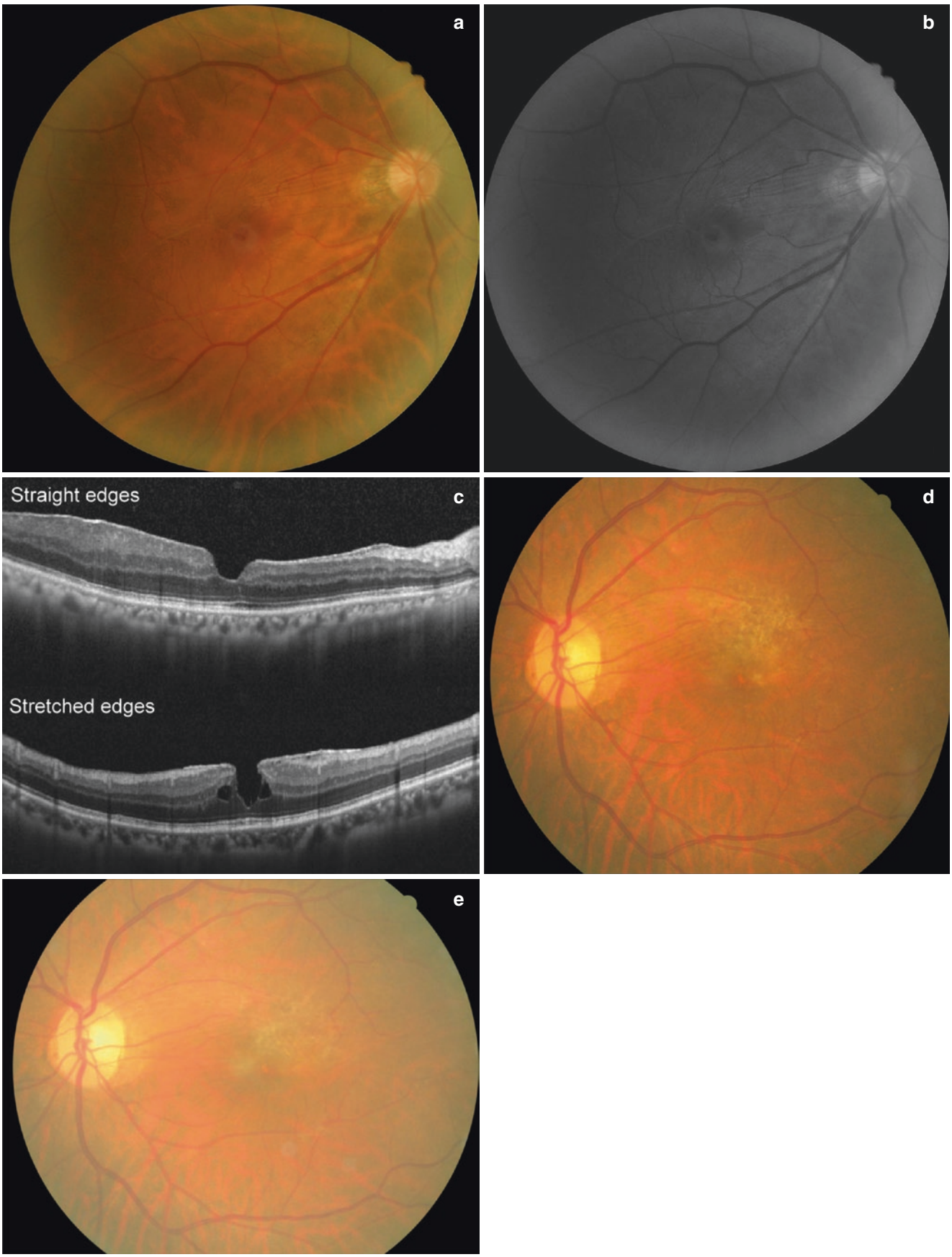

a
b
Straight edges
c
Stretched edges
d
e

Fig. 1.1 (**a**) This is a right eye fundus from a 66-year-old male patient. This color fundus picture shows central round reddish hole-like structure with contractile epiretinal membrane (ERM). Minimal vessel tortuosity could also be observed on the contractile ERM. (**b**) This is the same fundus of (**a**) under red-free filter. We could observe the more evident contractile folds around macula. (**c**) OCT image from two different patients showed macular pseudoholes with straight edges and stretched edges. (**d**) This was the left eye of a 53-year-old female. She complained of progressively blurred vision in the left eye with insidious onset. Fundoscopy showed yellow-grayish thick ERM with mild distortion of retinal surface and small vessels. Radial retinal folds could all be also appreciated. Red-free photography was not taken during this time point. (**e**) After 2 years of follow-up, the yellow-grayish thick ERM with mild distortion of retinal surface and small vessels. Radial retinal folds could all be also appreciated. The ERM was relatively stable. However, the VA deteriorated from 0.4 to 0.3 in Snellen chart. Red-free photography was not taken during this time point

the macula that mimicked a macular hole. In two patients, the clinical course was stable. One patient progressed to full-thickness macula hole. One patient had spontaneous peeling of epiretinal membrane and hole closure. All of the patients had normal or nearly normal visual acuity at first presentation. Three patients had a slight fluorescence in the base of the hole in fluorescein angiography (FA). The fluorescence is less than in true macular holes and not present in lamellar macular holes [18].

Due to advancement of optical coherence tomography (OCT), the characteristics and morphology of macular pseudohole had been redefined. In 2004, Haouchine et al. assessed 40 MPH cases and summarized a steepened foveal pit combined with thickened foveal edges and a small foveal pit diameter as the features of the MPH. Central foveal thickness was normal or slightly increased (167 ± 42 μm). Mean perifoveal thickness was greater than normal (363 ± 65 μm) [19]. Intraretinal split was considered to be only lamellar macula hole at that stage.

In 2008, Gupta, Sadun, and Sebag demonstrated ERM with multifocal contraction tends to result in retinal edema and intraretinal cystoid space [20]. In 2012, Michalewska et al. were the first to find all subtypes of non-full-thickness macular hole (NFMH) belong to the same entity of maculopathy due to ERM, internal limiting membrane (ILM), or hyaloid contraction [21].

In 2013, Gaudric et al. reviewed 54 eyes with MPH using the Cirrus SD-OCT (Carl Zeiss Meditec, Dublin, California, USA). They found 24 (44%) eyes had vertical foveal pit and straight, smooth edges on the OCT scan corresponding to centripetal contraction of the ERM. Nevertheless, 30 (56%) other eyes exhibited some degree of stretching and cleavage of the foveal pit edge resulting from asymmetrical tangential traction of the ERM between multiple epicenters of contraction. Thus, they proposed some lamellar macular holes (LMH) might be a subcategory of macular pseudohole (MPH).

1.2 Etiopathogenesis

1.2.1 ERM

The pathogenesis of ERM was believed to be discontinuity of the internal limiting membrane (ILM). Glial cells may proliferate onto the inner retinal surface. The collagen fibrils of the cortical vitreous may tangle with the proliferation and together form firm vitreoretinal attachment [9–11].

ERM can occur in eyes with posterior vitreous detachment (PVD) or no PVD yet. In 1977, Foos showed the internal limiting membrane (ILM) is especially thin over larger posterior retinal vessels [22, 23]. In these locations, discontinuity of ILM may occur, and glial cells may proliferate onto the inner retinal surface. The collagen fibrils of the cortical vitreous may tangle with the proliferation and together form firm vitreoretinal attachment [9–11]. Foos also raised that retinal ischemia and inflammation may produce enzymatic destruction of ILM integrity and induce glial proliferation [22, 23].

Michels also summarized the hypothesis in patients with PVD already [9]:

1. Full-thickness retinal breaks with liberation of retinal pigment epithelial (RPE) cells into the vitreous cavity
2. Disruption of the ILM, followed by proliferation of glial cells onto the inner retinal surface
3. Mechanical damage to the optic nerve head, where ILM is attenuated or absent, followed by glial cell proliferation
4. Intraocular hemorrhage or inflammation, or both, that, in turn, introduces other cells capable of proliferation [24, 25]

Epiretinal membrane in case with prior retinal break or detachment often had retinal pigmented epithelium (RPE) component and sometimes had pigmented appearance [12–14]. Several factors have been associated with formation of macular epiretinal membrane after retinal reattachment surgery [9]:

1. Increasing patient age [26]
2. Low preoperative visual acuity [26]
3. Total retinal detachment [27]
4. Preoperative evidence of epiretinal membrane formation elsewhere in the eye [26]
5. Vitreous hemorrhage [28, 29]
6. Drainage of subretinal fluid and multiple perforations [27, 29]
7. Intraoperative complications including vitreous loss [29]

There are two hypothesized sources of contraction: myofibroblasts and contraction of vitreous fibrils [30, 31].

Vascular leakage and intraretinal edema could be seen in cases with thick epiretinal membrane and retinal distortion. FA can detect chronic leakage in about 20% of cases, but these leakages did decrease overtime [9].

In 1981, Kampik and coworkers published the ultrastructural findings in 56 eyes with epiretinal membranes. Myofibroblast-like cells are seen in 91% of these eyes. RPE cells were identified only in eyes with retinal detachment with massive preretinal proliferation (MPP) (11 of 11 cases) or prior retinal detachment (11 of 23 cases). Fibrous astrocytes and fibroblasts were observed in 44 (79%) and 43 (77%) eyes, respectively. In eyes ($n = 23$) with prior retinal detachment, the percentage rose to 83% and 61%, respectively [31].

In 1982, Michels released a series of 74 cases. Forty-six eyes (62%) had prior retinal reattachment surgery. Nine cases (12%) were otherwise healthy eyes with PVD. Two eyes (3%) were considered developmental, while two eyes (3%) were considered acquired type in young patients. Fifteen eyes (20%) had history of uveitis, damage from a penetrating injury, vitreous hemorrhage, or prior photocoagulation or surgery not related to retinal detachment. In the membranes removed, he identified the following components:

1. Pigment epithelial cells
2. Fibrous astrocytes
3. Macrophage
4. Fibrocytes
5. Microfilaments and extracellular collagens

In a more recent report by Yazici et al. in 2011, the majority of ERM remained to be idiopathic in most eyes (43%) [32]. However, it is very difficult to compare these epidemiology studies, because the difference in patient population may influence these results greatly (Table 1.2).

In summary, the pathogenesis of ERM was believed to be discontinuity of the ILM. Glial cells may proliferate onto the inner retinal surface. The collagen fibrils of the cortical vitreous may tangle with the proliferation and together form firm vitreoretinal attachment. ERM can occur in eyes with posterior vitreous detachment (PVD) or no PVD yet. The grading of ERM still follows the Gass classification as grades 0, I, and II (Table 1.1). The pathology exam showed the component of ERM as pigment epithelial cells, fibrous astrocytes, macrophage, fibrocyte, microfilaments, and extracellular collagens.

1.2.2 MPH

There is currently no published histopathologic report of a macular pseudohole [34]. The pathogenesis of macular hole was initially proposed by Allen and Gass to be the contraction force of epiretinal membrane in 1976 [18]. There are two studies to support this assumption, and they provided more detailed proposals [21, 34] (Table 1.3).

Some pseudoholes have stretched edge or intraretinal cleavage that could not be simply explained by one center of centripetal contraction. Thus, Gaudric et al. studied the en face OCT images of 54 eyes with MPH. They found 24 eyes with straight edges and 30 eyes with stretched edges (Table 1.4 and Fig. 1.2). They found MPH with straight edges often had smooth ERM, contracted around pseudohole, causing radial retinal folds that converged toward the edge of the membrane, revealing the centripetal forces of

Table 1.2 Etiologies of epiretinal membrane

Study	ERM etiology
Michels [9]	Previous retinal detachment in 46 eyes (62%) Idiopathic in 9 eyes (12%) Developmental in 4 eyes (5%) Previous cataract extraction in 3 eyes (4%) Previous uveitis, vitreous hemorrhage, photocoagulation, penetrating injury, other kinds of surgery in 12 eyes (16%)
Poliner et al. [32]	Idiopathic in 61 eyes (69%) Previous retinal detachment in 27 eyes (31%)
Yazici et al. [31]	Idiopathic in 61 eyes (69%) Previous retinal detachment in 27 eyes (31%) Idiopathic in 125 eyes (43%) Diabetic retinopathy in 107 eyes (37%) Retinal vein occlusion in 28 eyes (10%) Uveitis in 12 eyes (4%) Previous retinal detachment in 5 eyes (2%) Other pathologies in 16 eyes (5%)

Table 1.3 Etiopathogenesis of macula pseudoholes (MPH)

Study	Etiopathogenesis
Allen and Gass [18]	Centripetal contraction of ERM
Gaudric et al. [33]	Centripetal force between eccentric epicenters
Michalewska et al. [20]	Hyperreflective linear structure, either epiretinal membrane, thickened internal limiting membrane, or hyaloids could be the common cause of all types of non-full-thickness macular holes (NFMH)

Table 1.4 Type of pseudohole features and epiretinal membrane contraction [34]

Pseudohole feature	ERM contraction
Straight foveal edge ($n = 24$)	Smooth ERM, contracted around pseudohole, causing radial retinal folds that converged toward the edge of the membrane, thus revealing the centripetal forces of contraction ($n = 18$) Complex pattern fold ($n = 4$) Smooth, no visible folds ($n = 2$)
Stretched edge with partial cleavage of inner and outer retina ($n = 30$)	Multiple epicenters of contraction, asymmetric distortion Eversion of foveal edge ($n = 22$) Smooth with few folds ($n = 4$) More or less radial ($n = 4$)

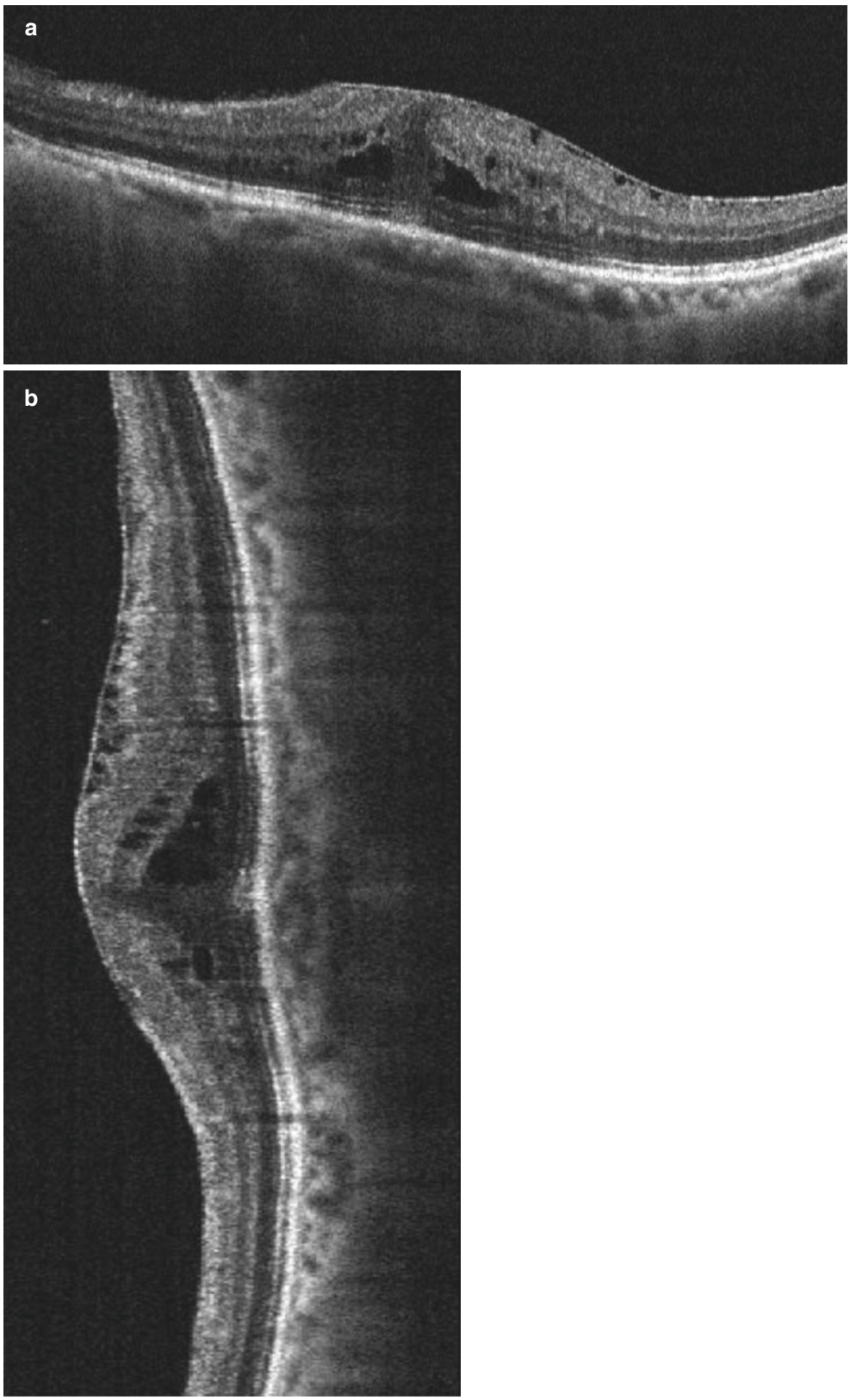


Fig. 1.2 (**a**) High-resolution optical coherence tomography (OCT) showed thickened ERM and central macula edema with intraretinal split, on both horizontal section (**a**) and vertical section (**b**). (**b**) High-resolution optical coherence tomography (OCT) showed thickened ERM and central macula edema with intraretinal split, on both horizontal section (**a**) and vertical section (**b**)

Table 1.5 Characteristics of ERMs on SD-OCT analysis [35]

ERM	Pseudohole eyes (n = 27)
Typical tractional ERM	24
Atypical epiretinal tissue	0
Combined	3

Table 1.6 Proposed stages of macular pseudoholes [36]

Stages	Number	Definition
1	14	No cleavage
2a	13	Localized cleavage not crossing fovea
2b	9	Localized cleavage crossing fovea
3b	14	Diffuse cleavage

contraction. They also noted MPH with stretched edges often had multiple epicenters of contraction and asymmetric distortions [34].

On the other hand, Michalewska et al. championed that not only epiretinal membrane could produce this contraction. They proposed that hyperreflective linear structure-like epiretinal membrane, thickened internal limiting membrane, or hyaloids could be the common cause of all types of non-full-thickness macular holes [21].

Besides these two theories, Schumann et al. analyzed the properties of epiretinal membrane of 27 eyes with MPH in 2015. They confirmed the majority of ERM are typical tractional ERM [35] (Table 1.5).

In 2016, Tomaya et al. proposed three stages of macular pseudoholes: no cleavage (stage 1), localized cleavage (stage 2) that does or does not cross the central fovea (stage 2b and 2a, respectively), and diffuse cleavage (stage 3) (Table 1.6). This reflected different levels of stretching and foveal morphology distortion [36].

1.3 Clinical Features

1.3.1 A Typical Case of ERM

This was the left eye of a 53-year-old female. She complained of progressively blurred vision in the left eye with insidious onset. Fundoscopy showed yellow-grayish thick ERM with mild distortion of retinal surface and small vessels. Radial retinal folds could all also be appreciated (Fig. 1.1d). She had been observed for 2 years and had relative stable clinical course with best-corrected VA deteriorating from 0.4 to 0.3 (Fig. 1.1e). High-resolution optical coherence tomography (OCT) showed thickened ERM and central macula edema with intraretinal split, on both horizontal section (Fig. 1.2a) and vertical section (Fig. 1.2b).

However, due to this worsening, the patient requested for operation. Microincisional sutureless 23G vitrectomy with double peeling with triamcinolone acetonide (TA) staining was performed. Air tamponade with head-positioning for 1 day were also administered. After 1.5 months postoperatively, follow-up OCT showed removal of ERM and ILM on central macula, on both horizontal section (Fig. 1.3a) and vertical section (Fig. 1.3b).

After 2.5 months postoperatively, the intraretinal split subsided and initial restoration of foveal depression could be observed (Fig. 1.4a, b). After 6.5 months postoperatively, the anatomical improvement had been stable (Fig. 1.5a, b).

After 2 years of follow-up, the macula seemed flat without recurrence of ERM. The VA was stable at 0.4. On the OCT, the retinal layers also showed adequate segmentation. Please note the remnant of ERM on the superior aspect of macula. The ERM did not extend to the parafoveal region. Please also note there were some epiretinal hyperreflectivities on the horizontal section, but these spots did not form contractile ERM (Fig. 1.6a–d).

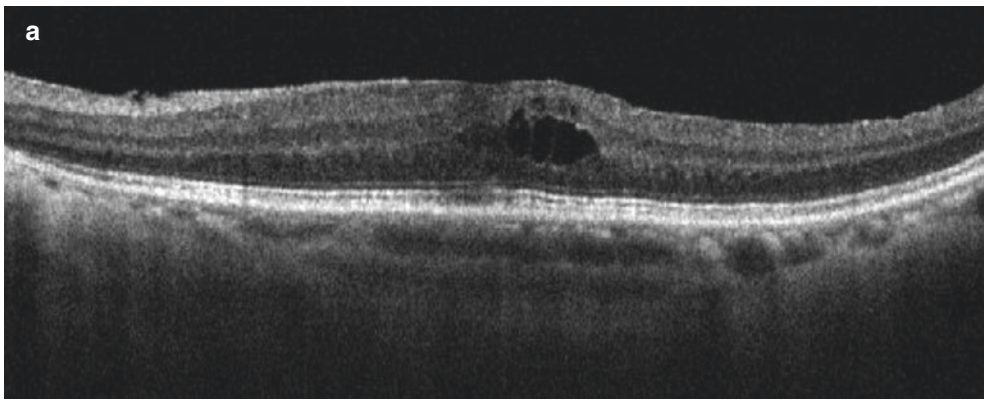
1.3.2 Examples of Secondary ERM

We demonstrate some cases of secondary ERM here. The first case was the left eye of a 29-year-old female. She suffered from poorly controlled diabetes mellitus. Proliferative diabetic retinopathy with tractional epiretinal membrane and vitreous hemorrhage. The second case was the left eye from a 74-year-old female with prior proliferative diabetic retinopathy with panretinal photocoagulation scars. Tractional membrane over disc and nasal side retina and yellow-grayish contractile macular ERM could be seen. The third case was the left eye from a 74-year-old female with prior proliferative diabetic retinopathy with pan-retinal photocoagulation scars. Tractional membrane over disc and nasal side retina and yellow-grayish contractile macular ERM could be seen. High-resolution OCT showed thickened ERM with attenuation of the foveal pit. No remaining macular ERM could be seen post-operatively. The contractile wrinkling had also been gone (Fig. 1.7).

1.3.3 Presenting Age, VA, and Laterality in ERM

Epiretinal membrane usually occurs in patients over 50 years old and could be seen in 10–30% of the general population over 70 years old. Bilateral involvement is present in 20% of these patients. Eighty percent of these membranes are idiopathic, while about 20% are secondary to previous retinal detachment, vascular, or inflammatory retinal diseases [1, 5] (Table 1.2). The initial presenting visual acuity is usually fair, 20/50, or better, and the progression is usually slow [5–7].

In 1982, Sidd et al. published a series of 98 eyes in 89 patients, with 83 more than 50 years old. Sixty eyes (60/98,



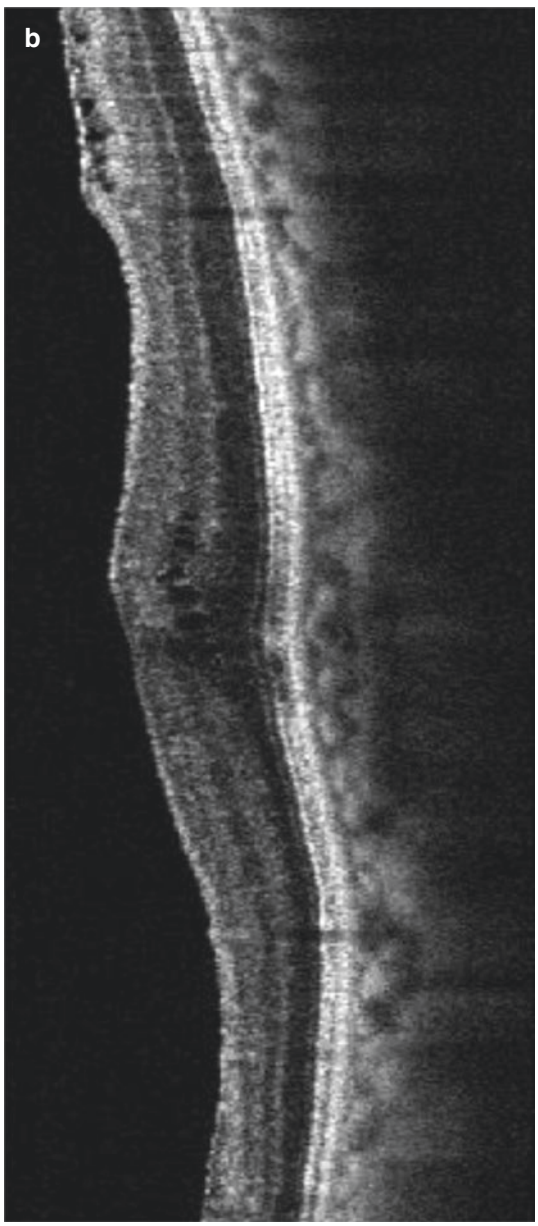
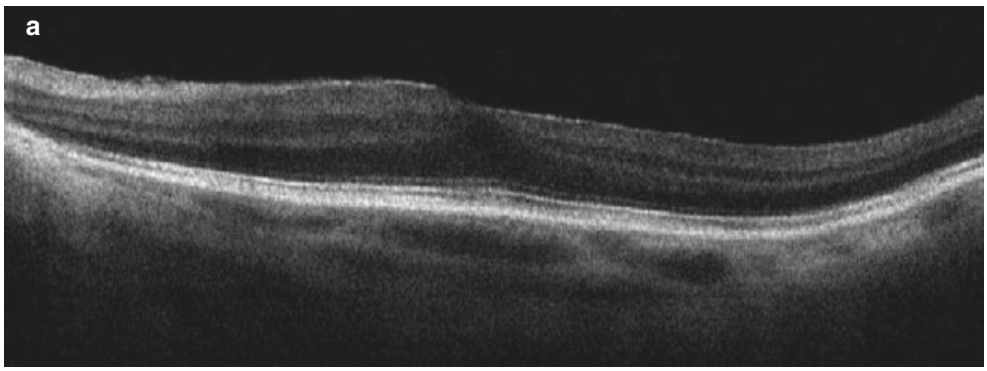


Fig. 1.3 (**a**) After 1.5 months postoperatively, follow-up OCT showed removal of ERM and ILM on central macula, on both horizontal section (**a**) and vertical section (**b**). The central foveal thickness decreased markedly, and the intraretinal splitting lessened. Please also note very thin ILM still evident on the side close to optic nerve head. We preferably perform limited ILM peeling in our cases. (**b**) After 1.5 months postoperatively, follow-up OCT showed removal of ERM and ILM on central macula, on both horizontal section and vertical section. The central foveal thickness decreased markedly, and the intraretinal splitting lessened. Please also note very thin ILM inferiorly and residual ERM-ILM superiorly. We preferably perform limited ILM peeling only in our cases



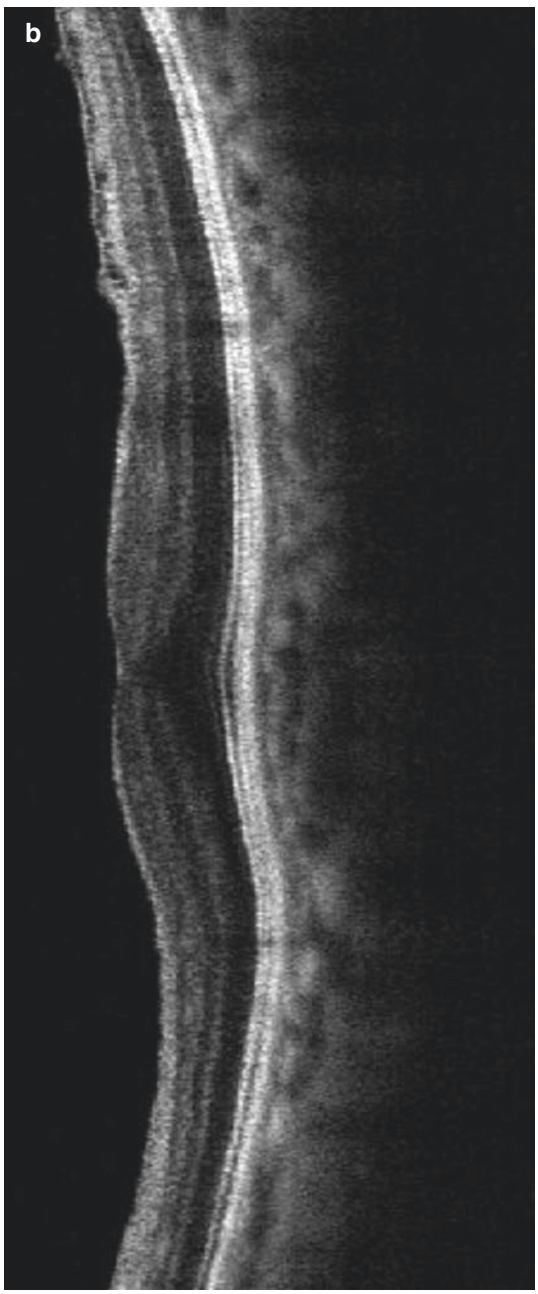


Fig. 1.4 (**a**) After 2.5 months postoperatively, the intraretinal split subsided, and initial restoration of foveal depression could be observed. (**b**) After 2.5 months postoperatively, the intraretinal split subsided, and initial restoration of foveal depression could be observed

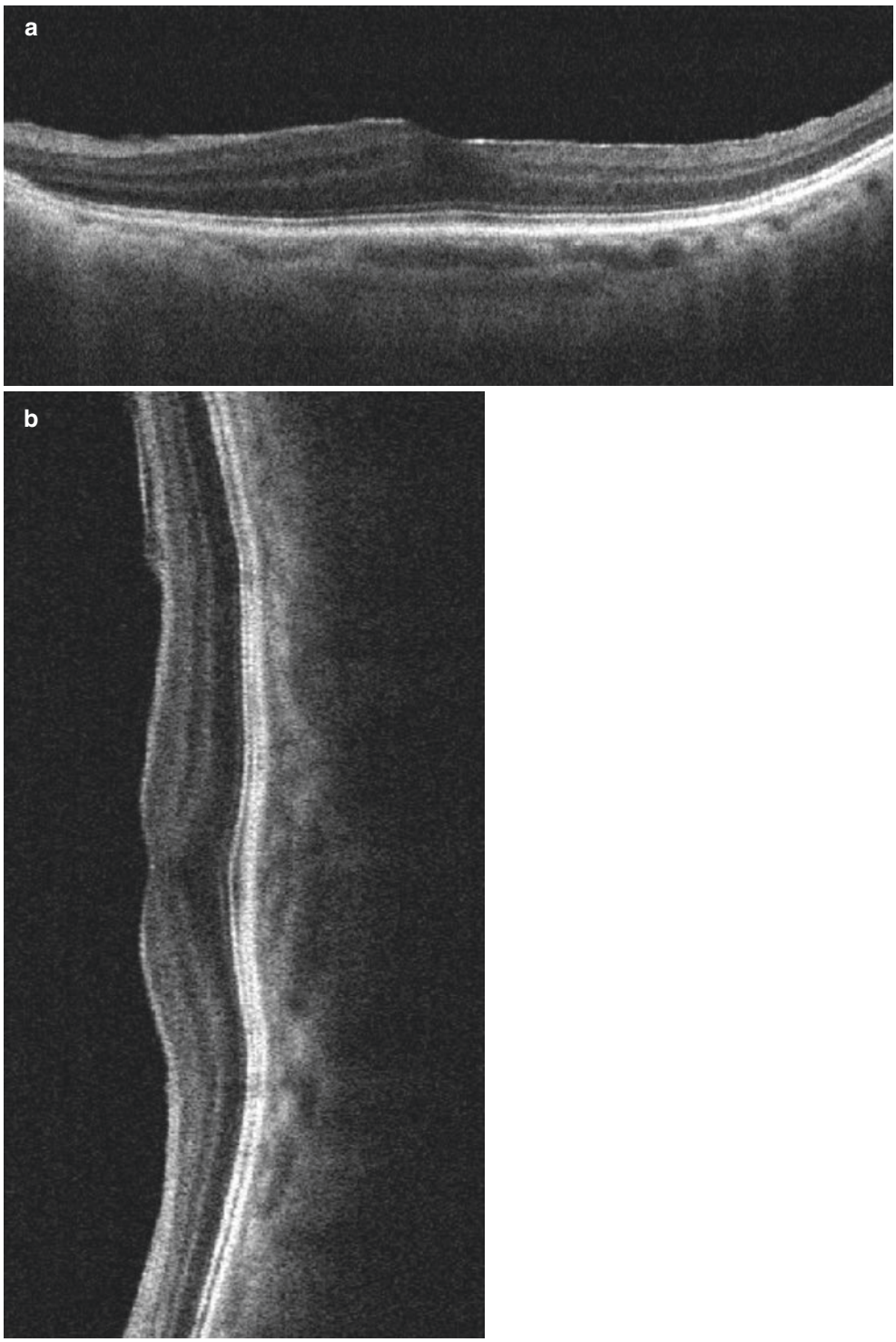


Fig. 1.5 (**a**) After 6.5 months postoperatively, the anatomical improvement had been stable. There was no more foveal cystic change, and the segmentation of retinal layers was well-defined. (**b**) After 6.5 months postoperatively, the anatomical improvement had been stable. There was no more foveal cystic change, and the segmentation of retinal layers was well-defined

61%) had initial presenting VA 6/12 (20/40) or better. Nine patients had initial bilateral epiretinal membrane, and a second eye became involved in one initially unilateral patient during the follow-up period. Sixteen of 74 eyes (21%) had fluorescein leakage into the macula [7].

In 1988, Appiah, Hirose, and Kado reviewed 395 eyes in 324 eyes with idiopathic premacular gliosis. The mean age of onset in these patients was 64.6 years old. Initial visual acuity was 20/40 or better in 214 eyes (54.2%), 20/50 to 20/100 in 136 eyes (34.4%), and poorer than 20/100 in 45 eyes (11.4%).

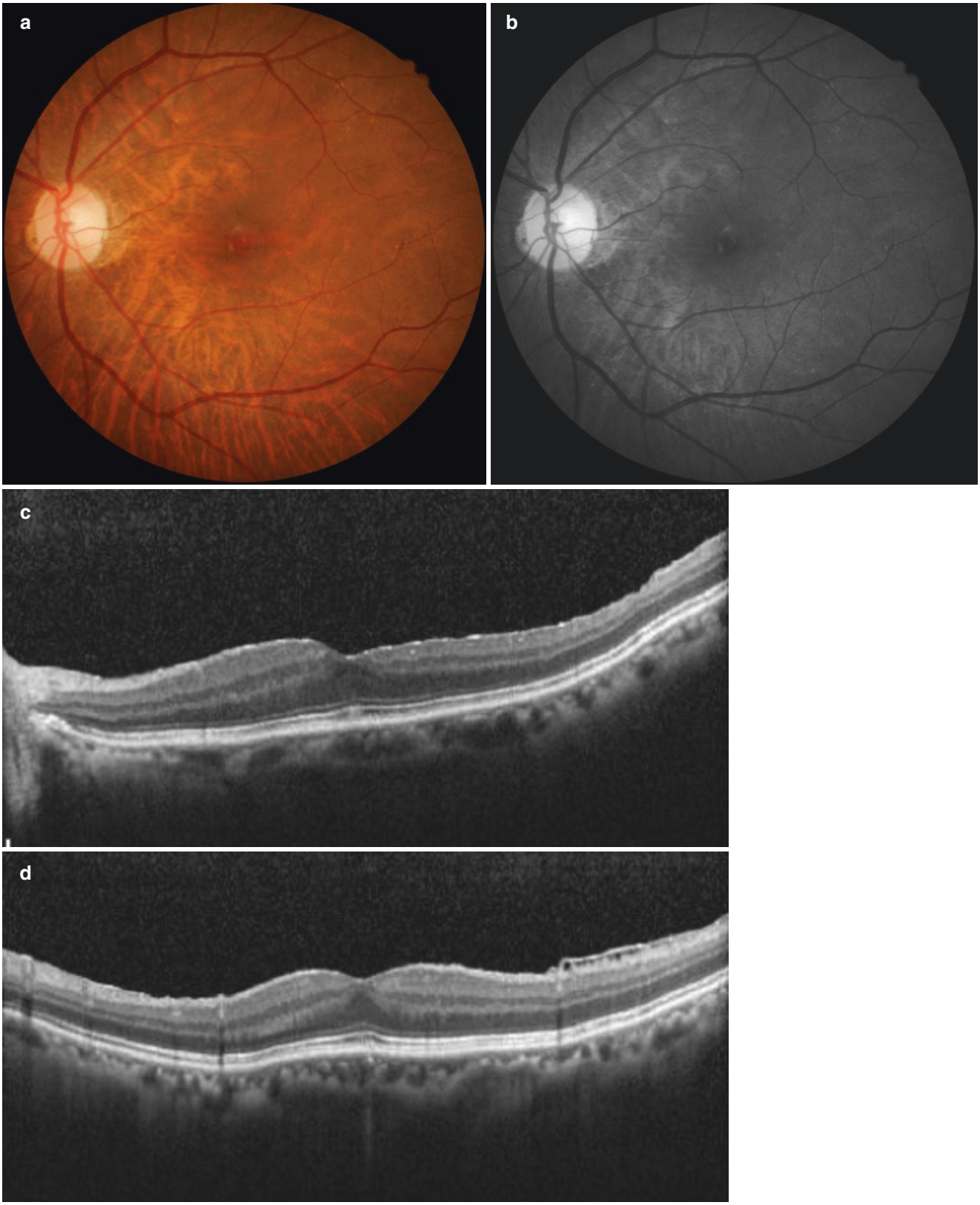


Fig. 1.6 (**a**) After 2 years of follow-up, the macula seemed flat without recurrence of ERM. There was also no retinal folding. (**b**) After 2 years of follow-up, the macula seemed flat without recurrence of ERM. There was also no retinal folding. (**c**, **d**) After 2 years of follow-up, the macula seemed flat without recurrence of ERM. On the OCT, the retinal layers also showed adequate segmentation. Please note the remnant of ERM on the superior aspect of macula. The ERM did not extend to the parafoveal region. Please also note there were some epiretinal hyperreflectivities on the horizontal section, but these spots did not form contractile ERM

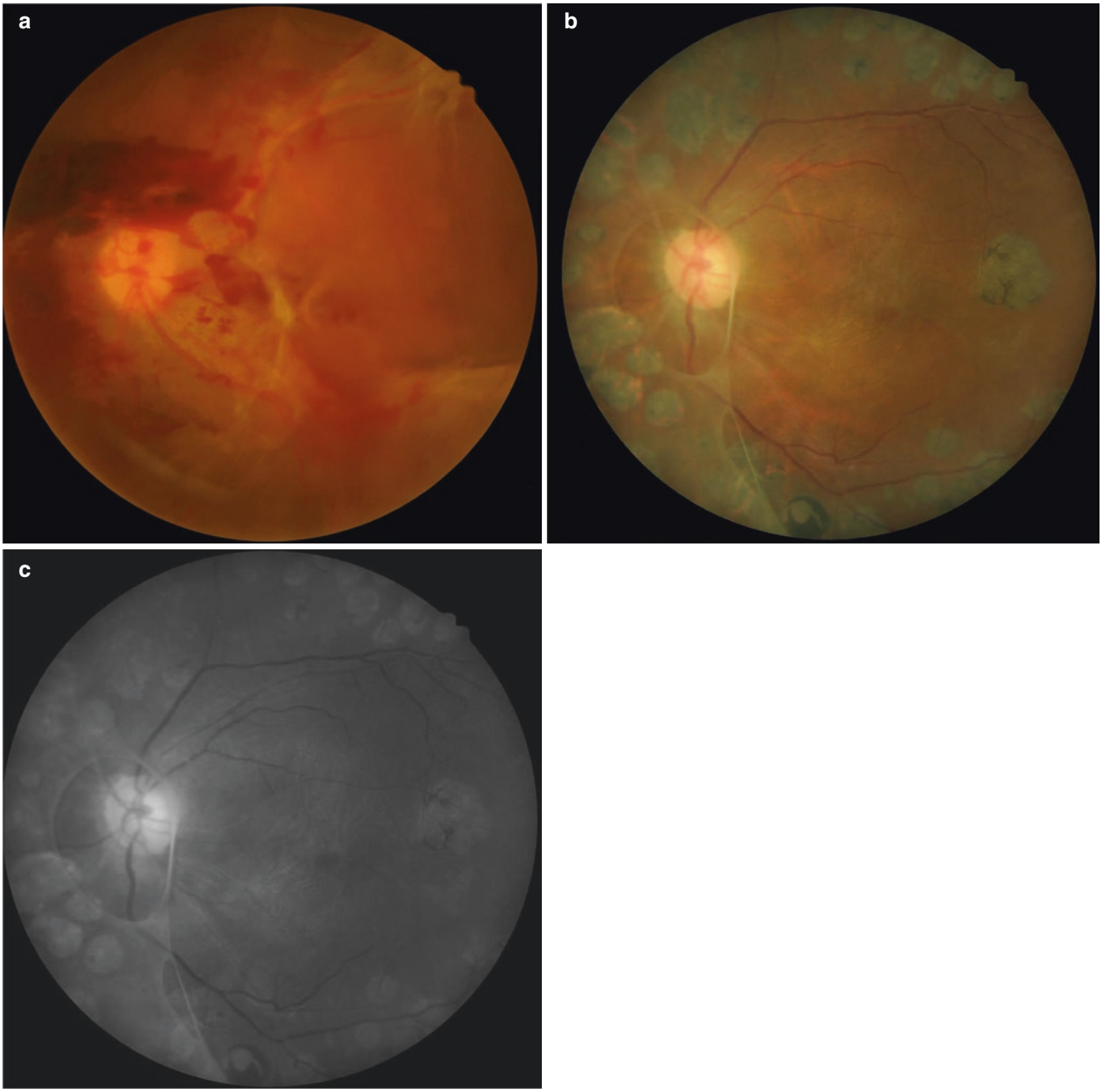


Fig. 1.7 (**a**) This was a left eye of a 29-year-old female. She suffered from poorly controlled diabetes mellitus. Proliferative diabetic retinopathy with tractional epiretinal membrane and vitreous hemorrhage could be seen in this fundus color photo. The postoperative photo was not available for this patient. (**b**) This was a left eye from a 74-year-old female with prior proliferative diabetic retinopathy with pan-retinal photocoagulation scars. Tractional membrane over disc and nasal side retina and yellow-grayish contractile macular ERM could be seen. (**c**) This was a left eye from a 74-year-old female with prior proliferative diabetic retinopathy with pan-retinal photocoagulation scars. Tractional membrane over disc and nasal side retina and yellow-grayish contractile macular ERM could be seen. Please note the contractile wrinkling of macular ERM being more evident under this red-free fundus photo. (**d**, **e**) High-resolution OCT showed thickened ERM with attenuation of the foveal pit. (**f**) One month after the vitrectomy and double membrane peeling. The macular tractional ERM and ILM were peeled off. No remaining macular ERM could be seen postoperatively. (**g**) One month after the vitrectomy and double membrane peeling. The macular tractional ERM and ILM were peeled off. No remaining macular ERM could be seen postoperatively. The contractile wrinkling had also been gone in this red-free photography. (**h**, **i**) One month after the vitrectomy and membrane peeling, there was mild restoration of the foveal contour. This patient was referred back to original ophthalmologist after this examination

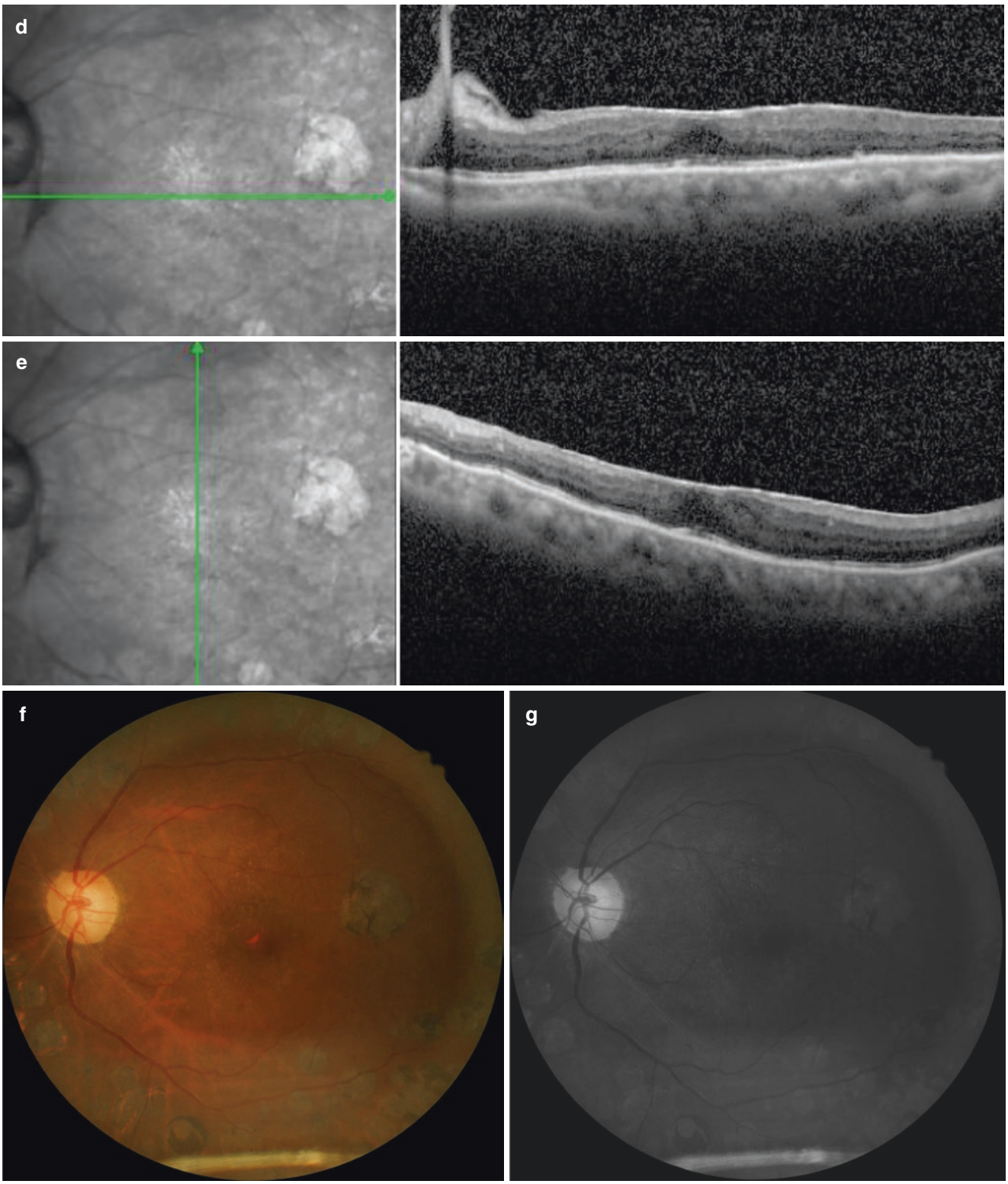


Fig. 1.7 (continued)

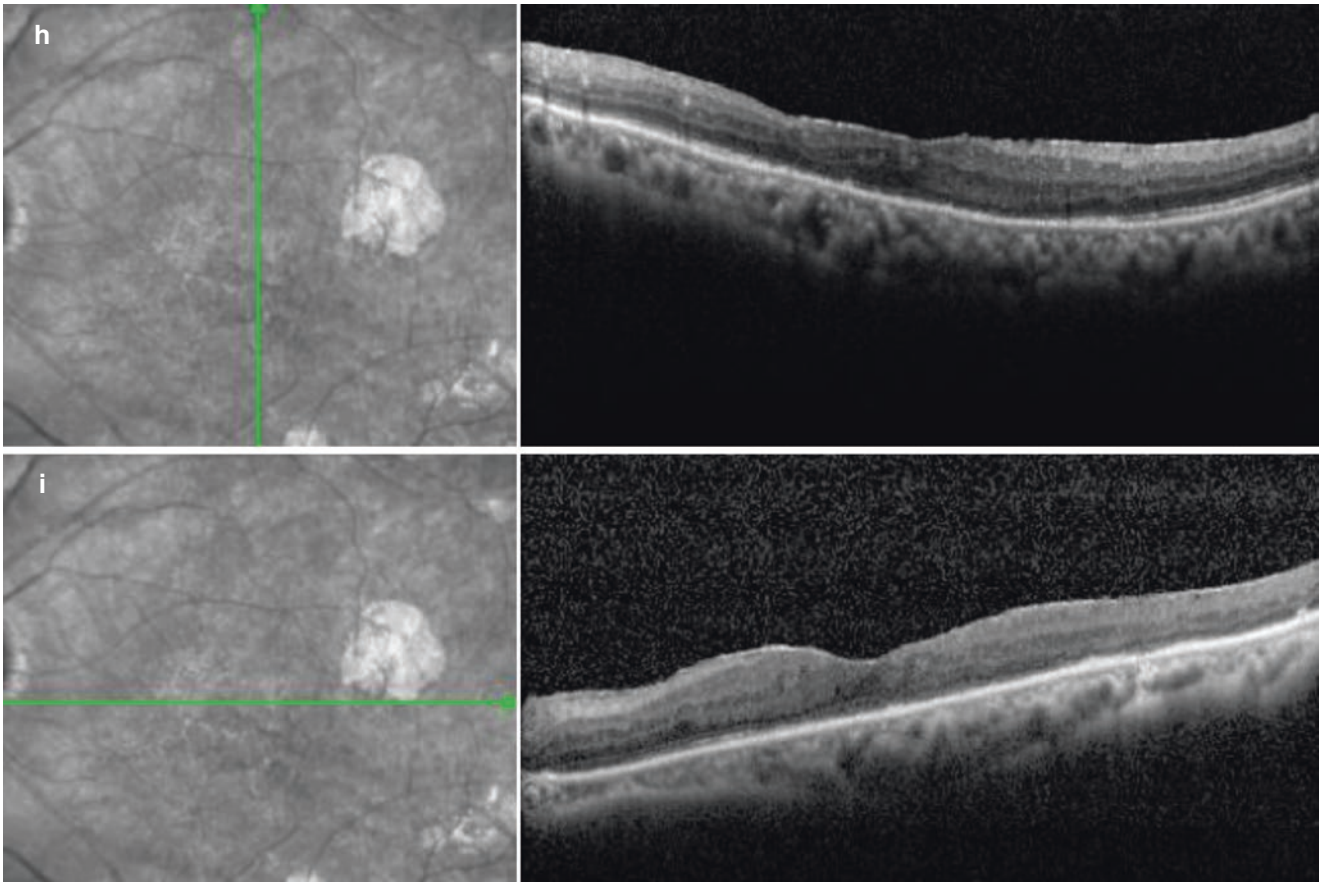


Fig. 1.7 (continued)

In a more recent nature-course observation, Hejsek et al. followed 53 eyes in 49 patients (average 21.3 months). No statistically significant anatomical or functional impairment was observed. BCVA remained constant in 29 eyes (54.7%), improvement by 1 or more lines (ETDRS) was observed in 12 eyes (22.6%), and impairment by 1 or more lines (ETDRS) was found in 12 eyes (22.6%). Only three eyes (5.6%) were worse by more than 1 line (ETDRS). This study further confirmed that the majority of eyes with idiopathic epiretinal membranes are functionally stable [16].

1.3.4 Status of Posterior Vitreous Detachment (PVD) in ERM

Most eyes with ERM, both idiopathic and secondary, have PVD, ranging from 84% to 98% from literature.

In 1975, Wise reviewed 137 eyes with idiopathic membranes involving the macula and found PVD 118 (86%) eyes [37].

In 1982, Sidd and coworkers published a series of 89 patients. Sixty-four eyes had been recorded for PVD status, and 59 eyes (92%) had PVD [7].

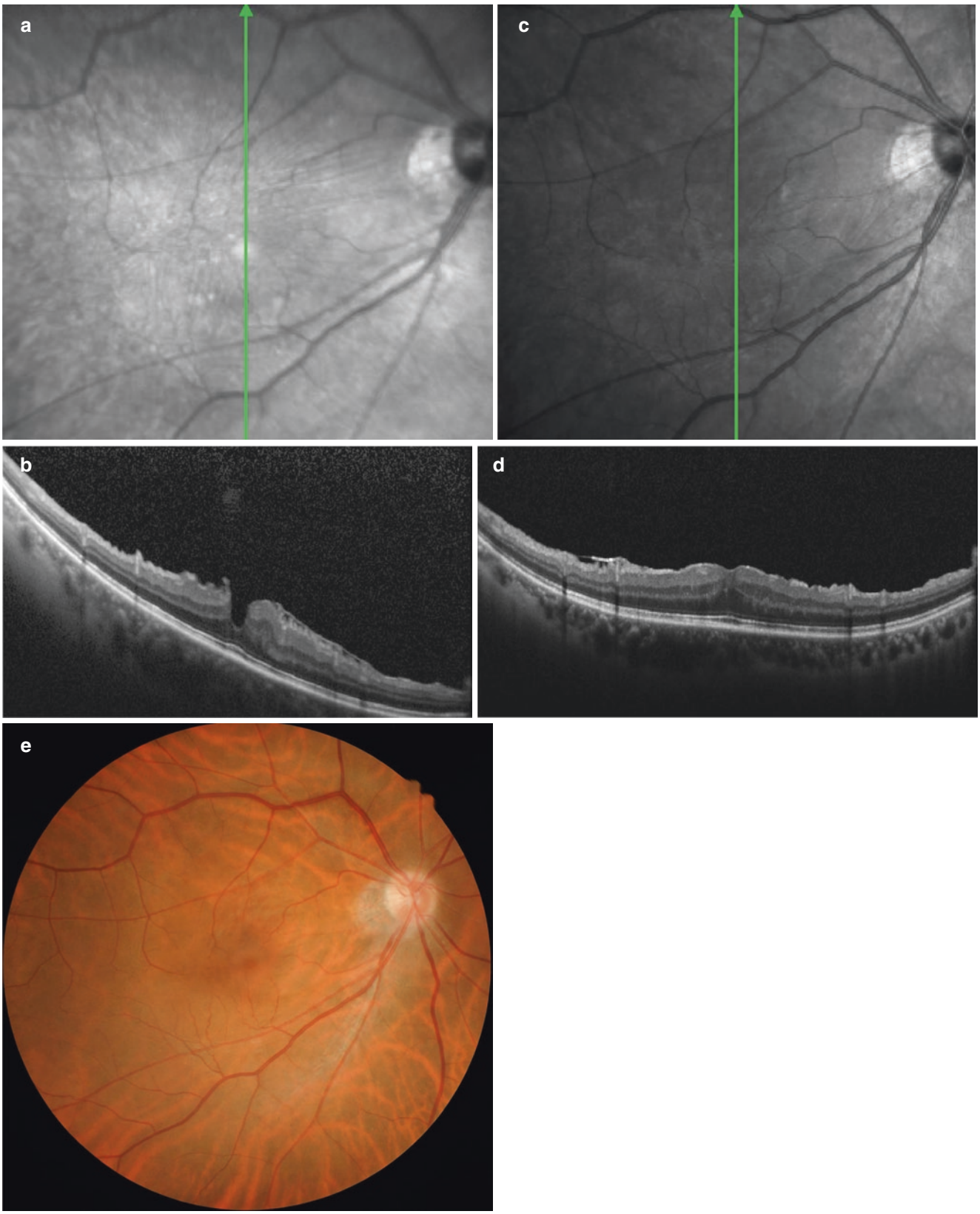
In 1988, Appiah et al. reviewed the vitreous status of 357 eyes. Partial or complete PVD was seen in 303 (84.9%) eyes. Forty-three (14.2%) of these 303 eyes had PVD with vitreous adhesion to the macula.

In a more recent series by Yazici et al., 125 eyes with idiopathic ERM and 168 eyes with secondary ERM were reviewed. PVD was seen in 98% of idiopathic ERM and 96% of secondary ERM [32].

1.3.5 Summary of Clinical Features in ERM

Epiretinal membrane usually occurs in patients over 50 years old and could be seen in 10–30% of the general population over 70 years old. Bilateral involvement is present in 20% of these patients. Eighty percent of these membranes are idiopathic, while about 20% are secondary to previous retinal detachment, vascular, or inflammatory retinal diseases. The initial presenting visual acuity is usually fair, 20/50, or better, and the progression is usually slow. Most eyes with ERM, both idiopathic and secondary, have PVD, ranging from 84% to 98% from literature.

MPH could be seen in 8–20% of eyes with ERM.


a
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e

Fig. 1.8 (**a**) This shows the vertical section of an eye with macular pseudohole under high-resolution spectral domain optical coherence tomography (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany). Please also note the centripetal contraction folds clearly shown. (**b**) This section shows the classic steepened foveal edge with increased foveal thickness under the centripetal traction from epiretinal membrane (ERM) high-resolution spectral domain OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany). (**c**) This shows the vertical section of the same eye with macular pseudohole, 1 year after 23-gauge vitrectomy, epiretinal membrane and internal limiting membrane peeling, air tamponade, and prone positioning, under high-resolution spectral domain OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany). Note the closure of the macular pseudohole. (**d**) This shows the vertical section of the same eye with macular pseudohole, 1 year after 23-gauge vitrectomy, epiretinal membrane and internal limiting membrane peeling, air tamponade, and prone positioning, under high-resolution spectral domain OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany). Please note the closure of the macular pseudohole and moderate restoration and normal foveal structure. (**e**) This color fundus shows the same eye with macular pseudohole, 1 year after 23-gauge vitrectomy, epiretinal membrane and internal limiting membrane peeling, air tamponade, and prone positioning. Please note the closure of the macular pseudohole and disappearance of epiretinal membrane and contractile folds

1.3.6 A Typical Case of MPH

This is a right eye from a 66 years old male patient. Epiretinal membrane with contractile wrinkling could be observed under color fundus and red-free photo (Fig. 1.1a, b). Under high-resolution spectral domain optical coherence tomography (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) (Fig. 1.8a, b), classic steepened foveal edge with increased foveal thickness under the centripetal traction from epiretinal membrane (ERM) is shown. The preoperative visual acuity (VA) was 0.6 (0.22 logMAR). One year after small-gauge vitrectomy, epiretinal membrane and internal limiting membrane peeling, air tamponade, and prone positioning, the pseudohole is closed with moderate restoration of normal foveal structure (Fig. 1.8c–e). The postoperative VA was 0.7 (0.15 logMAR).

1.3.7 Presenting Age, Visual Acuity, and Fluorescein Angiography in MPH

In 1992, Fish et al. reviewed 14 eyes with epimacular membrane and pseudohole. The mean age of patients was 61.6 years, and median visual acuity was 20/30. Mean horizontal and vertical diameters of the pseudoholes were 384 μm and 410 μm, respectively. FA showed three eyes with increased tortuosity or abnormal straightening of the perifoveal vessels; three eyes with a foveal window defect; and three eyes with late leakage from the perifoveal vessels [38].

The visual function of MPH eyes was often fair but varied from reports. In 1999, Massin et al. had case-control comparison of 50 eyes with idiopathic ERMs only and ERMs combined with pseudohole. The median preoperative visual acuity (VA) was the same as 20/63 (range, 20/32–20/860). In 1997, Tsujikawa et al. observed 49 eyes diagnosed with macular pseudoholes or impending macular holes. The median VA was 20/25 (range, 20/15–20/100). Only one eye showed a relative scotoma in perimetry, compared with 100% in full-thickness macular hole [39]. In 2008, Chen and Lee reviewed 92 eyes of macular lamellar defects, comprised of MPH, LMH, and foveal pseudocyst (FP). The MPH had the best VA of 0.1 (SD = 0.15) logMAR (equivalent to 20/25 Snellen acuity) compared with that of the LMH group (0.28 (SD = 0.25) logMAR; p = 0.005) and the FP group 0.30 (SD = 0.26; p = 0.01) [40]. In 2012, Michalewska and colleague reviewed 21 eyes with MPH, and the mean VA was 0.58. After excluding eyes with photoreceptor defects, the mean VA was 0.54 [21].

1.3.8 Status of PVD in MPH

The status of posterior vitreous detachment had been shown in one report. Schumann et al. had a series of 23 MPH underwent vitrectomy. They found eight (35%) eyes with vitreous attached, five (22%) eyes with vitreous partially detached, and ten (43%) eyes with complete PVD [35].

1.3.9 Detailed MPH Characteristic Discovery Under OCT Advances

The detailed characteristics of MPH had been revealed as OCT technology advanced. In 2004, Haouchine et al. observed 40 eyes with MPH. They summarized MPH as a steepened foveal pit combined with thickened foveal edges and a small foveal pit diameter. Central foveal thickness was normal or slightly increased (167 ± 42 μm). Mean perifoveal thickness was greater than normal (363 ± 65 μm) [19]. Intraretinal split was considered as hallmark for lamellar macula hole at then. Also, photoreceptor layer was considered as intact [41].

However, Gupta, Sadun, and Sebag demonstrated ERM with multifocal contraction tends to result in intraretinal cystoid space, in 2008. In 2013, Gaudric et al. reviewed 54 eyes with MPH using the Cirrus SD-OCT (Carl Zeiss Meditec,

Dublin, California, USA). They found 24 (44%) eyes had vertical foveal pit and straight, smooth edges on the OCT scan corresponding to centripetal contraction of the ERM. Nevertheless, 30 (56%) other eyes exhibited some degree of stretching and cleavage of the foveal pit edge resulting from asymmetrical tangential traction of the ERM between multiple epicenters of contraction. Thus, they proposed some lamellar macular hole (LMH) might be a subcategory of macular pseudohole (MPH).

Gaudric and colleagues further elaborated the ERM contraction by the en face OCT image. In the group with straight foveal edges, 18 of 24 (75%) eyes had a characteristic pattern of a smooth ERM, contracted around the pseudohole, causing radial retinal folds that converged toward the edge of the membrane, thus revealing the centripetal forces of contraction generated by the membrane. Four other eyes had a more complex pattern of folds, and in the two remaining eyes, the membrane was smooth with no visible folds. In the group with stretched edges combined with a partial cleavage between the inner and outer retina, 22 of 30 (73%) eyes displayed a characteristic pattern of multiple epicenters of contraction at the peripheral edge of the membrane, which resulted in an asymmetric distortion of the fovea and explained the eversion of the foveal edge on OCT scans. In four eyes, the ERM was smooth, with few retinal folds, and in the four other eyes, the folds were more or less radial. There was no significant difference in gender, age, posterior vitreous detachment (PVD), VA, central macular thickness (CMT), and central foveal pit thickness between two groups [34].

In 2015, Schumann et al. proved photoreceptor and external limiting membrane (ELM) damage from 39 eyes with MPH. Among the 39 eyes, 27 eyes had examination by high-resolution spectral domain OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany). They stratified ERM to "typical tractional ERM" and "atypical epiretinal tissue." Defect of inner and outer segment (IS/OS) and ELM was seen in 11% of MPH eyes. The median best-corrected visual acuity (BCVA) was 0.30 logMAR. Metamorphopsia was complained in 59% (n = 23) of the patients, and 59% (n = 23) had vitrectomy during follow-up.

They found a lower BCVA in the disrupted IS/OS and ELM group; and there was no significant difference in the intact IS/OS and ELM group and disrupted IS/OS-only group. In the nonoperated eyes (31 LMH and 16 MPH eyes), there is no BCVA difference in the subgroups. They did not reveal the independent result of MPH eyes in this analysis.

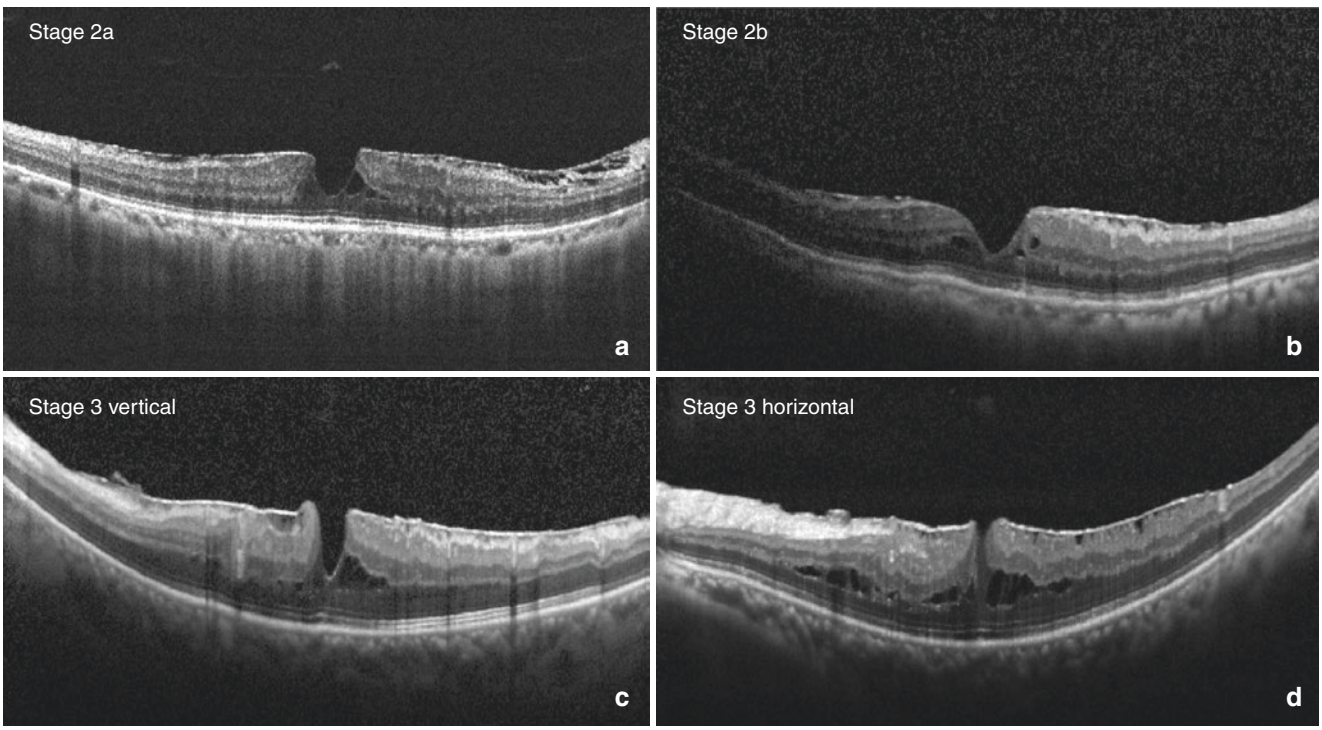

Fig. 1.9 (**a**) This optical coherence tomography section showed localized cleavage on only one side of the foveal edge. This is a stage 2a macular pseudohole according to Toyama's report in 2016. (**b**) This optical coherence tomography section showed localized cleavage crossing both sides of the foveal edge. This is a stage 2b macular pseudohole according to Toyama's report in 2016. (**c**, **d**) This optical coherence tomography section showed diffuse cleavage crossing both sides of the foveal edge. This is a stage 3 macular pseudohole according to Toyama's report in 2016. Please note that the diffuse cleavage might only be seen on some sections, usually not shown in all section. The same condition is also demonstrated in Toyama's paper

On the contrary, Toyama and colleague did not observe any disruption in the ellipsoid zone and ELM in 50 eyes with MPH [36].

In the same report, Toyama et al. further categorized the foveal edge to three stages of stretch cleavage between outer plexiform layer and the outer nuclear layer. The stages are as follows: no cleavage (stage 1), localized cleavage (stage 2) that does or does not cross the central fovea (stage 2b and 2a, respectively), and diffuse cleavage (stage 3). We used our patient's OCT to demonstrate these stages (Figs. 1.8b and 1.9a–d).

The number of patients categorized into each stage was 14 (28.0%), 13 (26.0%), 9 (18.0%), and 14 (28.0%) for stages 1, 2a, 2b, and 3, respectively. Temporal (12.3%) or nasal (11.1%) cleavage was more common than inferior (8.0%) or superior (9.3%) cleavage [36].

There was a significant difference in VA between the stages 2a and 2b ($p = 0.0099$ by multiple regression model). Therefore, the patients were categorized into two groups, the no/mild cleavage group (stage 1/2a) and the extensive cleavage group (stage 2b/3). They also found age, gender, and phakic status were not significant in affecting VA [36].

1.3.10 How to Differentiate Between Lamellar Macular Hole (LMH) and MPH

On biomicroscopy, the diagnosis of MPH is based on the presence of a well-delineated round or oval image of the macula with definite ERM with retinal folds. The diagnosis of LMH is described as a round- or petal-shaped reddish lesion with flat, sharply circumscribed edges. The center sometimes slightly depressed. Paler thin tracts could occasionally be seen. However, in 2004, Haouchine and coworkers had shown considerable misdiagnosis when confirmed by OCT. Among the 40 eyes diagnosed as MPH on OCT, 35 were also diagnosed as MPH, and two were diagnosed as LMH on biomicroscopy. Among the 29 cases diagnosed as LMH on OCT, 14 were diagnosed as MPH and eight as LMH on biomicroscopy [19] (Fig. 1.10a).

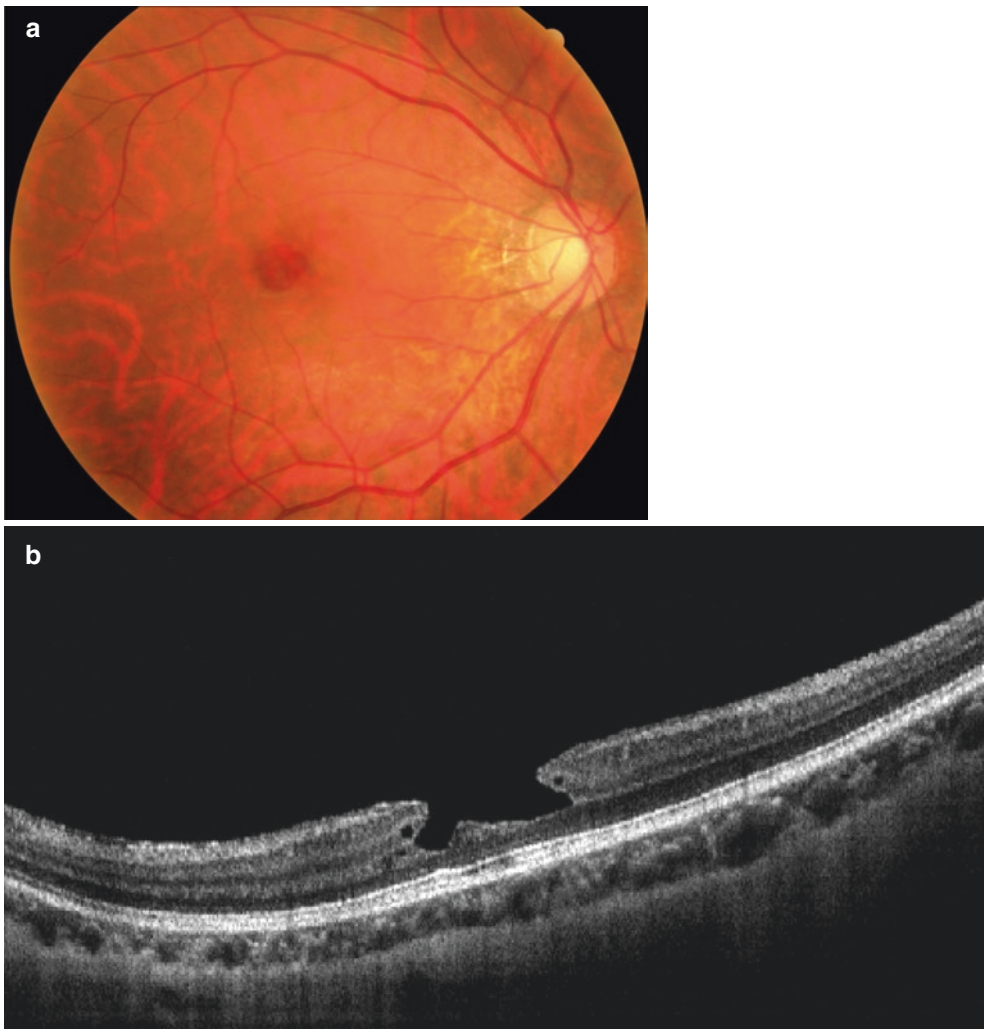

Fig. 1.10 (**a**) This is a right eye fundus photo of a 36-year-old female. Round and also mild petal-shaped reddish lesion with flat, sharply circumscribed edges could be appreciated. The center also seems slightly depressed. This represents a typical case of lamellar macular hole (LMH). (**b**) This is the OCT image of the right eye of the 36-year-old female shown in Fig. 1.9a. Please note that all the four criteria described by Haouchine et al. could be seen: (1) thin irregular foveal floor, (2) split foveal edges, (3) near-normal perifoveal retinal thickness, and (4) central foveolar thickness thinner than normal

They published their observation of 71 eyes from 70 patients. Characteristic of OCT in LMH was defined as the following and now being well adapted [19] (Fig. 1.10b).

1. Thin irregular foveal floor
2. Split foveal edges
3. Near-normal perifoveal retinal thickness
4. Central foveolar thickness thinner than normal

These criteria defined by Haouchine et al. are still widely used today. We may use these criteria to differentiate LMH from MPH.

1.3.11 Summary of Clinical Features in MPH

The mean age of patient was 61.6 years. The VA was generally fair, but with various median VA reported from 20/63 to 20/25. Metamorphopsia was complained in 59% of the patients. Mean horizontal and vertical diameters of the pseudoholes were 384 μm and 410 μm, respectively. Thirty-five percent of the eyes had vitreous attached. Twenty-two percent of the eyes had vitreous partially detached; and 43% of the eyes had complete PVD.

MPH generally has steepened foveal pit combined with thickened foveal edges and a small foveal pit diameter. Central foveal thickness was normal or slightly increased. Mean perifoveal thickness was greater than normal. With the advance of OCT, MPH could be classified into groups with straight edges and stretched edges. In the group with straight foveal edges, most eyes had a characteristic pattern of a smooth ERM. In the group with stretched edges combined with a partial cleavage, most eyes displayed a characteristic pattern of multiple epicenters of ERM contraction. There is a lower BCVA in the disrupted IS/OS and ELM group; and there was no significant difference in the intact IS/OS and ELM group and disrupted IS/OS only group.

Three stages of stretch cleavage had been defined as no cleavage (stage 1), localized cleavage (stage 2) that does or does not cross the central fovea (stage 2b and 2a, respectively), and diffuse cleavage (stage 3). There was a significant difference in VA between the stages 2a and 2b.

1.4 Management

The management of epiretinal membrane (ERM) includes observation and vitreoretinal surgery. Surgery is advised to patients [9, 16]:

1. VA deteriorates under 20/100–20/50 or worse.
2. Intolerable metamorphopsia.

The management of macular pseudohole (MPH) includes observation and vitreoretinal surgery. Surgery is advised to patients:

1. Visual acuity decreases more than two Snellen lines during the follow-up.
2. Initial visual acuity below 0.6, disturbing to the patient.
3. Visual acuity is better than 0.6, but disturbing metamorphopsia [21].

1.4.1 Observation in ERM and MPH

Generally speaking, the majority of patients had relatively stable clinical course [6, 7, 16]. Therefore, observation is suggested unless the criteria of surgery are met.

In 1982, Sidd et al. published their observation in 98 eyes with epiretinal membrane. Seventy-two eyes completed follow-up, with mean of 31.1 months. The fundus remained grossly unchanged in 65 eyes (90%). Fifty-one eyes (71%) had final VA deterioration within one line. Decrease in retinal wrinkling and VA improvement of two lines or more occurred in only two patients (2%) [7].

In 1988, Appiah, Hirose, and Kado reviewed 395 eyes in 324 eyes with idiopathic premacular gliosis, in which 214 eyes completed follow-up, with mean follow-up period of 33.6 months. One hundred and six (49.5%) of the 214 eyes maintained within 1 line of initial VA, 28 (13.1%) were more than 1 line better, and 80 (37.4%) were poorer [6].

In rare cases, epiretinal membrane will spontaneously peel off from the retina, and VA improvement may be observed [42].

In a more recent nature-course observation, Hejsek et al. followed 53 eyes in 49 patients (average 21.3 months). No statistically significant anatomical or functional impairment was observed. BCVA remained constant in 29 eyes (54.7%), improvement by 1 or more lines (ETDRS) was observed in 12 eyes (22.6%), and impairment by 1 or more lines (ETDRS) was found in 12 eyes (22.6%). Only three eyes (5.6%) were worse by more than 1 line (ETDRS). This study further confirmed that the majority of eyes with idiopathic epiretinal membranes are functionally stable [16].

Generally speaking, the majority of patients with MPH had relatively stable clinical course [18, 21]. Therefore, observation is suggested unless the criteria of surgery are met.

In 1976, Allen and Gass witnessed one in four pseudoholes that progressed to full-thickness macular hole [18].

In 2012, Michalewska et al. published an observation of 125 eyes (116 patients) with non-full-thickness macular hole (NFMH), including 21 eyes with macular pseudohole (MPH), during 2006–2009. None of the MPH progressed to full-thickness macula hole (FTMH) [21].

1.4.2 Vitreoretinal Surgery in ERM

In 1978, Machemer reported the first pars plana vitrectomy for visually distorting epiretinal membrane removal [43].

Shea, Michels and Gilbert, and Margheiro and coworkers were the pioneers to report fair results after epiretinal membrane peeling in eyes with prior retinal detachments. They reported VA improvement in 88–90% of the cases [44–47]. However, the postoperative VA is usually between 20/30 and 20/100 [43, 47, 48].

1.4.2.1 Indication for Surgery in ERM

In 1982, Michels supported that surgery be considered in eyes with visual acuity of 20/100 or less, because final VA in successful cases often ranges between 20/30 and 20/70 at then [9].

In a more recent review by Hejsek et al. in 2017, they suggested vitrectomy in:

1. VA deteriorates under 20/50 or worse.
2. Intolerable metamorphopsia.

However, no recommendation has yet been established on the exact timing of the surgery [16].

1.4.2.2 ERM Peeling in ERM

In 1996, Shimada et al. compared ERM peeling by one of the three following methods: without staining in 46 eyes, triamcinolone acetonide (TA) staining in 42, and brilliant blue G (BBG) staining in 54. They found in the BBG group, 61% (33/54) achieved double peeling during the initial ERM peeling [49].

1.4.2.3 ILM Peeling in ERM

In 1996, Shimada et al. conducted internal limiting membrane (ILM) peeling using brilliant blue G (BBG). They also compared 104 eyes with single peeling and 142 eyes with double peeling and found the VA improvement was similar. However, the recurrence rate was much lower in the double peeling group [49].

In 2003, Park et al. collected 22 eyes (55%) with single peeling and 20 eyes (45%) with double peeling. VA improved or was unchanged in 79% in single peeling group and 100% in double peeling group. VA improved five or more lines in 25% in single peeling group and 30% in double peeling group [50].

In 2012, Chuang et al. followed 104 eyes from 104 patients that underwent double peeling. They compared no staining ($n = 61$), triamcinolone acetonide (TA) ($n = 20$), and indocyanine green (ICG) ($n = 23$). The improvement of VA and central foveal thickness (CFT) were similar. However, the recurrence was 13.1% in the no staining group, compared with TA- or ICG-assisted group ($p = 0.011$) [51].

In 2017, Chang et al. published extensive review and meta-analysis including 11 retrospective studies and one randomized controlled trial involving 756 eyes. They found that the postoperative BCVA within 12 months was significantly better in the non-ILM peeling group ($p = 0.0460$). However, the double peeling group achieved significantly better postoperative BCVA after 18 months ($p = 0.0049$). Single peeling group exhibited a higher reduction in postoperative CRT ($p = 0.0020$) and a higher recurrence rate of ERM ($p = 0.0048$) than the double peeling group. However, the rate of improvement in BCVA and postoperative CRTs were similar in these two groups [52].

1.4.2.4 Postoperative VA Improvement in ERM

In 1982, Michels published a series of 74 eyes. Sixty-two eyes (84%) had VA improvement of two or more lines. The rest 12 eyes (16%) had unchanged VA. He raise predicting factors as (1) age of the patient, (2) preexisting damage to the macula before occurrence of the epiretinal membrane, (3) severity of macular distortion because of the membrane or secondary changes or both in the retina or pigment epithelium, (4) length of time the membrane had been present, and (5) ease or difficulty of removal of the membrane.

He had shown the group with duration longer than 12 months had inferior VA than those less than 6 months. He also showed that in group with previous RD, those with macula spared had better final VA. In total, however, only 5 (7%) of the 74 eye operated achieved VA of 20/20.

Twenty-one (28%) eyes reached final VA of 20/40 or better, and 37 (50%) eyes had final VA ranged from 20/50 to 20/100. Thus, he suggested surgery be considered in eyes with visual acuity of 20/100 or less [9].

For eyes with recurrence, Grewing and Mester reported 42 recurrences (12%) from 350 eyes vitrectomized for epiretinal membrane. They found VA improvement was still significant albeit the existence of recurrent epiretinal membrane. Eight (19%) of these 42 eyes had second vitrectomy, but their final VA is not different from the 32 eyes without second vitrectomy. Also, eyes with or without recurrence had similar VA improvement [53].

1.4.2.5 Recurrence Rate in ERM

Surgical removal of epiretinal membranes has infrequent recurrence. In 1981, Michels reported only 2 recurrences in 50 cases [48].

In 1996, Grewing and Mester reported 42 recurrences (12%) from 350 eyes vitrectomized for epiretinal membrane. Type of membrane (thick or thin) nor completeness of membrane removal did not affect recurrence rate [53].

In 2003, Park et al. reported a recurrence or persistent contraction to ILM in 21% of single peeling group. They found none of these in double peeling group [50].

In 2009, Shimada et al. reported 104 eyes that underwent single ERM peeling, and 17 eyes (16.3%) had recurrence. They also reported no recurrence in 142 eyes that underwent double ERM and ILM peeling [49].

In summary, the recurrence rate is significantly lowering in the double peeling group.

1.4.3 Vitreoretinal Surgery in MPH

Not all of the MPH eyes need vitreoretinal surgery unless they show signs of progressive loss of vision or increased visual symptoms such as metamorphopsia. Surgery of MPH typically requires ERM removal, and incidentally the internal limiting membrane (ILM), to improve the macular profile [34].

In 1999, Massin and colleagues reported the postoperative results for 50 eyes with pseudohole and a paired series of idiopathic ERMs without pseudohole operated on during the same period. All patients underwent standard three-port pars plana core vitrectomy and ERM peeling. For the patients with pseudohole, median preoperative visual acuity was 20/63 (range, 20/32–20/860), and median postoperative visual acuity was 20/40 (range, 20/20–20/860). Vision improved by 2 or more lines in 31 (62%) of 50 eyes. Forty eyes (80%) reached visual acuity of 20/50 or more. Pseudohole persisted in 22 eyes (44%) 3 months after surgery and in 15 eyes (30%) at 6 months. There was no difference in visual acuity, whether or not the pseudohole persisted [54].

In 2013, Gaudric et al. published a series of 33 patients, 14 eyes with straight foveal edges and 19 eyes with stretched edges, who underwent core vitrectomy and ERM removal. Trypan blue staining, followed by ILM peeling, was performed in 23 of the 33 patients. Short-acting gas tamponade (20% SF_6 air) was used only in four cases (two in each group) because of the intraoperative retinal tear. Mean macular thickness decreased equally in the two groups, and postoperative thickness was similar (363.8 μm vs. 345.3 μm; $p < 0.12$). The macular profile improved in all patients, with the disappearance or attenuation of the verticalization of the foveal edges. Of the 19 patients with stretched and cleaved edges, the cleavage completely disappeared in 14 patients, was attenuated in three patients, and remained unchanged in the two remaining patients. En face OCT images showed, in all patients, an alteration of the macular surface known as the dissociated optic nerve fiber layer, commonly seen after ILM peeling. The mean VA of the 33 eyes that underwent surgery improved from 0.44 logMAR (Snellen equivalent, 20/50) before surgery to 0.28 logMAR (Snellen equivalent, 20/40) after surgery ($p = 0.001$). There was no significant difference between the two groups in preoperative or postoperative VA ($p = 0.44$ and $p = 0.65$, respectively) and no difference in visual gain [34].

In 2015, Schumann et al. reviewed 39 eyes with MPH, and 59% of eyes ($n = 23$) had vitrectomy during follow-up. For the operated eyes, the preoperative BCVA was 0.40 logMAR (mean ± SD, 0.46 ± 0.26 logMAR). The postoperative BCVA was 0.10 logMAR (mean ± SD, 0.22 ± 0.21 logMAR). It was not superior using gas tamponade and prone positioning. They also published a mixed postoperative data comprised of 17 LMH eyes and 23 MPH eyes. They found a lower BCVA in the disrupted IS/OS and ELM group; and there was so significant difference in the intact IS/OS and ELM group and disrupted IS/OS-only group. In the nonoperated eyes (31 LMH and 16 MPH eyes), there is no BCVA difference in the subgroups. They did not reveal the independent result of MPH eyes in this analysis [35].

In 2015, Hirota et al. reported 31 eyes with a macular pseudohole underwent vitrectomy with internal limiting membrane removal. The BCVA improved significantly, and the length of the interdigitation zone (IZ) band defect decreased significantly after the surgery. Length of the IZ band defect is associated with preoperative and postoperative BCVA ($p < 0.001$ for all). The BCVA was not significantly correlated with the length of the ellipsoid zone, external limiting membrane band defect (ELM), and the central foveal thickness [55].

In 2016, Toyama and coworkers publish a series of 50 eyes with MPH, in which 36 eyes were evaluated by SD-OCT postoperatively. Lamellar cleavage subsided in 32 (88.9%) eyes [36].

To sum up, surgery is advised in patients whose visual acuity decreases more than two Snellen lines during the follow-up, initial visual acuity below 0.6, or disturbing metamorphopsia. With or without air/gas tamponade and prone positioning, the results are comparable. The anatomical improvement could be seen in the majority of patients, ranging from 70% to 90%, of operated eyes [36, 52]. Based on group analysis, VA would improve in both straight and smooth edges. Worse postoperative VA could be seen in eyes with disrupted IS/OS and interdigitation zone defect.

References

1. Dupas B, Tadayoni R, Gaudric A. Epiretinal membranes. J Fr Ophtalmol. 2015;38(9):861–75.
2. Fraser-Bell S, Guzowski M, Rochtchina E, Wang JJ, Mitchell P. Five-year cumulative incidence and progression of epiretinal membranes: the Blue Mountains Eye Study. Ophthalmology. 2003;110(1):34–40.
3. Klein R, Klein BE, Wang Q, Moss SE. The epidemiology of epiretinal membranes. Trans Am Ophthalmol Soc. 1994;92:403–30.

4. Mitchell P, Smith W, Chey T, Wang JJ, Chang A. Prevalence and associations of epiretinal membranes. The Blue Mountains Eye Study, Australia. Ophthalmology. 1997;104(6):1033–40.
5. Sheard RM, Sethi C, Gregor Z. Acute macular pucker. Ophthalmology. 2003;110(6):1178–84.
6. Appiah AP, Hirose T, Kado M. A review of 324 cases of idiopathic premacular gliosis. Am J Ophthalmol. 1998;106:533–5.
7. Sidd RJ, Fine SL, Owens SL, Patz A. Idiopathic preretinal gliosis. Am J Ophthalmol. 1982;94:44–8.
8. Iwanoff A. Beitraege zur normalen und pathologischen Anatomie des Auges: A. Zur pathologischen Anatomie der Retina. B. Zur normalen und pathologischen Anatomie des Glaskoerpers. Albrecht Von Graefes Arch Klin Exp Ophthalmol. 1865;11:135–70.
9. Michels RG. A clinical and histopathologic study of epiretinal membranes affecting the macula and removed by vitreous surgery. Trans Am Ophthalmol Soc. 1982;80:580–656.
10. Bellhorn MB, Friedman AH, Wise GN, et al. Ultrastructure and clinicopathologic correlation of idiopathic preretinal macular fibrosis. Am J Ophthalmol. 1975;79:366–73.
11. Foos RY. Ultrastructural features of posterior vitreous detachment. Albrecht Von Graefes Arch Klin Exp Ophthalmol. 1975;196:103–11.
12. Dellaporta A. Macular pucker and peripheral retinal lesions. Trans Am Ophthalmol Soc. 1973;71:329–40.
13. Laqua H. Pigmented macular pucker. Am J Ophthalmol. 1978;86:56–8.
14. Robertson DM, Buettner H. Pigmented preretinal membranes. Am J Ophthalmol. 1977;83:824–9.
15. Gass JD. Stereoscopic atlas of macular diseases: diagnosis and treatment. St. Louis, MO: CV Mosby Co; 1977. p. 344–66.
16. Hejsek L, Stepanov A, Dohnalova A, Rehakova T, Jiraskova N. The natural evolution of idiopathic epimacular membrane. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2017;161(1):100–6.
17. Klein BR, Hiner CJ, Glaser BM, et al. Fundus photographic and fluorescein angiographic characteristics of pseudoholes of the macula in eyes with epiretinal membranes. Ophthalmology. 1995;102:768–74.
18. Allen AW Jr, Gass JD. Contraction of a perifoveal epiretinal membrane simulating a macular hole. Am J Ophthalmol. 1976;82(5):684–91.
19. Haouchine B, Massin P, Tadayoni R, et al. Diagnosis of macular pseudoholes and lamellar macular holes by optical coherence tomography. Am J Ophthalmol. 2004;138:732–9.
20. Gupta P, Sadun AA, Sebag J. Multifocal retinal contraction in macular pucker analyzed by combined optical coherence tomography/scanning laser ophthalmoscopy. Retina. 2008;28(3):447–52.
21. Michalewska Z, Michalewski J, Odrobina D, et al. Non-full-thickness macular holes reassessed with spectral domain optical coherence tomography. Retina. 2012;32:922–9.
22. Foos RY. Vitreoretinal juncture over retinal vessels. Albrecht Von Graefes Arch Klin Exp Ophthalmol. 1977a;204:223–34.
23. Foos RY. Vitreoretinal juncture: epiretinal membranes and vitreous. Invest Ophthalmol Vis Sci. 1977b;16:416–22.
24. Burke JM, Sipos E, Cross HE. Cell proliferation in response to vitreous hemoglobin. Invest Ophthalmol Vis Sci. 1981;20:575–81.
25. Burke JM, Smith JM. Retinal proliferation in response to vitreous hemoglobin or iron. Invest Ophthalmol Vis Sci. 1981;20:582–92.
26. Lobes LA Jr, Burton TC. The incidence of macular pucker after retinal detachment surgery. Am J Ophthalmol. 1978;85:72–7.
27. Francois J, Verbraeken H. Relationship between the drainage of the subretinal fluid in retinal detachment surgery and the appearance of macular pucker. Ophthalmologica. 1979;179:111–4.
28. Hagler WS, Aturaliya U. Macular puckers after retinal detachment surgery. Br J Ophthalmol. 1971;55:451–7.
29. Tanenbaum HL, Schepens CL, Elzeneiny I, et al. Macular pucker following retinal detachment surgery. Arch Ophthalmol. 1970;83:286–93.
30. Daicker B, Guggenheim R. Studies on fibrous and fibro-glial surface wrinkling retinopathy by scanning electron microscopy. Albrecht Von Graefes Arch Klin Exp Ophthalmol. 1978;207:229–42.
31. Kampik A, Kenyon KR, Michels RG, et al. Epiretinal and vitreous membranes: comparative study of 56 cases. Arch Ophthalmol. 1981;99:1445–54.
32. Yazici AT, Alagöz N, Celik HU, et al. Idiopathic and secondary epiretinal membranes: do they differ in terms of morphology? An optical coherence tomography-based study. Retina. 2011;31(4):779–84.
33. Poliner LS, Olk RJ, Grand MG, Escoffery RF, Okun E, Boniuk I. Surgical management of premacular fibroplasia. Arch Ophthalmol. 1988;106(6):761–4.
34. Gaudric A, Aloulou Y, Tadayoni R, et al. Macular pseudoholes with lamellar cleavage of their edge remain pseudoholes. Am J Ophthalmol. 2013;155:733–42, 742.e1-4.
35. Schumann RG, Compera D, Schaumberger MM, Wolf A, Fazekas C, Mayer WJ, Kampik A, Haritoglou C. Epiretinal membrane characteristics correlate with photoreceptor layer defects in lamellar macular holes and macular pseudoholes. Retina. 2015;35(4):727–35.
36. Toyama T, Foggia MF, Yamaguchi T, Noda Y, Ueta T. The extent of stretched lamellar cleavage and visual acuity in macular pseudoholes. Br J Ophthalmol. 2016;100(9):1227–31.
37. Wise GN. Schoenberg lecture: clinical features of idiopathic preretinal macular fibrosis. Am J Ophthalmol. 1975;79:349–57.
38. Fish RH, Anand R, Izbrand DJ. Macular pseudoholes. Clinical features and accuracy of diagnosis. Ophthalmology. 1992;99(11):1665–70.
39. Tsujikawa M, Ohji M, Fujikado T, et al. Differentiating full thickness macular holes from impending macular holes and macular pseudoholes. Br J Ophthalmol. 1997;81(2):117–22.
40. Chen JC, Lee LR. Clinical spectrum of lamellar macular defects including pseudoholes and pseudocysts defined by optical coherence tomography. Br J Ophthalmol. 2008;92:1342–6.
41. Witkin AJ, Ko TH, Fujimoto JG, et al. Redefining lamellar holes and the vitreomacular interface: an ultrahigh-resolution optical coherence tomography study. Ophthalmology. 2006;113:388–97.
42. Messner KH. Spontaneous separation of preretinal macular fibrosis. Am J Ophthalmol. 1977;83:9–11.
43. Machemer R. The surgical removal of epiretinal macular membranes (macular puckers). Klin Monbl Augenheilkd. 1978;173:36–42.
44. Margheiro AR, Nachazel DP, Murphy PL, et al. The surgical management of epiretinal membranes, scientific exhibit, American Academy of Ophthalmology Annual Meeting, 1981. Ophthalmology. 1981;88(September suppl):82.
45. Michels RG, Gilbert HD. Surgical management of macular pucker after retinal reattachment surgery. Am J Ophthalmol. 1979;88:925–9.
46. Shea M. The surgical management of macular pucker. Can J Ophthalmol. 1979;14:110–3.
47. Shea M. The surgical management of macular pucker in rhegmatogenous retinal detachment. Ophthalmology. 1980;87:70–4.
48. Michels RG. Vitreous surgery for macular pucker. Am J Ophthalmol. 1981;92:628–39.
49. Shimada H, Nakashizuka H, Hattori T, Mori R, Mizutani Y, Yuzawa M. Double staining with brilliant blue G and double peeling for epiretinal membranes. Ophthalmology. 2009;116(7):1370–6.
50. Park DW, Dugel PU, Garda J, Sipperley JO, Thach A, Sneed SR, et al. Macular pucker removal with and without internal limiting membrane peeling: pilot study. Ophthalmology. 2003;110(1):62–4.

51. Chuang LHWN, Chen YP, Hwang YS, et al. Comparison of visual outcomes after epiretinal membrane surgery. Taiwan Journal of. Ophthalmology. 2012;2:56–9.
52. Chang WC, Lin C, Lee CH, Sung TL, Tung TH, Liu JH. Vitrectomy with or without internal limiting membrane peeling for idiopathic epiretinal membrane: a meta-analysis. PLoS One. 2017;12(6):e0179105.
53. Grewing R, Mester U. Results of surgery for epiretinal membranes and their recurrences. Br J Ophthalmol. 1996;80(4):323–6.
54. Massin P, Paques M, Masri H, et al. Visual outcome of surgery for epiretinal membranes with macular pseudoholes. Ophthalmology. 1999;106(3):580–5.
55. Hirota K, Itoh Y, Rii T, et al. Correlation between foveal interdigitation zone band defect and visual acuity after surgery for macular pseudohole. Retina. 2015;35:908–14.

Vitreomacular Traction Syndrome

2

Yusuke Ichiyama and Masahito Ohji

2.1 Introduction

Posterior vitreous detachment (PVD) is commonly seen in the aging eye [1]. Although the majority of PVDs occur without complication, a small proportion can be associated with excessive traction on the macula, resulting in retinal anatomic changes. These eyes are characterized as having vitreomacular traction (VMT). VMT can lead to functional changes such as metamorphopsia and blurring of visual acuity with central visual field defects.

VMT is prevalent in women (about 65%), and most patients are in their sixth or seventh decade [2, 3]. To diagnose VMT, optical coherence tomography (OCT) is a very useful tool, because it is frequently difficult to distinguish VMT from other retinal diseases such as epiretinal membrane (ERM) or macular hole (MH) using slit-lamp examination (Fig. 2.1). Some eyes with VMT progress to macular hole (MH) in their natural history, and therefore VMT is considered to be one of the initiating causes of MH [4, 5].

2.2 Etiopathogenesis

The vitreous consists of approximately 98% water and 2% structural macromolecules forming a gel-like structure [6, 7]. In our early life, the vitreous is attached to all contiguous structures of the inner eye, including the internal limiting membrane (ILM) of the retina. As the eye ages, gel liquefaction and weakening of vitreoretinal adhesion occur, resulting in PVD. These changes typically begin in the perifoveal macula (Fig. 2.2) [8, 9], and this process proceeds for years

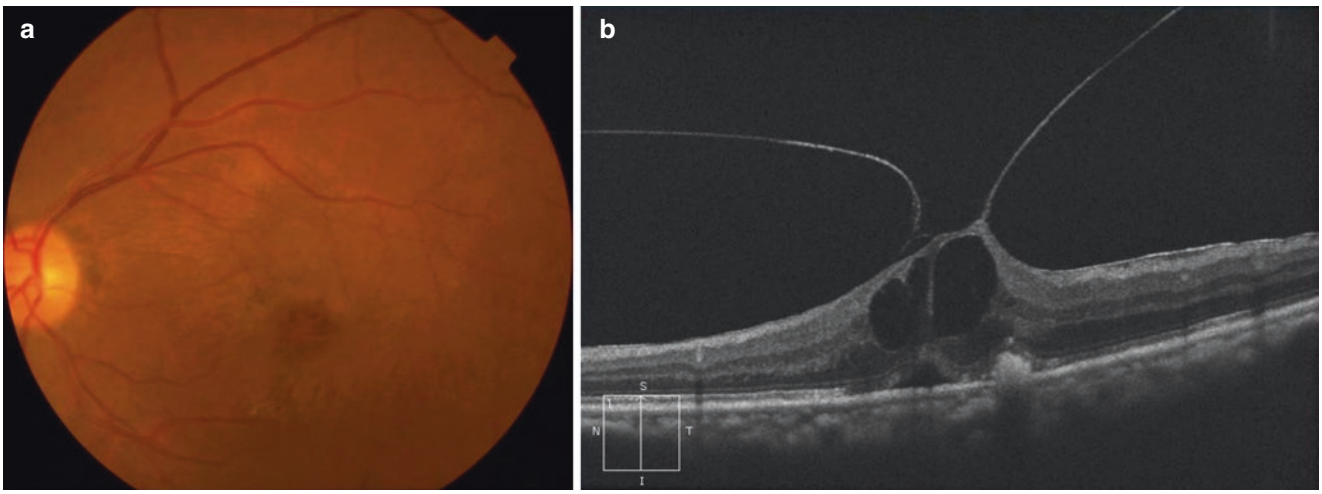

Fig. 2.1 (**a**) Color fundus photograph shows irregular reflex on vitreoretinal interface and retinal fold around fovea, but it is difficult to detect VMT from this photograph. (**b**) On the other hand, OCT clearly shows vitreomacular traction on fovea

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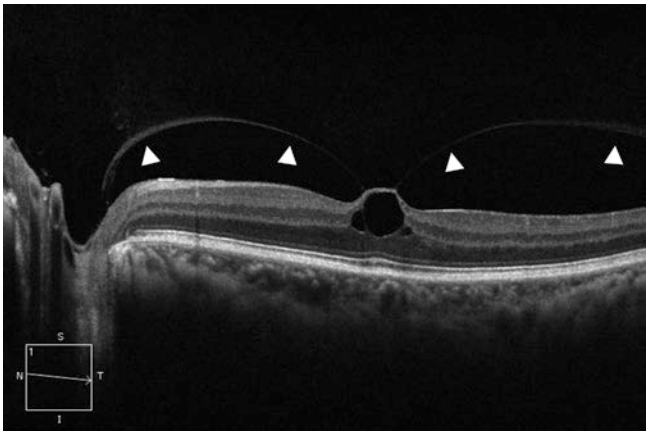

Fig. 2.2 OCT shows PVD that began in the perifoveal macula (arrowheads), and remaining vitreous attachment caused cystoid macular edema

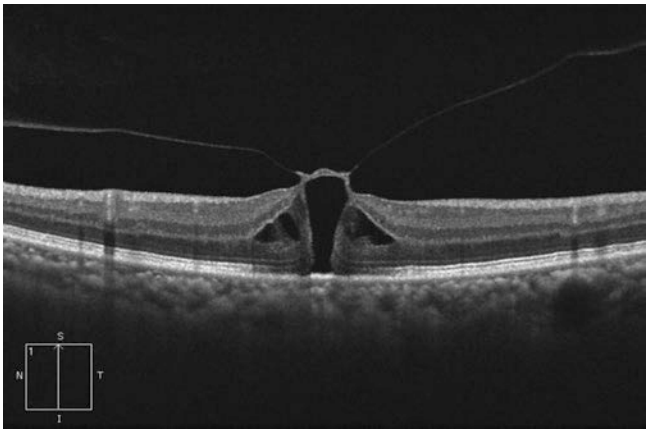

Fig. 2.3 OCT shows outer retinal macular hole with vitreous traction on fovea. It would remain controversial to define this case as VMT or MH

to decades into final separation of the vitreous from the macula and the optic nerve, resulting in a complete PVD. Although the majority of PVDs occur without complication, the retinal anatomic changes can develop in a small proportion of cases, because the strength and position of the remaining attachments vary among individuals [10].

2.3 Definition and Classification

2.3.1 Definition

Reese et al. first described VMT as a condition characterized by persistent vitreous attachment in the central macula, causing a cystoid configuration and decreased vision [11, 12]. Recently, the International Vitreomacular Traction Study Group suggested an OCT-based classification of vitreomacular interface disorders, including VMT [13]. They defined eyes with all of the following anatomic criteria on at least one B-mode OCT scan as having VMT: (1) evidence of perifoveal vitreous cortex detachment from the retinal surface; (2) macular attachment of the vitreous cortex within a 3-mm radius of the fovea; and (3) association of attachment with distortion of the foveal surface, intraretinal structural changes, elevation of the fovea above the RPE, or a combination thereof, but no full-thickness interruption of all retinal layers. This definition includes eyes with outer retinal macular hole due to VMT (Stage 1b of Gass' MH classification, Fig. 2.3), which remains controversial.

2.3.2 Classification

The International Vitreomacular Traction Study Group also suggested. that eyes with VMT are to be classified by the size of the vitreomacular adhesion (VMA) into either (1) focal (≤1500 μm, Fig. 2.4a) or (2) broad (>1500 μm; Fig. 2.4b). Focal areas of vitreous attachment with traction tend to distort the foveal surface, form cystoid macular edema, and sometimes combine with subretinal fluid. Broad areas of attachment with traction can cause generalized thickening of the macula, vascular leakage on fluorescein angiography, macular schisis, and cystoid macular edema. However, it remains unclear whether there is any prognostic difference between focal and broad VMT, so this criterion is currently considered to be tentative.

2.4 Management

The management strategies of VMT include observation, medical therapy, and surgery. The choice depends on the degree of subjective symptoms and the severity of retinal damage. If the subjective symptoms are limited and retinal damage is mild, observation is preferentially selected. However, if progressive traction and rapid visual loss occurs, prompt interventions should be considered, because irresponsible observation is associated with irreversible retinal damage and poor prognosis [14].

2.4.1 Observation

Several observational studies reported the natural history of VMT [4, 14–16]. Hikichi et al. reported that spontaneous release was observed in 11% of eyes with VMT during a median of 60 months of follow-up. Tzu et al. followed 230 eyes with VMT for a mean of 32 months, and they found spontaneous VMT release in 73 eyes (31.7%) at a mean of 18 months after initial visit. Theodossiadis et al. reported release of VMT in 26% (12 of 46 eyes) at a mean of 8.75 months from initial visit. Almeida et al. reported release

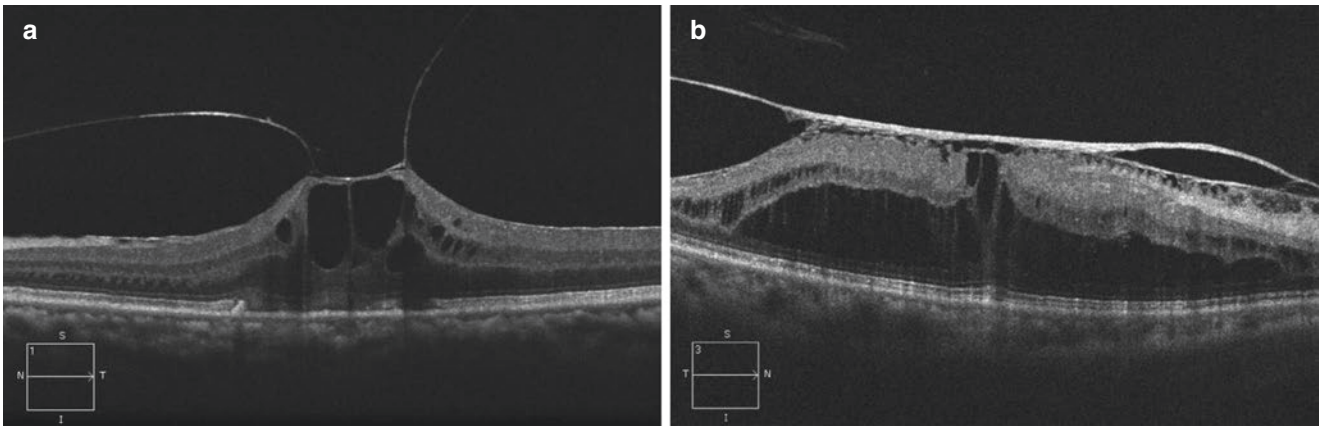

Fig. 2.4 (**a**) OCT shows distortion of foveal surface and cystoid macular edema with focal type of VMT. (**b**) OCT shows generalized thickening of the macula, macular schisis, and cystoid macular edema with broad type of VMT

of VMT in 35% (21 of 61 eyes) during a mean of 13.7 months of follow-up. These reports also suggested prognostic factors for spontaneous VMT release, including VMA diameter <400 μm and isolated inner retinal distortion.

2.4.2 Medical Therapy

Medical therapy for VMT currently includes intravitreal ocriplasmin (Jetrea; Thrombogenics, Leuven, Belgium) or intravitreal gas injection.

Intravitreal ocriplasmin injection: The enzyme ocriplasmin was approved for the treatment of symptomatic VMT in 2012 by the US Food and Drug Administration. The multicenter, randomized, double-blind, phase 3 clinical trials (MIVI-TRUST trials) revealed that the proportion of eyes with nonsurgical resolution of VMA on OCT at day 28 was significantly higher in ocriplasmin-injected group than that in placebo group (26.5% vs. 10.1%, respectively; $p < 0.001$) [2]. They also revealed that higher odds of VMT resolution were associated with younger age (<65 years), smaller adhesions (<1500 μm), phakic eyes, absence of ERM, and presence of a full-thickness MH with VMA. According to MIVI-TRUST trials, several groups have reported "real world" results using ocriplasmin ranging from a VMT release rate of 43–50% [17–19]. Therefore, ocriplasmin injection might be effective for about half of eyes with VMT if indication of treatment is closely examined.

Intravitreal gas injection: Several retrospective reports recently demonstrated that intravitreal gas injection was effective for resolution of VMT [20, 21]. Rodriguez et al. reported 60% resolution of VMT using intravitreal perfluoropropane (C_3F_8) injection. They included 15 eyes with focal VMT (size of VMA <1500 μm), without peripheral retinal degeneration that could cause retinal breaks. Steinle et al. reported 83% resolution of VMT with intravitreal C_3F_8 injection, including consecutive cases with VMT (size of VMA <400 μm). This report did not have exclusion criteria, so eyes with ERM, concurrent diabetes mellitus, or eyes previously treated with ocriplasmin without release of VMT were also included and successfully treated with C_3F_8 gas. In both the Rodriguez and the Steinle series, no case of retinal breaks or detachment was observed during follow-up periods.

2.4.3 Surgery

Pars plana vitrectomy (PPV) is the most established treatment for VMT (Fig. 2.5) [3, 22]. Moreover, in the recent era of small-gauge vitrectomy, the risk/benefit profile of PPV is more favorable with shorter operating times [23]. A systematic literature review about effectiveness of vitrectomy for VMT reported that mean logMAR visual acuity improved from 0.67 ± 0.55 to 0.42 ± 0.45 after surgery (from 20/94 to 20/53 Snellen, n = 259 eyes) [3]. Other reports regarding predictive factors after vitrectomy demonstrated that shorter symptom duration, younger age, better preoperative visual acuity, and less damage to outer retina were associated with good visual outcome [24–26]. Therefore, earlier vitrectomy seems to deliver a better result for patients with VMT. On the other hand, vitrectomy has potential disadvantages, including cost, cataract formation, endophthalmitis, and ERM formation. To prevent postoperative ERM formation, internal limiting membrane (ILM) peeling could be an optional procedure for surgeons [27, 28]. However, a recent report suggested that there was no difference in outcome between surgeries performed with and without ILM peeling [3], and ILM peeling had adverse effects, including thinning of the temporal retina and reduced retinal sensitivity [29, 30]. Therefore, whether to perform ILM peeling for eyes with VMT is now under debate.

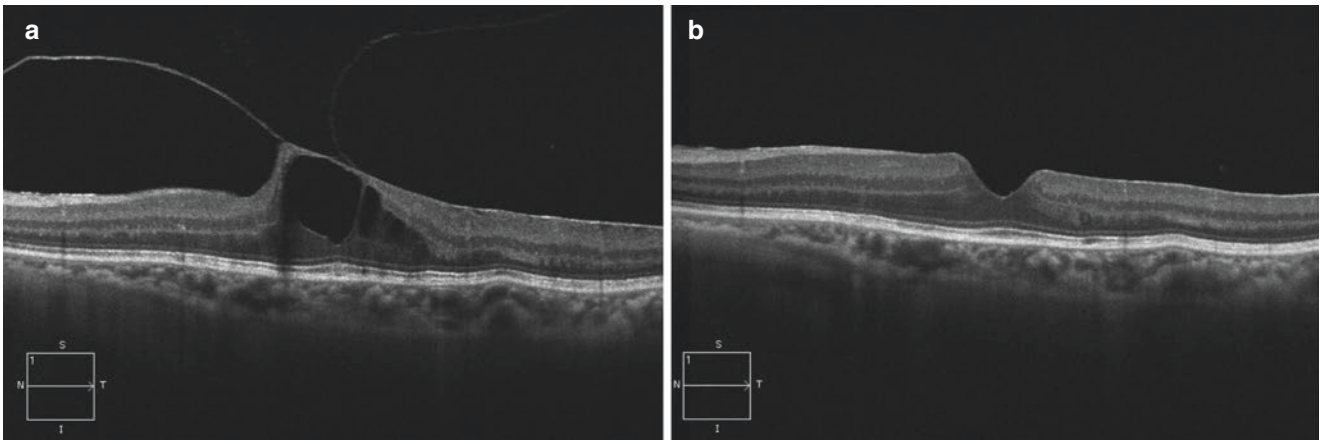

Fig. 2.5 (**a**) OCT shows cystoid macular edema and lack of foveal pit due to VMT. The best-corrected visual acuity was decreased to 12/20. (**b**) One month after vitrectomy, macular edema was completely resolved, and foveal pit was recovered. The best-corrected visual acuity was improved to 20/20

References

1. Foos RY, Wheeler NC. Vitreoretinal juncture. Synchysis senilis and posterior vitreous detachment. Ophthalmology. 1982;89:1502–12.
2. Stalmans P, Benz MS, Gandorfer A, et al. Enzymatic vitreolysis with ocriplasmin for vitreomacular traction and macular holes. N Engl J Med. 2012;367:606–15.
3. Jackson TL, Nicod E, Anglis A, et al. Pars plana vitrectomy for vitreomacular traction syndrome: a systemic review and metaanalysis of safety and efficacy. Retina. 2013;33:2012–7.
4. Tzu JH, John VJ, Flynn HW Jr, et al. Clinical course of vitreomacular traction managed initially by observation. Ophthalmic Surg Lasers Imaging. Retina. 2015;46:571–6.
5. Gaudric A, Haouchine B, Massin P, et al. Macular hole formation: new data provided by optical coherence tomography. Arch Ophthalmol 1999;117:744-51.
6. Bishop PN. Structural macromolecules and supramolecular organisation of the vitreous gel. Prog Retin Eye Res. 2000;19:323–44.
7. Sebag J. Vitreous: the resplendent enigma. Br J Ophthalmol. 2009;93:989–91.
8. Uchino E, Uemura A, Ohba N. Initial stages of posterior vitreous detachment in healthy eyes of older persons evaluated by optical coherence tomography. Arch Ophthalmol. 2001;119:1475–9.
9. Johnson MW. Posterior vitreous detachment: evolution and complications of its early stages. Am J Ophthalmol. 2010;149:371–82.
10. Sebag J. Anomalous posterior vitreous detachment: a unifying concept in vitreo-retinal disease. Graefes Arch Clin Exp Ophthalmol. 2004;242:690–8.
11. Reese AB, Jones IR, Cooper WC. Macular changes secondary to vitreous traction. Am J Ophthalmol. 1967;64:544–9.
12. Reese AB, Jones IR, Cooper WC. Vitreomacular traction syndrome confirmed histologically. Am J Ophthalmol. 1970;69:975–7.
13. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013;120:2611–9.
14. Hikichi T, Yoshida A, Trempe CL. Course of vitreomacular traction syndrome. Am J Ophthalmol. 1995;119:55–61.
15. Theodossiadis GP, Grigoropoulos VG, Theodoropoulou S, et al. Spontaneous resolution of vitreomacular traction demonstrated by spectral-domain optical coherence tomography. Am J Ophthalmol. 2014;157:842–51.
16. Almeida DR, Chin EK, Rahim K, et al. Factors associated with spontaneous release of vitreomacular traction. Retina. 2015; 35:492–7.
17. Singh RP, Li A, Bedi R, et al. Anatomical and visual outcomes following ocriplasmin treatment for symptomatic vitreomacular traction syndrome. Br J Ophthalmol. 2014;98:356–60.
18. Sharma P, Juhn A, Houston SK, et al. Efficacy of intravitreal ocriplasmin on vitreomacular traction and full-thickness macular holes. Am J Ophthalmol. 2015;159:861–7.
19. Warrow DJ, Lai MM, Patel A, et al. Treatment outcomes and spectral-domain optical coherence tomography findings of eyes with symptomatic vitreomacular adhesion treated with intravitreal ocriplasmin. Am J Ophthalmol. 2015;159:20–30.
20. Rodrigues IA, Stangos AN, McHugh DA, et al. Intravitreal injection of expansile perfluoropropane (c(3)f(8)) for the treatment of vitreomacular traction. Am J Ophthalmol. 2013;155:270–6.
21. Steinle NC, Dhoot DS, Quezada Ruiz C, et al. Treatment of vitreomacular traction with intravitreal perfluoropropane (C3f8) injection. Retina. 2017;37:643–50.
22. Chang JS, Smiddy WE. Cost evaluation of surgical and pharmaceutical options in treatment for vitreomacular adhesions and macular holes. Ophthalmology. 2014;121:1720–6.
23. Neffendorf JE, Gupta B, Williamson TH. Intraoperative complications of patients undergoing small-gauge and 20-gauge vitrectomy: a database study of 4,274 procedures. Eur J Ophthalmol. 2017;27:226–30.
24. Ichiyama Y, Kawamura H, Fujikawa M, et al. Photoreceptor outer segment length and outer foveal thickness as factors associated with visual outcome after vitrectomy for vitreomacular traction syndrome. Retina. 2016;36:1707–12.
25. Petrou P, Kontos A, Errera MH, et al. Pars plana vitrectomy for vitreomacular traction syndrome: analysing the preoperative prognostic factors. Semin Ophthalmol. 2016;9:1–5.
26. Yang CS, Hsieh MH, Chang YF, et al. Predictive factors of visual outcome for vitreomacular traction syndrome after vitrectomy. Retina. 2018;38:1533.
27. Park DW, Dugel PU, Garda J, et al. Macular pucker removal with and without internal limiting membrane peeling: pilot study. Ophthalmology. 2003;110:62–4.
28. Obata S, Fujikawa M, Iwasaki K, et al. Changes in retinal thickness after vitrectomy for epiretinal membrane with and without internal limiting membrane peeling. Ophthalmic Res. 2017;57:135–40.
29. Kumagai K, Ogino N, Furukawa M, et al. Retinal thickness after vitrectomy and internal limiting membrane peeling for macular hole and epiretinal membrane. Clin Ophthalmol. 2012;6:679–88.
30. Ripandelli G, Scarinci F, Piaggi P, et al. Macular pucker: to peel or not to peel the internal limiting membrane? A microperimetric response. Retina. 2015;35:498–507.

Macular Holes

3

Daniele Veritti, Valentina Sarao, Carla Danese, and Paolo Lanzetta

3.1 Definition

A full-thickness macular hole (FTMH) is an anatomic discontinuity of the foveal retina, involving all the neural layers between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE). Mechanical forces mainly arising from the vitreous are thought to be responsible for FTMH formation, including the development of tractional foveal cystoid space, breakdown and elevation of the external retina, and traction on the inner retina. The hole's edge is usually rounded and possibly contains intraretinal pseudocysts. Intraretinal fluid can accumulate, leading to edge thickening and elevation from the RPE plane. Vitreous can be either attached or separated from the hole's edge. A FTMH is usually easily diagnosed via multiple optical coherence tomography (OCT) foveal B-scans, even though in many cases just a single B-scan is sufficient. As far as shape is concerned, the OCT scans usually show an hourglass shape, varying depending on OCT scan orientation (Fig. 3.1). If the defect involves the retinal thickness only partially, this condition is named lamellar macular hole (LMH). A macular pseudohole, instead, is a circle- or oval-shaped lesion in the presence of an epiretinal membrane, which clinically mimics the appearance of a FTMH [1, 2].

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3.2 Epidemiology

Population studies report that 1.5% of the general population presents ocular pathologies associated with symptomatic vitreomacular adhesion (VMA). FTMHs occur more frequently in people older than 65, with a prevalence ranging from 0%, in people aged between 43 and 54 years, to 0.8%, and in patients older than 75 years, with an age- and sex-adjusted incidence of 8.5 cases per 100,000 people per year. A peak incidence is observed in women (72%) and in people aged between 65 and 74 years, while people less than 50 years old account for only 3% of all FTMHs. FTMHs are unilateral at diagnosis in more than 80% of the cases. Even though studies have been conducted in order to associate systemic risk factors to this demographic distribution, they ended up to be inconclusive, with some exception: elevated plasma fibrinogen increases the risk, which, on the opposite, decreases in women taking estrogen replacement therapy. The risk is more elevated in patients with severe myopia, reaching 6% in eyes between −14 and −32 diopters. There is a 15.6% risk of developing a FTMH in the fellow eye within 5 years, 17% within 10 years. This percentage falls to less than 2% when the fellow eye presents a complete posterior vitreous detachment (PVD) [3, 4].

3.3 Classification

The first classification of macular holes, realized by Gass, dates back to the 1990s. It categorizes macular holes according to their clinical appearance. This now seems to be obsolete, since the wide usage of OCT has provided a large amount of anatomic data, which is very useful to better understand the pathogenesis and progression of FTMHs. The International Vitreomacular Traction Study Group has therefore realized a new classification, considering different parameters, such as hole's size, eventual vitreomacular traction, and etiology [1, 5].

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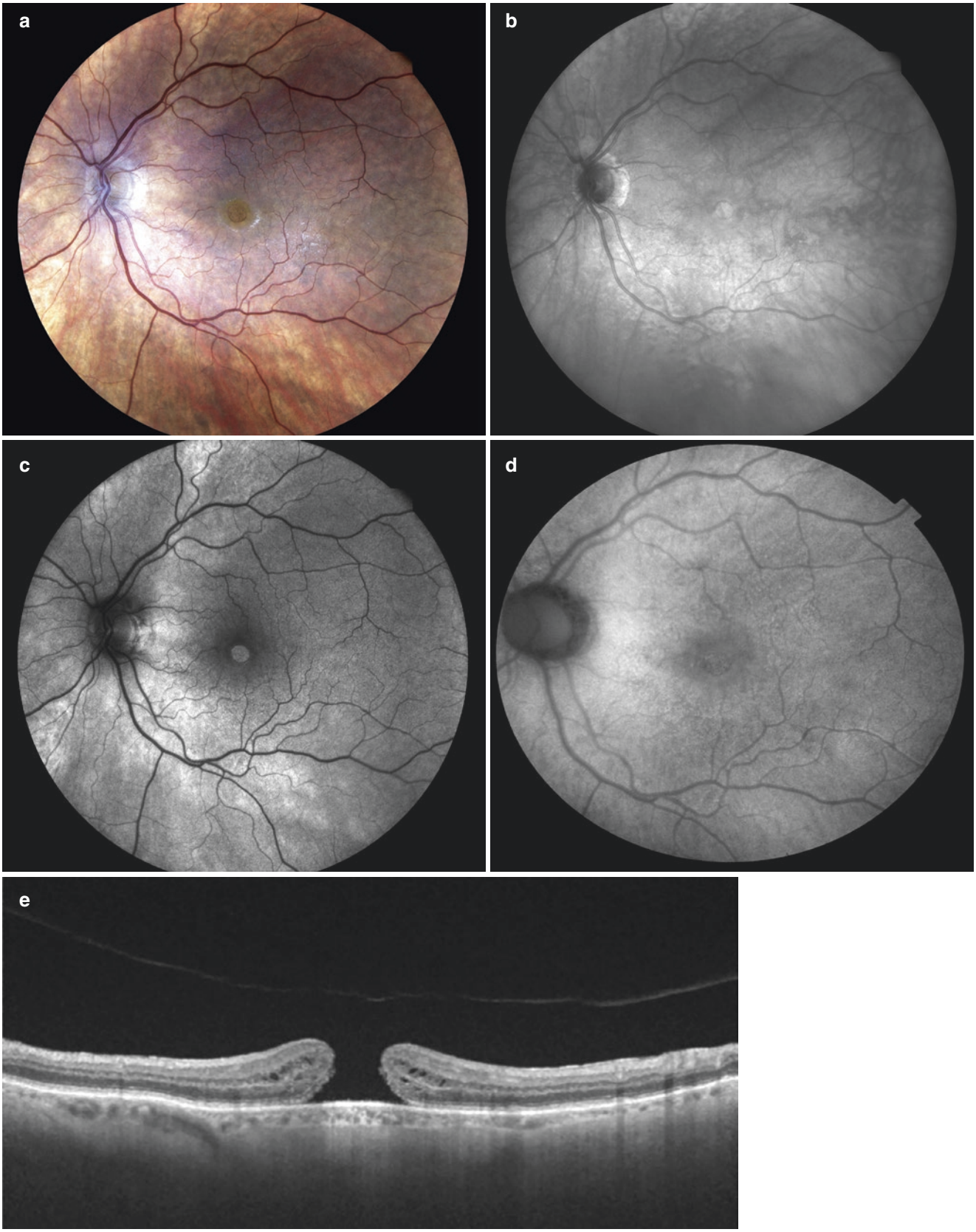

Fig. 3.1 A typical case of full-thickness macular hole as it appears at true-color fundus image (**a**), infrared (**b**), blue autofluorescence (**c**), green autofluorescence (**d**), swept-source optical coherence tomography (**e**)

3.3.1 Gass Classification

In 1988 Gass realized a biomicroscopic classification of idiopathic age-related macular holes, which he subsequently modified according to a more accurate anatomical description [6].

- Stage 1: includes modifications of the vitreoretinal interface and of the foveal neuroepithelium, which will lead to FTMH formation. There are two subgroups:
  - Stage 1a: a foveal yellow spot is visible ophthalmoscopically, associated with loss of physiological foveal depression, in absence of a complete PVD.
  - Stage 1b: the yellow spot evolves in a yellowish, ring-shaped reflex, associated with horizontalization of the foveal profile, corresponding to a foveolar serous detachment with marginal dislocation of the xantophyll.
- Stage 2: a rupture in the roof of the foveolar serous detachment, made of thin retinal tissue, leads to FTMH formation.
- Stage 3: the hole becomes bigger than 400 μm, and it is associated with persistence of vitreoretinal adhesions generated by the PVD.
- Stage 4: this stage includes holes larger than 400 μm, which are associated with complete resolution of the VMAs.

Even though Gass classification takes into account only ophthalmoscopic parameters, it correlates well with the morphological features recently highlighted by OCT and autofluorescence. Also the treatment choice has been guided by this classification until recently. Stage 1 holes required observation and serial evaluations every 4–6 months, while in stage 2, options were a strict follow-up or surgical intervention; vitrectomy was the only viable strategy for stage 3 and 4 holes.

3.3.2 International Vitreomacular Traction Study Group Classification

3.3.2.1 Vitreomacular Adhesion and Vitreomacular Traction

Reese, based on histological studies, was the first to describe an abnormal macular traction exerted by a PVD on the macular tissue, thus providing the first description of vitreomacular traction (VMT) [7]. The new classification includes not only macular holes but also VMA and VMT, since they all are closely related vitreomacular diseases. VMA is defined as a perifoveal vitreous separation with remaining vitreomacular attachment and unperturbed foveal morphology, while VMT is characterized by anomalous vitreous detachment accompanied by anatomic foveal distortion, including pseudocysts, macular schisis, cystoid macular edema, and subretinal fluid [1, 8].

Increasing VMA width is associated with a decreased tractional force, thus leading to reduced foveal deformation. Indeed, small and focal foveal adhesions, i.e., less than 500 μm, exert high tractional forces, causing macular hole formation, foveal inner retinal cavitations, and foveal retinal detachment, while larger vitreoretinal adhesions typically lead to a generalized foveal profile flattening, being also associated with ERM development and retinal thickening. The differentiation between VMA and VMT is guided by clinical symptoms, such as visual loss, blurred vision, and metamorphopsia. It must be noted that some cases of VMT do not determine visual impairment. Specifically, the presence of symptoms together with OCT alterations suggests the progression from VMA to VMT. The OCT criteria needed to classify an eye as having a VMT are:

- Partial perifoveal vitreous cortex separation from the retinal surface.
- Macular attachment of the vitreous cortex within a 3-mm radius of the fovea.
- Distortion of the foveal surface, intraretinal structural changes, foveal elevation above the RPE, or a combination thereof, but no full-thickness interruption of all retinal layers.

Many VMTs are complicated by the development of an ERM 10–20 μm thick, during the early perifoveal stages of PVD. If the VMT is associated with visual loss, a condition named vitreomacular traction syndrome is present.

VMT may determine the occurrence of macular edema, due to a dynamic traction caused by ocular movements and elastic tractional forces, exerted by posterior vitreous cortex, specifically macular stretching. Tractional cystoid macular edema, characterized by metamorphopsia and mild asymmetry of the foveal thickening, may be considered as a variant of symptomatic VMT.

Finally, in the complex pathogenesis of a macular hole, VMT plays an important role, since it represents a strong risk factor not only for contralateral FTMH development but also for maintenance of the hole itself.

As to the classification, VMAs and VMTs can be differentiated as follows:

- Focal: adhesion area ≤1500 μm
- Extended: adhesion area <1500 μm, parallel to the RPE and eventually associated with dehiscence areas
- Isolated
- With concurrent retinal conditions

3.3.2.2 Full-Thickness Macular Hole

Macular Hole Size

The OCT-based measurements of minimum hole width—i.e., aperture size—represent a valid treatment guidance. OCT devices are provided with a caliper function, which allows measurement of the minimum hole width.

Three categories can therefore be distinguished:

- Small FTMHs—aperture size smaller than 250 μm. They are associated with a small chance of spontaneous closure, while the closure rate after vitrectomy approaches 100%. This subtype appears to be the most responsive to pharmacologic vitreolysis (Fig. 3.2).
- Medium FTMHs—aperture size from 250 to 400 μm. More than 90% of these holes close after vitrectomy when a complete removal of residual hyaloid is performed, with or without ILM peeling. The results of pharmacological therapy, instead, are less satisfying than in small FTMHs (Fig. 3.3).
- Large FTMHs—aperture size larger than 400 μm. This group accounts for nearly half of all FTMHs. A 90–95% closure rate can be achieved after vitrectomy with ILM peeling. Pharmacologic vitreolysis has little success in these cases (Fig. 3.4).

Macular Holes Associated with Vitreomacular Traction

It is important to understand if FTMHs are associated with VMT, since pharmacologic vitreolysis is viable only in case of concurrent VMT. Around 55% of patients with a FTMH present with a VMT at the hole edge.

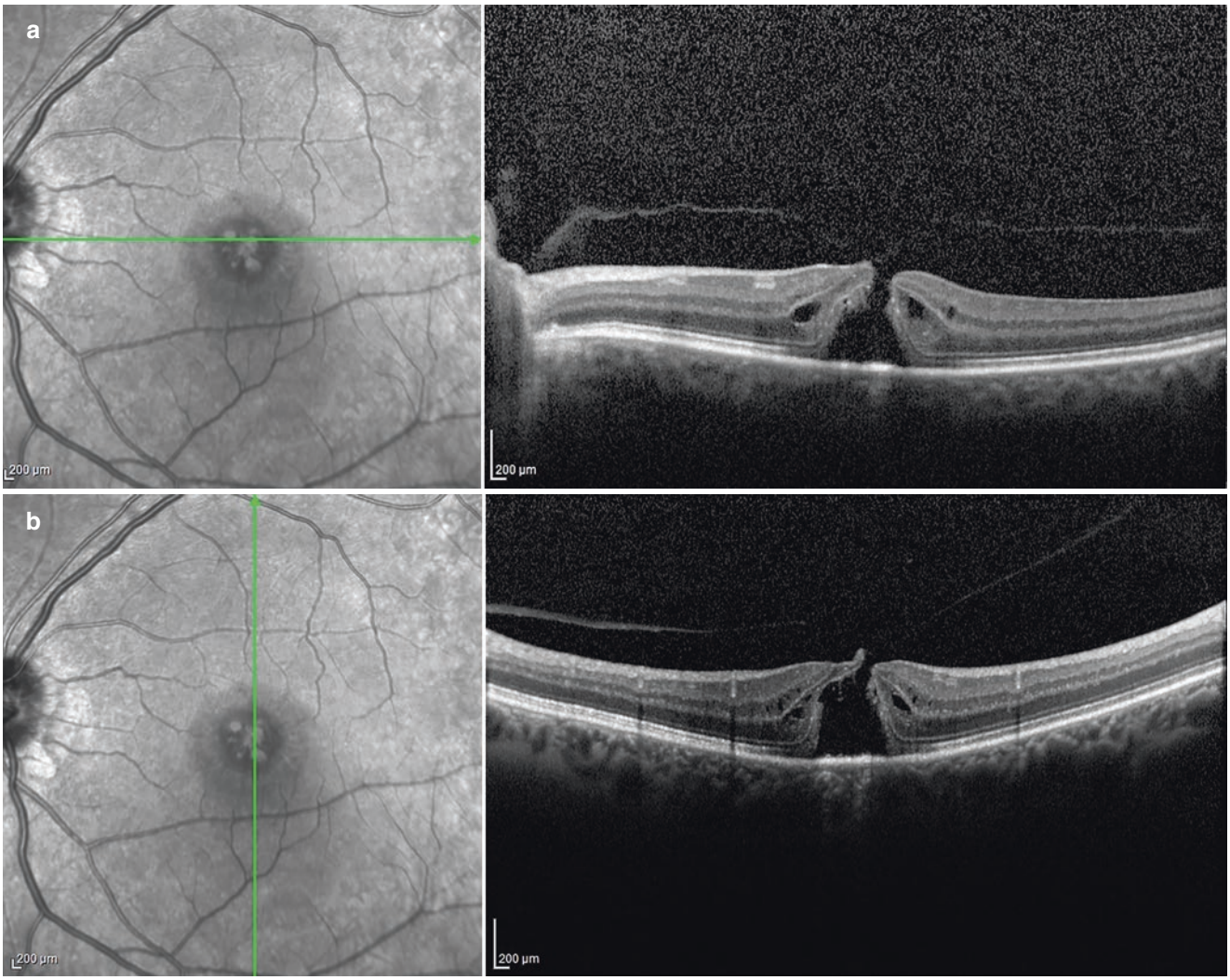

Fig. 3.2 A case of small full-thickness macular hole with vitreomacular traction. Spectralis optical coherence tomography (OCT) horizontal scan (**a**) and vertical scan (**b**) shows a full-thickness macular hole inferior to 250 μm with intraretinal fluid and a foveal traction on its edge due to an incomplete posterior vitreous detachment. Green line corresponds with level of OCT image

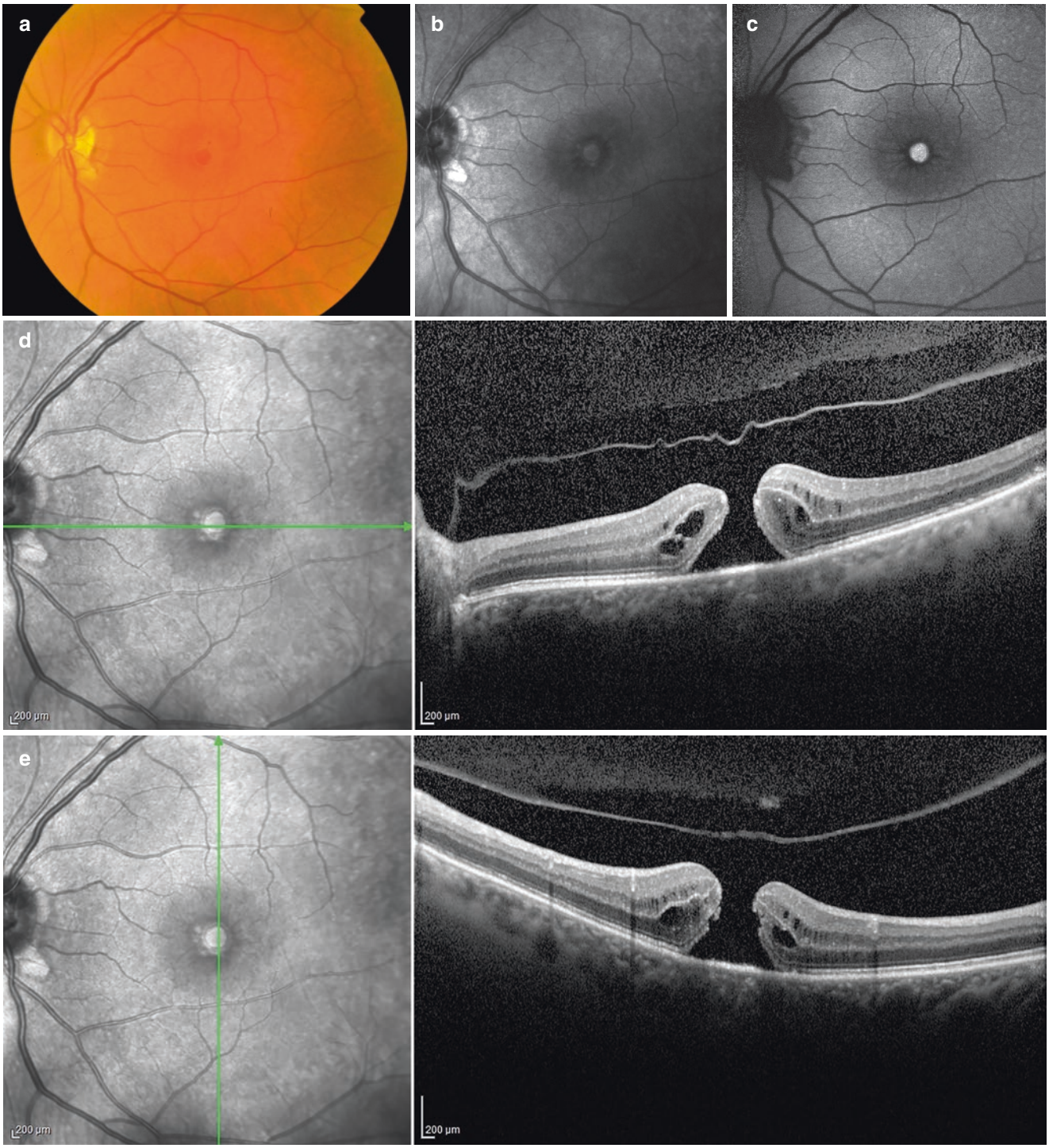

Fig. 3.3 A case of medium full-thickness macular hole without vitreomacular traction. Color fundus (**a**) reveals a well-defined roundish defect at the foveal region. Infrared reflectance imaging (**b**) shows an hyper-reflective foveal area surrounded by an hypo-reflective ring. Blue light autofluorescence (**c**) reveals an increased autofluorescent signal corresponding to the macular hole surrounded by a halo of hypo-autofluorescence. Spectralis optical coherence tomography (OCT) horizontal scan (**d**) and vertical scan (**e**) confirms a full-thickness macular hole with a diameter ranging between 250 and 400 µm with intraretinal cysts. The presence of a complete posterior vitreous detachment is clearly visible on OCT. Green line corresponds with level of OCT image

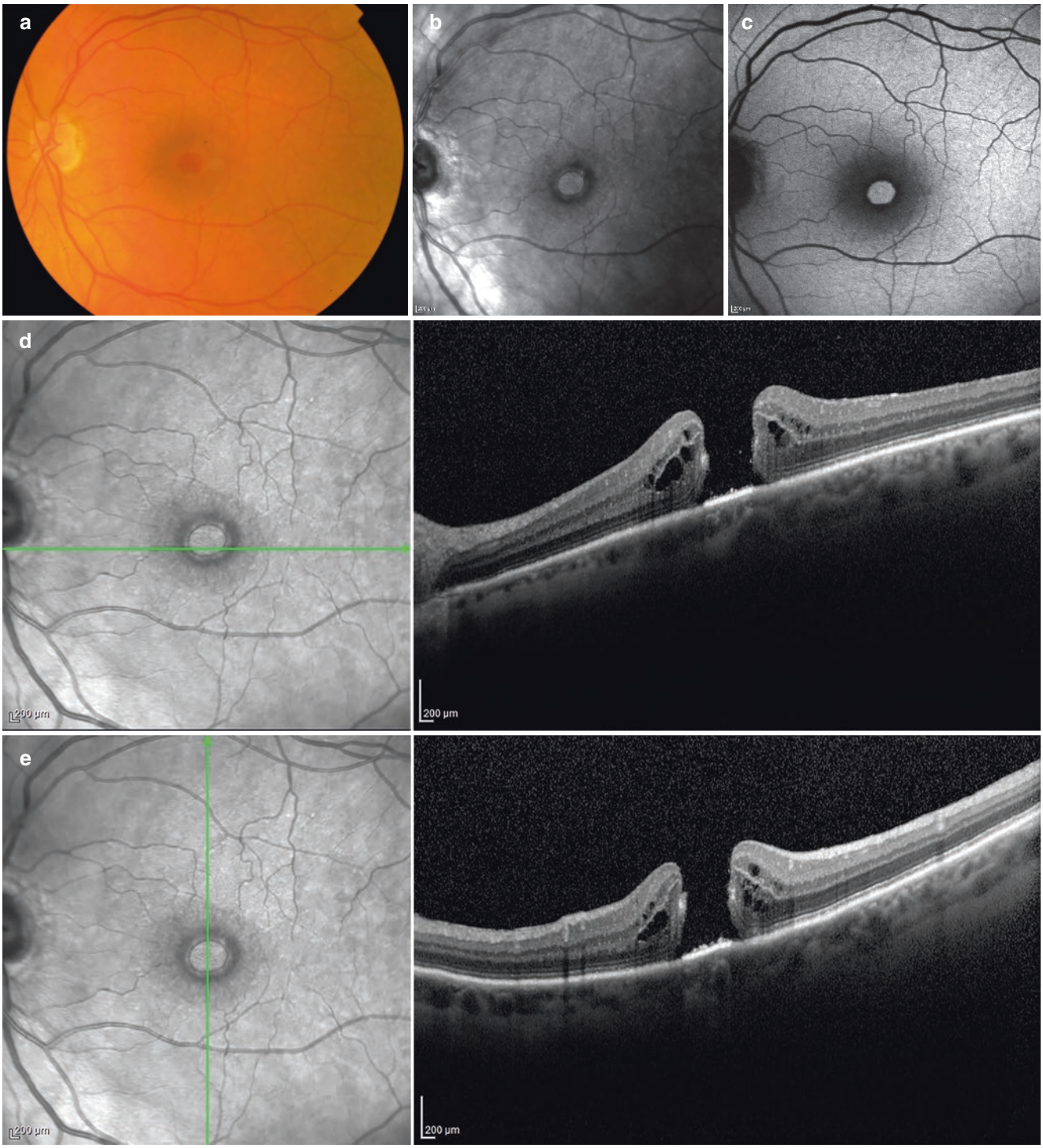

Fig. 3.4 A case of large full-thickness macular hole. Color fundus (**a**) reveals a single, round, well-circumscribed reddish lesion located over the fovea. Infrared reflectance imaging (**b**) shows a normal reflective small foveal area surrounded by hyper- and hypo-reflective zone. Blue light autofluorescence (**c**) reveals a foveal hyper-autofluorescence surrounded by a ring of hypo-autofluorescence. Spectralis optical coherence tomography (OCT) horizontal scan (**d**) and vertical scan (**e**) confirms a full-thickness macular defect with a diameter ranging superior to 400 µm with intraretinal cysts at the edges of the hole. Green line corresponds with level of OCT image

Etiology

FTMHs can be differentiated between primary and secondary forms.

- Primary FTMHs (formerly referred to as "idiopathic") are caused by vitreous traction on the fovea, due to an anomalous PVD. In some cases, patients with high myopia present a VMT, precursive of a FTMH.
- Secondary FTMHs are not associated with VMT. They are, instead, caused by other pathologic conditions, such as blunt trauma, lightning strike, high myopia, macular schisis, type 2 macular telangiectasia, wet age-related macular degeneration, and macroaneurysms. Among secondary FTMHs, those occurring immediately after surgical procedures—such as vitrectomy for retinal detachment—must be mentioned, these probably being caused by traction-induced damage to the inner fovea, leading to foveal destabilization, before or coincident with spontaneous vitreofoveal separation.

In some cases, FTMHs are concomitant with macular edema associated with various other diseases, such as diabetic macular edema, age-related macular degeneration, retinal vascular occlusions, and uveitis [1].

3.3.2.3 Impending Macular Hole

Previously referred to as "stage 0 macular hole," this definition indicates a patient with a FTMH in one eye and VMA or VMT, demonstrated via OCT, in the fellow eye, which is therefore at risk of developing a FTMH, although there are also chances of spontaneous traction/adhesion resolution.

3.3.2.4 Lamellar Macular Hole

A LMH is a partial-thickness foveal defect, visible at biomicroscopy as a round or oval, reddish, well-circumscribed lesion (Fig. 3.5). OCT is very useful in detecting LMH, since the diagnosis can be difficult using biomicroscopy alone. The tomographic findings are:

- An irregular foveal contour.
- A defect in the inner retina, with intact outer retina and a near-normal perifoveal retinal thickness.
- Intraretinal schisis, usually between the outer plexiform and outer nuclear layers.
- Intact photoreceptor layer. This is the main feature differentiating a LMH from a FTMH.

Detailed knowledge regarding the natural history and surgical indication for LMHs is still lacking. It is thought that the progression is slow and either incomplete FTMH formation or an ERM exerting centripetal traction or both may represent the causative process. In addition, varying anteroposterior and tangential forces from the vitreous may play a role.

A LMH usually determines mild metamorphopsia and limited central vision loss. A deterioration in reading vision is usually caused by the progression of an associated ERM. LMHs may be associated with myopia, uveitis, exudative age-related macular degeneration, and retinal detachment, and they are also being described following cataract surgery. Concerning treatment, surgical indication for LMH remains controversial: between 25% and 75% of patients undergoing vitrectomy experience an improvement in visual acuity, which is mainly due to the associated ERM peeling. Further studies are needed in order to define adequate guidelines [9].

3.3.2.5 Macular Pseudohole

Macular pseudohole is a discrete, reddish, round or oval foveal lesion, with a diameter between 200 and 400 μm, mimicking the biomicroscopic aspect of a FTMH, thus deserving the definition of pseudohole. In these situations, an OCT scan with multiple foveal lines is required to rule out a FTMH, showing no loss of foveal tissue and a normal or slightly reduced central foveal thickness.

The OCT features defining a macular pseudohole are the following:

- Invaginated or heaped foveal edges
- Concomitant ERM with central opening
- Steep macular contour to the central fovea with near-normal central foveal thickness
- No loss of retinal tissue

The most relevant characteristic of a macular pseudohole is the etiological role of a coexisting macular ERM, which contracts and therefore pulls the underlying retinal tissue toward the foveal center, thus causing an invagination of the perifoveal retina into a shape mimicking a hole and altering the light reflex, without any actual loss of foveal tissue. The neurosensory retina is thickened but intact, with thickened foveal edges of a steep foveal pit of small diameter (Fig. 3.6).

The management of a macular pseudohole is usually conservative, a vitrectomy with membrane peeling being needed only when the ERM determines a significant visual loss [10].

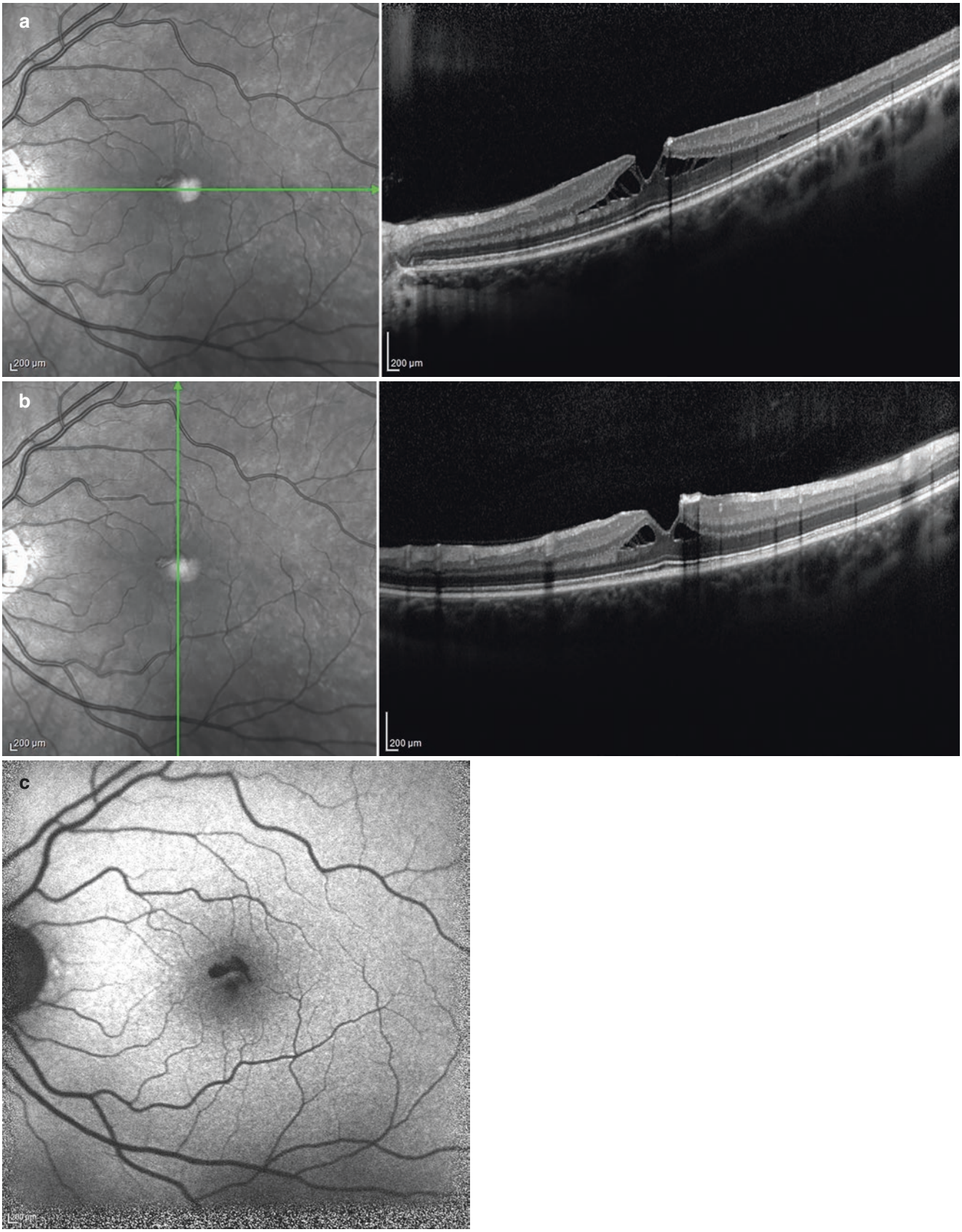

Fig. 3.5 A case of lamellar macular hole. Spectralis optical coherence tomography (OCT) horizontal scan (**a**) and vertical scan (**b**) shows an irregularity in the foveal contour, defects in the inner retina, and thinning of the retina at the base of the fovea without a full-thickness defect. An intraretinal schisis is clearly visible. Please note the presence of epiretinal membrane superiorly at the fovea that appears as an hyper-reflective signal on OCT. Blue autofluorescence (**c**) reveals an hyper-autofluorescence due to loss of foveal tissue and a decrease of autofluorescence signal corresponding to the epiretinal membrane

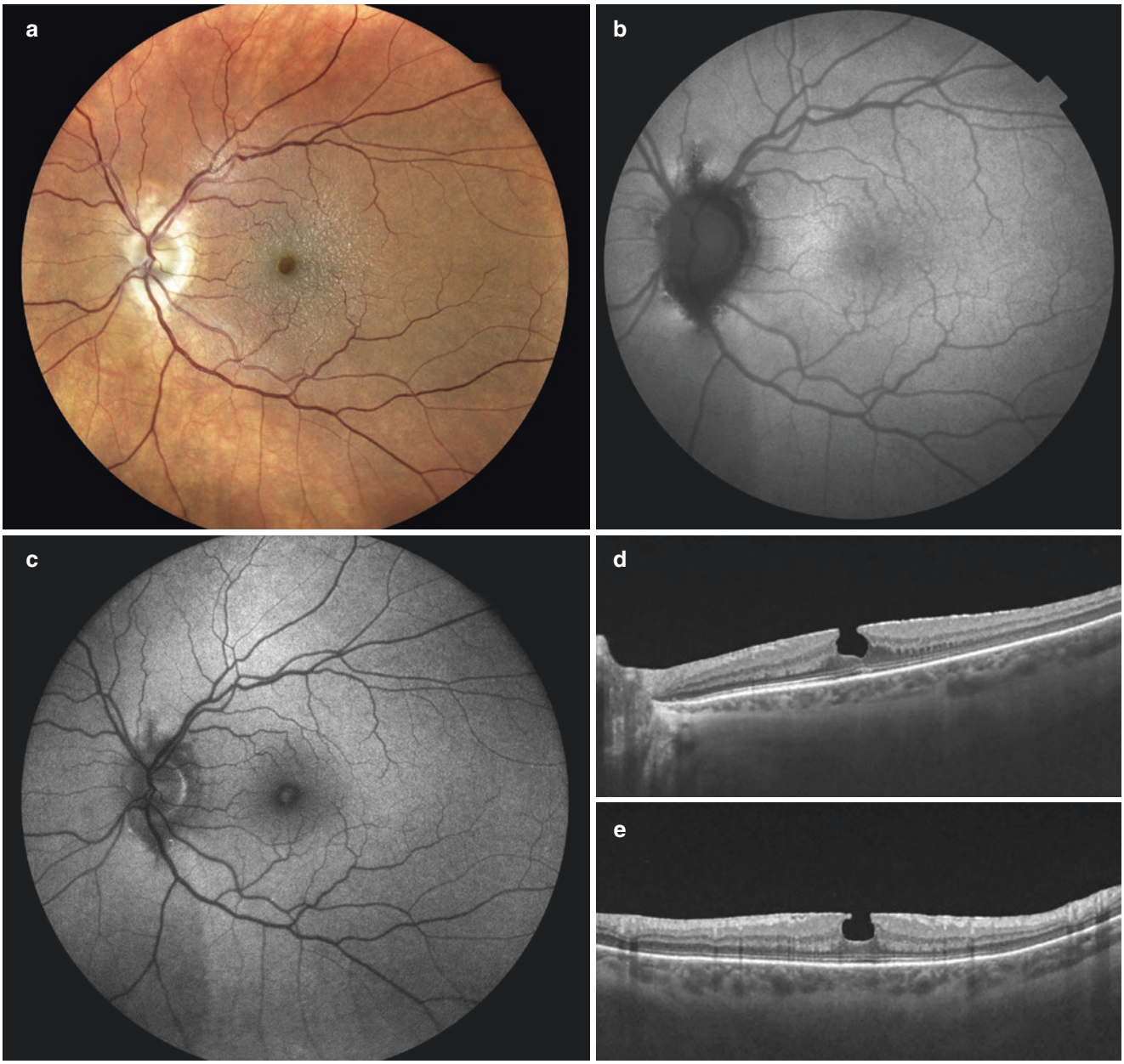

Fig. 3.6 A case of macular pseudohole. True-color image (**a**) clearly shows a single, round, well-circumscribed reddish lesion located over the fovea. Please note a wrinkling of the retinal surface at the posterior pole consistent with epiretinal membrane. Compared with green autofluorescence (**b**), blue autofluorescence (**c**) shows an increased autofluorescent signal corresponding to the macular hole. A halo of hypo-autofluorescence surrounding the hole is clearly visible, and it could be due to the displacement of macular pigment at the edge of the hole. The presence of macular pseudohole was confirmed by swept-source optical coherence tomography horizontal (**d**) and vertical scan (**e**), which reveals an irregular foveal contour characterized by a break of the inner retinal layers but leaving intact the photoreceptors in foveal region. The presence of epiretinal membrane is confirmed by the detection of an highly reflective layer on the surface of the retina

3.4 Pathophysiology

Historically, the first description of a macular hole dates back to 1869, when Knapp documented a FTMH in a patient who had sustained a blunt trauma to the eye. Therefore, at first, macular holes were considered etiologically related to episodes of ocular trauma. However, it is now recognized that traumas account only for less than 10% of all macular holes, while more than 80% are idiopathic.

Gass first reported the potential pathogenesis of primary macular holes based on biomicroscopic findings, hypothesizing the role of a tangential traction exerted by the perifoveal vitreous cortex, resulting in a foveal dehiscence progressing from foveolar detachment to a FTMH.

Later on, the wide usage of OCT imaging has made clear that the pathogenetic process of FTMHs starts during perifoveal PVD, as a consequence of anteroposterior, dynamic VMT.

The anterior tractional forces on the foveola firstly determine an intrafoveal split, which evolves into a foveal pseudocyst, which subsequently extends, disrupting and separating the outer retinal layers and then raising into the inner layers. Moreover, these tractional forces also cause degeneration of the retinal tissue, which facilitates the entire process. Afterward, dehiscence of the foveal cyst creates a full-thickness defect, involving also the IS/OS junction of the photoreceptor layer. An operculum—visible within the vitreous gel—is also formed, being the completely detached cyst roof, made of glial tissue, hyperplastic Muller cells from inner retinal surface, and components of the outer retina, such as cone cells, in an up to 65% of cases [4, 8].

3.5 Natural History and Clinical Features

A macular hole usually evolves over a period of weeks to months, but in some cases, the development may also be more abrupt. The diagnosis is typically made when a sudden change in patient's symptoms is noticed. Visual dysfunction in patients with a macular hole is directly related to the absence of retinal tissue in the fovea. Additionally, it may also be related to the presence of a cuff of subretinal fluid with associated photoreceptor atrophy. FTMHs are associated with significantly reduced visual acuity—inversely related to the size of the hole—metamorphopsia, loss of central vision with a central scotoma. It must be noted that the prognosis of untreated FTMHs is poor, resulting in a progressive worsening of visual acuity over time, falling between 20/100 and 20/400, and then stabilizing with a good peripheral vision. If, instead, a FTMH closes spontaneously, visual acuity may noticeably improve. A small FTMH may repair itself after complete PVD has occurred, via proliferation of retinal glial cells. However, if this repair mechanism fails, the glial cell migration at the edge of the hole can progressively contract, determining the enlargement of the hole itself. Moreover, the edge may elevate due to the presence of a cuff of subretinal fluid, with eventual association of neurosensory retinal tissue thickening [4, 5].

3.5.1 The Fellow Eye

Fellow eyes are at higher risk of developing a macular hole, in absence of PVD. Thus, since macular holes are not by any means preventable, an early diagnosis is crucial, since it appears to be associated with both a higher closure rate after vitrectomy and better postoperative visual acuity. Therefore, in order to achieve the earliest diagnosis possible, not only the fellow eye must be carefully examined, but also the patient has to be carefully instructed about warning signs, such as metamorphopsia and mild decrease in central visual acuity. OCT scans are useful to identify at-risk eyes, characterized by vitreous traction at or near the center of the macula [11].

3.6 Diagnosis

When evaluating a patient who may have a FTMH, some conditions, such as central serous retinopathy, subfoveolar drusen, and solar maculopathy, must be taken into account and excluded [4]. The patient's history thus appears to be fundamental, especially regarding:

- Duration of symptoms
- Ocular history: glaucoma, retinal detachment or retinal tear, traumas, ocular surgery, sun, or eclipse gazing
- Medications associated with macular cystoid edema, such as systemic niacin, topical prostaglandin analogues

3.6.1 Slit-Lamp Examination

At fundus examination, FTMH can present the following features: fine, drusen-like yellow deposits in the hole base, a surrounding cuff of subretinal fluid, a distinct circular margin around the hole, and an operculum—appearing as a small round opacity suspended within the vitreous above the fovea. At first, the retinal pigment epithelium appears normal, while chronic changes, such as atrophy and hyperplasia, may appear over time. The additional presence of an overlying epiretinal membrane causes a fine crinkling of the inner retinal surface or even a distortion of the hole itself [4].

3.6.2 Diagnostic Tests

3.6.2.1 Watzke-Allen Test

The Watzke-Allen test is performed at the slit lamp, directing a narrow vertical and horizontal slit through the fovea. If the patient detects a break in the light due to the lack of retinal tissue in the hole region, the test is positive. The perception of a narrowing or of a distortion of the bar of light is not diagnostic of a macular hole and must be carefully interpreted.

3.6.2.2 Laser Aiming Beam Test

It is similar to the Watzke-Allen test. A small, 50-μm spot-size laser aiming beam is placed within the lesion. The test results positive when the patient cannot detect the aiming beam.

3.6.2.3 Amsler Grid

It usually shows a non-specific central distortion, rather than a scotoma. Bowing of the lines and micropsia are frequent, mainly due to the presence of retinal edema and intraretinal cysts surrounding the hole.

3.6.3 Imaging

3.6.3.1 Optical Coherence Tomography

OCT is the most accurate technique for visualizing the vitreoretinal interface, thus identifying VMTs and FTMHs. This technology has experienced significant improvements in the recent years, with the introduction of spectral domain and swept-source technology. New generation OCTs can provide 5-μm axial resolution images, with reduced artifacts. It is therefore possible to visualize VMTs, ERMs, retinal distortion, and macular detachment. In the case a VMT is present, horizontal and vertical vitreous adhesions and foveal cavitation can be accurately studied. Moreover, a differentiation between VMT-associated pseudocysts and cystoid macular edema is also achievable.

As discussed in the previous paragraph, OCT is fundamental for FTMH staging, thanks to accurate visualization of foveal anatomy, including intraretinal cavitation, thus identifying changes associated with impending macular holes and allowing an early intervention. Many measurements of the macular hole can also be taken, such as base width, minimum and maximum linear diameter, and macular hole height. Moreover, a differential diagnosis between FTMH, pseudohole, and lamellar macular hole is possible.

It is important to underline that it is fundamental to choose the correct OCT scanning protocol, in order to avoid to underestimate the FTMH size, or even missing areas of focal vitreous attachment or full-thickness retinal defects. Therefore, the lowest line spacing protocol available or a radial pattern scan through the fovea should be used.

Considering all the described features, it is important to use OCT imaging for observation of lesions over time and for follow-up after treatment. Some positive prognostic features may be assessed as well, such as the structural integrity of the photoreceptors at the IS/OS junction defect, ELM integrity, and outer diameter of the foveal defect before and after intervention. Additionally, preoperative base diameter, inner opening diameter, and minimum linear diameter can predict the post-vitrectomy outcomes [4].

3.6.3.2 Fluorescein Angiography

A FTMH determines an early well-defined window defect, due to xantophyll displacement and possible RPE atrophy, not expanding with time, while the surrounding subretinal fluid and displaced macular pigments can be seen as a hyperfluorescent halo in late frames. The arteriovenous phase of the angiogram best demonstrates a granular hyperfluorescent window, associated with the overlying pigment layer changes. Fluorescein angiography (FA) is useful when other pathologies are suspected, such as choroidal neovascularization, parafoveal telangiectasia, or clinically occult retinal vein occlusion [4].

3.6.3.3 B-Scan Ultrasonography

B-scan ultrasonography used to be useful for the study of the vitreomacular interface, since it allows visualization of early-stage PVDs and it may allow an easier distinction between a FTMH and an idiopathic macular pucker secondary to an ERM, presenting with a complete PVD and Weiss ring. Nowadays, OCT represents a much more accurate imaging tool [4].

3.6.3.4 Fundus Autofluorescence

FTMH appears on fundus autofluorescence (FAF) as an hyper-autofluorescent area, corresponding to the hole area. Because the macular pigments absorbing the blue light are absent, the light reaches directly the lipofuscin within the RPE appearing pathologically hyper-autofluorescent. An hypo-autofluorescent ring may surround the lesion due to retinal thickening. Hyper-autofluorescence typically resolves upon anatomic hole closure.

3.6.3.5 Fundus Photography

Fundus photography can highlight an eventual ERM, associated with vascular distortion or macular pseudohole, especially when using red-free or blue-reflectance technology.

3.7 Prognosis and Treatment

For a long time, macular holes were regarded as an incurable disease, until Kelly and Wendel reported that visual acuity could be stabilized—or even improved—after vitrectomy and intraocular gas tamponade, thus relieving tangential traction on the macula, reducing the cystic changes, and reattaching the cuff of detached retina surrounding the hole.

In the early days of macular hole surgery, patients were instructed to maintain a prone position up to 14 days, to achieve the best possible outcomes, while nowadays the most recent studies report excellent results with a face-down positioning of 1–3 days [8, 12].

Although there is no general consensus about the management of VMTs, some recommendations can be made:

- Patients should be observed for 2–3 months, since an eventual spontaneous release may occur, even though this depends on symptoms severity and impact on the patient's life quality.
- In case of no resolution, ocriplasmin treatment should be taken into account, considering factors such as VMA width, eventual ERM presence, status of the lens, and patient age.
- Surgery is recommended in case of significant ERM.

As far as FTMHs are concerned, instead, current recommendations are:

- Early treatment is indicated, especially if symptoms are significantly affecting life quality.
- Ocriplasmin is a viable treatment if the diameter of the hole is less than 400 μm, and there is an associated VMT. Some patient-related variables must also be considered, such as systemic morbidity, VMA width, eventual ERM presence, status of the lens, and patient age.
- If 1 month after ocriplasmin injection the hole is still open, vitrectomy should be performed.
- Surgery is the option of choice if the hole is bigger than 400 μm in diameter and VMT is not present. In this setting, ILM peeling—using the minimum effective amount of dye—gas tamponade, and face-down posturing improve results. Simultaneous cataract surgery can be performed, especially if the patient is older than 60.

3.7.1 Observation

Some patients with VMA and VMT may have foveal cysts, possibly resolving completely without any treatment. In these cases, visual acuity may improve when the posterior vitreous completely detaches from the central macula. Only 50% of VMAs and VMTs evolve to FTMHs, while in the other 50% of cases, a complete PVD occurs, therefore leading to a normalization of the appearance of the fovea. As a consequence, cautious observation of VMAs and VMTs is recommended, using OCT imaging to monitor eventual changes. The spontaneous detachment of the vitreous often determines a rapid improvement in visual symptoms.

There is a remote chance of a spontaneous resolution of a FTMH, especially if the hole is small, with a subsequent visual benefit which depends from duration and size of the hole itself. Even though in the majority of cases no treatment is needed for spontaneously healed holes, vitrectomy with ERM peeling is sometimes indicated [13].

3.7.2 Treatment

When a VMT is associated with a FTMH, not only further vision loss is described in absence of treatment but also the success rate falls because of the eventual development of an ERM [12].

3.7.2.1 Vitrectomy

Surgery is recommended for every FTMH associated with VMT, even if the hole is small or medium, since visual acuity results are good and it prevents further visual loss, avoiding progression to a bigger hole. It is usually performed under local anesthesia. Indications for surgical repair of macular holes are based on the presence of a full-thickness defect, since once it has developed, the potential for spontaneous resolution is low. At present, the anatomic success rate of vitrectomy ranges between 82% and 100%, depending on the case series. The surgical technique consists in a standard three-port pars plana small gauge vitrectomy. The main goal is the separation of the posterior cortical hyaloid from the retinal surface, with the eventual aid of triamcinolone acetonide staining to highlight the posterior vitreous. These eyes are prone to the development of retinal breaks. Therefore, an examination of the peripheral retina must always be conducted. Moreover, if there is marked traction and the OCT shows a highly elevated flap, traction in that direction must be avoided, since it may determine further enlargement of the hole during posterior hyaloid separation.

In order to achieve postoperative anatomic closure of the hole, several tamponade agents may be used, with different effect duration:

- Air: days
- SF_6 gas: from 2 to 4 weeks
- C_3F_8 gas: from 1 to 3 months
- Silicone oil: long-term closure

There is no consensus regarding the best tamponade agent. One study has reported 98% closure rate when using SF_6. When gas tamponade is used, patients must be instructed to maintain a face-down prone position. However, the optimal tamponade duration is debated. One week face-down positioning is optimal, while some surgeons advocate 1–3 days or even none. Even though there is no consensus, a longer face-down positioning may be needed in case of large holes—i.e., diameter more than 400 μm. In some studies, early postoperative OCT is used to monitor the progression of the hole closure, the findings being used to curtail positioning. In any case, the patient needs to avoid any position requiring the head tilting up. Even though anatomic and visual results seem to be better with gas tamponade, silicone oil may be useful for patients who are not able to position face-down. When using silicone, the

need for a second operation for silicone oil removal must be taken into account.

Generally, the highest closure rates are reported with the association of air tamponade and ILM peeling. The ILM, indeed, acts as a scaffold for cellular proliferation or attachment of contractile tissue elements, resulting in persistent VMT. On the other hand, detrimental effects may be generated by the loss of its structural role or secondary collateral nerve fiber layer loss. There is no consensus regarding the best peeling technique: some surgeons do not use dyes, while others prefer to optimize ILM visualization with vital dyes [14]. Recently, the inverted flap technique has been proposed for treating large FTMHs. In this technique, after core vitrectomy and dye staining, the ILM is not completely removed from the retina, but it is left in place, attached to the edges of the MH. This ILM remnant is then inverted to cover and fill the MH. It is supposed that inverted ILM, containing Müller cell fragments, may induce glial cell proliferation, filling the MH and supporting MH closure, acting as a scaffold for tissue proliferation [15].

Surgical Outcomes

The studies conducted to investigate the outcomes of vitrectomy for the treatment of FTMHs are coherent, estimating a closure rate after surgery between 91% and 98%, with a median postoperative visual acuity of 20/40. The success rate is highest for holes lasting less than 6 months, while it falls to 63% when considering holes present for more than 2–3 years. Visual acuity outcomes follow the same pattern.

In case of first surgery failure, despite a 70% sealing rate after a second operation, the resulting visual acuity is poor, approximately 20/100. The results are, instead, better for those patients experiencing a successful closure after the first vitrectomy and then a late reopening.

Visual improvement, in terms of visual acuity and recovery from distortion, occurs gradually after macular hole surgery, involving mechanisms that are not completely known. According to postoperative OCT findings, the first layer to recover its integrity is the external limiting membrane, followed by the inner segment/outer segment (IS/OS) junction line. Patients with a good quality of these structures tend to have a better visual outcome. The diameter of the IS/OS junction discontinuity 3 months after surgery also plays a role. If it is greater than 1500 μm, it is associated with a poorer visual acuity. The eventual presence of subfoveal fluid 3 months after surgery is not relevant in terms of visual outcomes [16].

3.7.2.2 Pharmacologic Treatment

In October 2012, ocriplasmin (Jetrea) was approved by the US Food and Drug Administration (FDA) for enzymatic dissection of the vitreous from the retinal surface. Ocriplasmin is a recombinant proteolytic enzyme, with activity against fibronectin and laminin, that underwent a multicenter, randomized, double-blind phase III trial by the MIVI-TRUST study group, which demonstrated a 40.6% closure rate of FTMHs using a single intravitreal injection of ocriplasmin (125 μg), compared to a 10.6% closure rate injecting intravitreal saline placebo. Also in the VMA group, the results were better with ocriplasmin than with placebo, with success rates of 26.5% vs. 10.1%, respectively. Best results are obtained in small FTMH with limited and focal VMA [13, 17].

An example of treatment employing both ocriplasmin and vitrectomy is presented in Figs. 3.7, 3.8, and 3.9.

3.8 Traumatic Macular Hole

Traumatic macular holes (TMHs) are usually associated with forceful blunt injury and, occasionally, with inadvertent Neodymium YAG laser burn. After the first description in 1869 by Knapp, the main etiology was thought to be a direct impact on the eyeball. It is now renown, however, that a hole can occur not only immediately after injury but also days or weeks later. Foveal detachment determines immediate vision loss, while progression of cystic changes and photoreceptor loss may account for delayed visual compromise. Moreover, the different impact forces and the material features of the object account for various TMHs subtypes.

According to their OCT morphology, TMHs can be classified in five groups:

- Type 1 (27.4%): macular hole with cystic edema of the neurosensory retina on both margins of the hole on both horizontal and vertical OCT scans, being therefore similar to idiopathic macular holes
- Type 2 (24.7%): macular hole with cystic edema of the neurosensory retina on only one margin of the hole, either on the horizontal or on the vertical OCT scan
- Type 3 (19.2%): macular hole with full-thickness defect of the neurosensory retina without cystic edema or margin detachment
- Type 4 (23.3%): macular hole with localized detachment of the neurosensory retina at the margin without cystic edema
- Type 5 (5.5%): macular hole with thinning of the neurosensory retina

Type 1 and 2, in which macular edema is evident, have a greater average retinal thickness than the other groups. Type 4 presents a localized retinal detachment, which results in a significant basal area increase, while type 5 has a greater apical area than type 4. As far as time of presentation is concerned, patients with type 1 holes seem to seek medical advice later than those with type 4 holes,

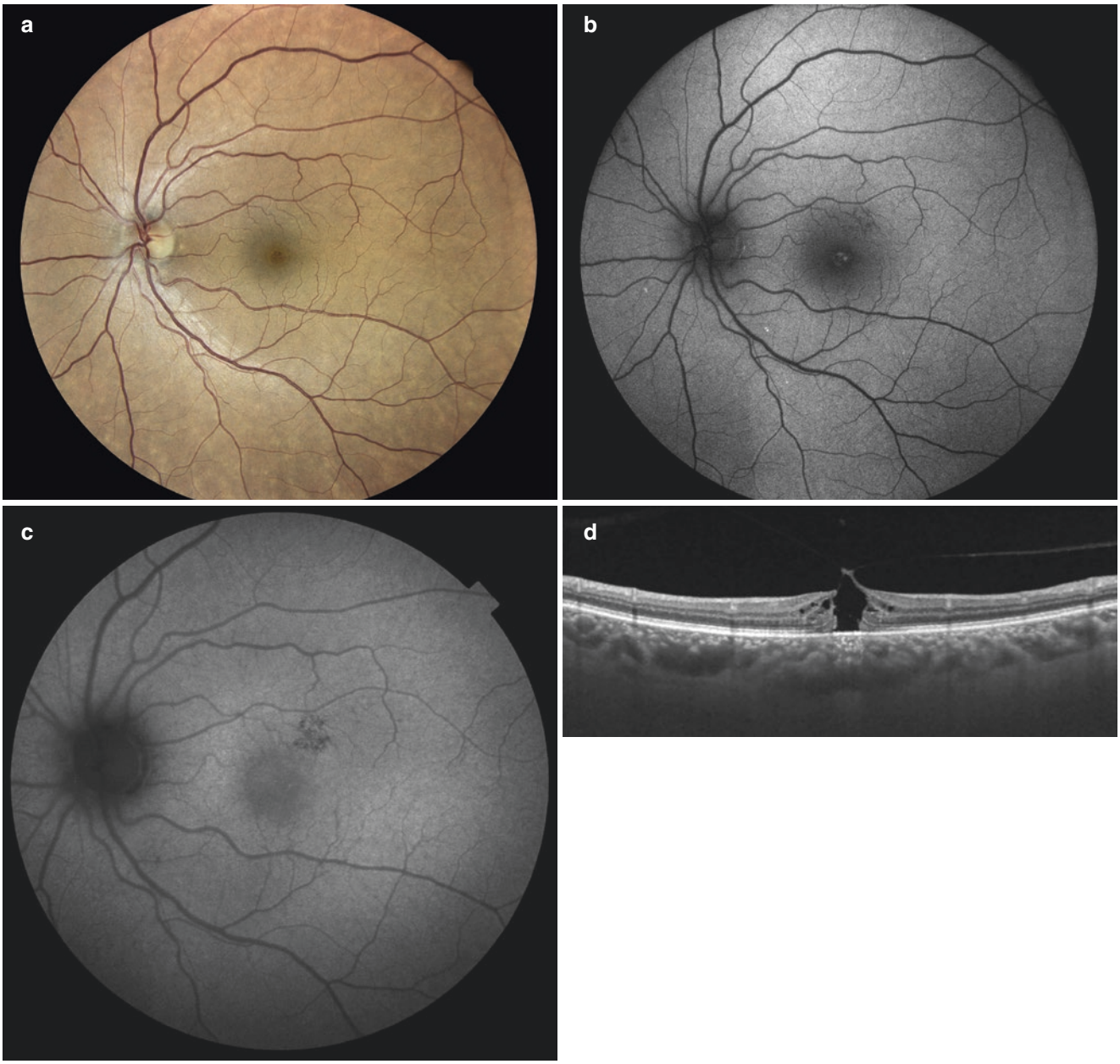

Fig. 3.7 Case presentation: A 66-year-old female complained of a visual loss and metamorphopsia in the left eye for 2 months. At the presentation visual acuity in the left eye was 20/40. Color fundus (**a**), blue autofluorescence (**b**), and green autofluorescence (**c**) showed findings consistent with the presence of small full-thickness macular hole. (**d**) Swept-source optical coherence tomography revealed also the presence of a foveal traction. The patient received an intravitreal injection of ocriplasmin

while no difference can be underlined in terms of gender, age, visual acuity, and eccentricity. It seems that some TMHs may evolve in type 1 holes, with an increase in retinal edema, possibly due to injury-induced abnormal capillary permeability in the parafoveal region and vitreous traction. Evidence suggests that patients with a late presentation have larger apical areas, since TMHs may enlarge, while the retina thickens over time. On the other hand, some TMHs may close spontaneously, especially among young patients, thanks to both glial and retinal pigment epithelial cell proliferation from the hole edges toward the bottom of the hole and to contractile forces, which pull the neurosensory retinal tissues together [18].

3.8.1 Mechanism of Hole Formation

The formation of a TMH can be ascribed to two different mechanisms: indeed, one type forms directly after the trauma, with avulsion and rupture of the fovea, causing acute

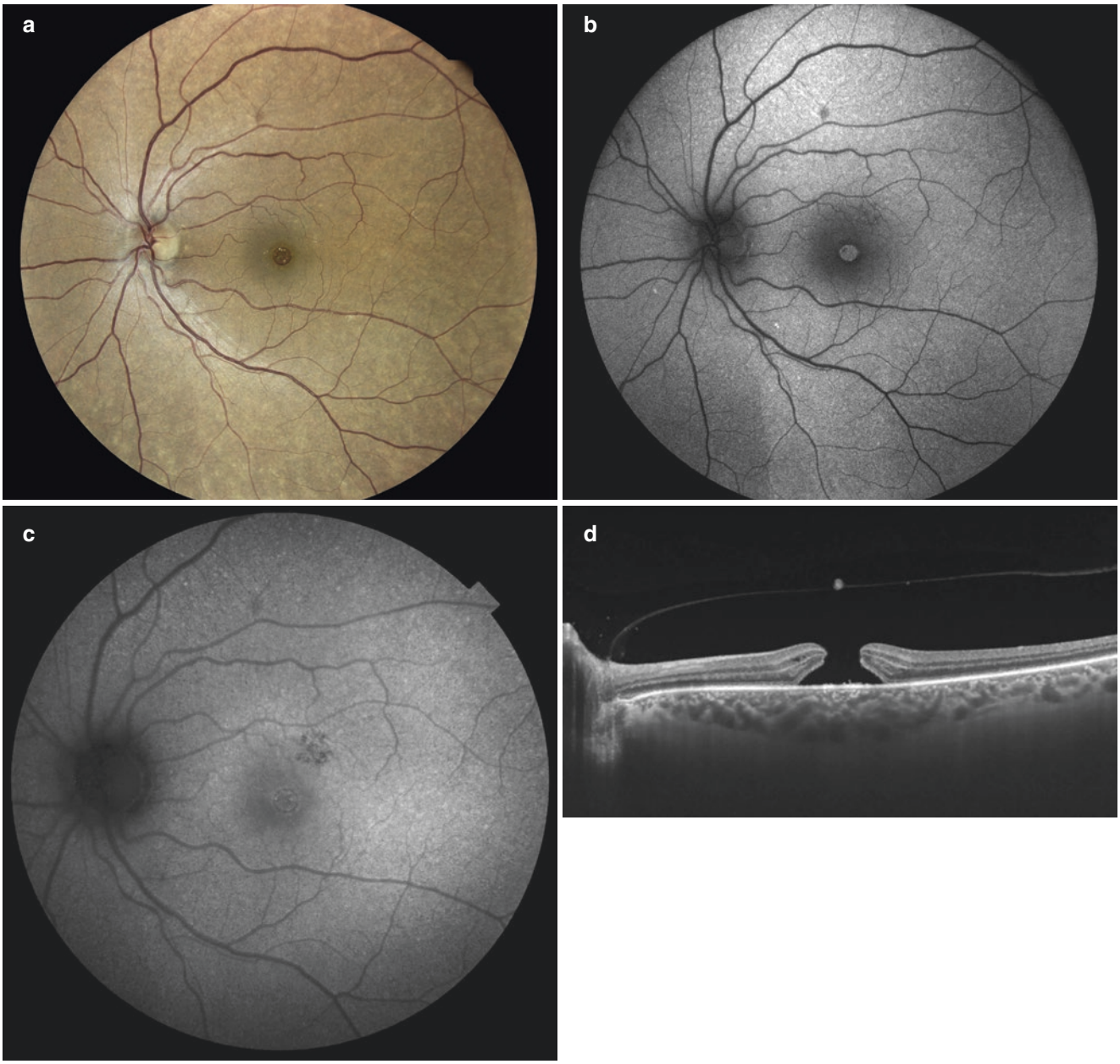

Fig. 3.8 One month after vitreolysis with ocriplasmin. Visual acuity in the left eye was unchanged to 20/40. Color fundus (**a**), blue autofluorescence (**b**), and green autofluorescence (**c**) showed an increase in size of full-thickness macular hole. (**d**) Swept-source optical coherence tomography (OCT) revealed the complete release of the vitreomacular attachment. The OCT scan confirmed the presence of a large full-thickness macular hole with an overlying operculum. The patient underwent a surgical intervention

visual loss, while the second one has a more gradual onset, from several days to months after the trauma, with a mechanism similar to the vitreomacular traction syndrome. This theory is supported by histological studies, demonstrating that, in some cases, the formation of TMHs is preceded by macular edema and cysts [19].

3.8.1.1 Rapid Onset TMH

Blunt trauma causes a sudden anteroposterior compression and equatorial expansion of the globe, resulting in significant stress on the retina in the points of vitreous attachment. Since young patients have the greatest vitreofoveal adherence, a sudden foveal traction can easily cause a macular hole immediately after the injury, especially in closed eye trauma. At the opposite, patients with vitreous foveal detachment result in having less chance of developing TMH. At the same time, PVD can be determined by the injury itself. Moreover, the equatorial expansion directly stretches the posterior pole, therefore pulling apart the fovea, since the elasticity and strength of Bruch's

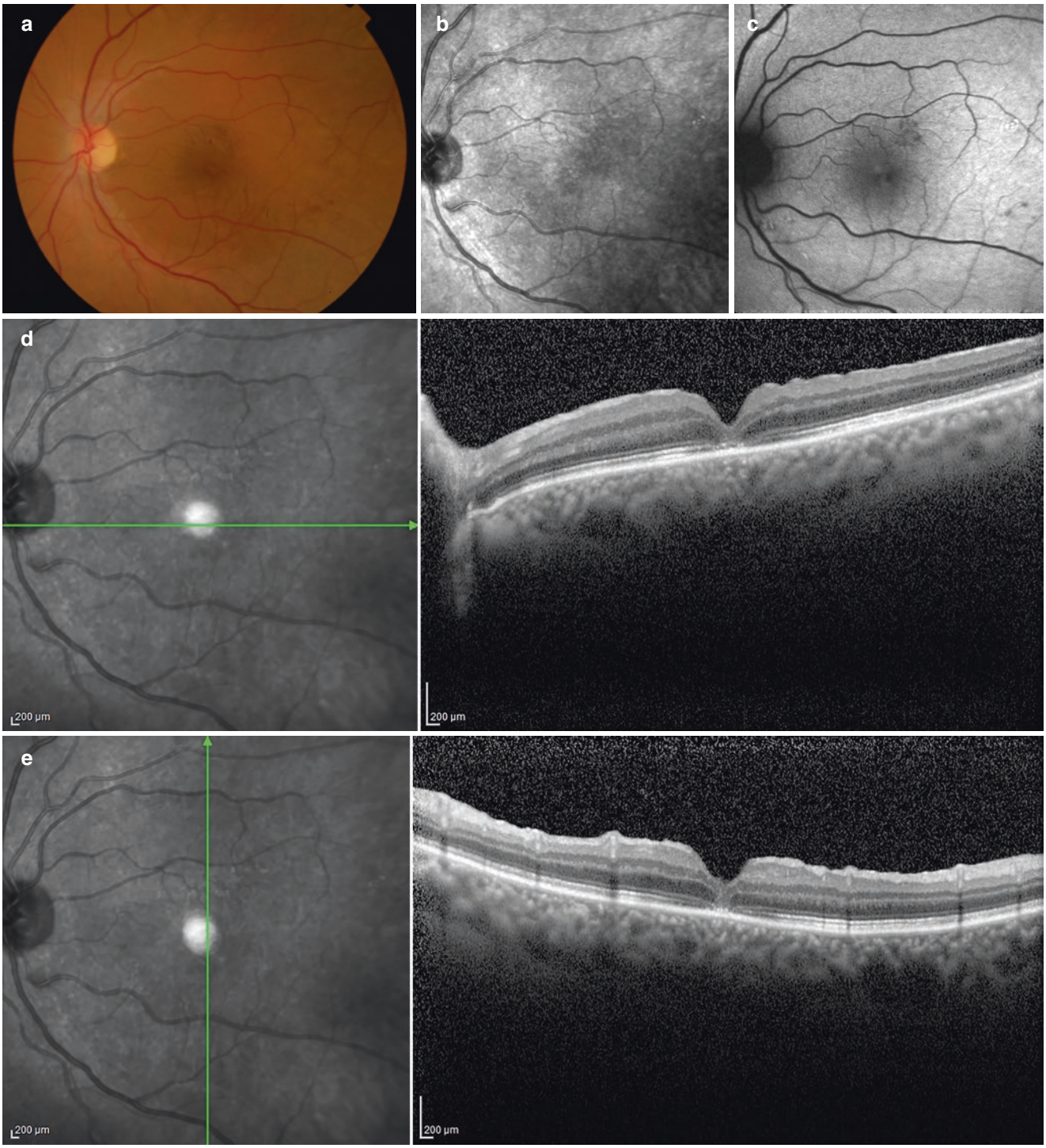

Fig. 3.9 One month after 27-gauge pars plana vitrectomy. Visual acuity in the left eye improved to 20/25. Color fundus (**a**), infrared (**b**), and blue autofluorescence (**c**) showed the closure of macular hole. Spectralis optical coherence tomography horizontal scan (**d**) and vertical scan (**e**) revealed the restoration of the outer retina including the external limiting membrane and photoreceptors. Green line corresponds with level of OCT image

membrane and ILM are not as great as those of the sclera. As far as shape is concerned, it is thought that TMHs arise in an elliptical or irregular morphology and gradually become more circular.

3.8.1.2 Delayed Onset TMH

Some TMHs form within days, or even weeks, after the injury, probably because of persistent vitreofoveal adhesions. This hypothesis is confirmed by the fact that vitrectomy with vitreofoveal adhesion release typically leads to hole resolution. The role of retinal cyst development in the delayed formation of TMHs is not clear. It seems that cystoid macular edema leads to the formation of lamellar holes, while posttraumatic cystic retinal changes precede the development of foveal atrophy. Older patients have weaker vitreofoveal adhesions, which not only determines a reduced average retinal thickness but also results in a prolonged period of time preceding TMH formation, thus leading to a circle-shaped hole, since the forces have more time to distribute evenly around the fovea.

3.8.2 TMH and Visual Acuity

No correlation has been found between TMH subtype and visual acuity. Average retinal thickness seems to be positively correlated with visual acuity. Indeed, a thin retina not only implies a less severe edema but may also indicate a more extensive retinal atrophy. This suggests that retinal thickness alone is not an adequate visual acuity predictor. Patients presenting late to medical attention seem to have better visual acuity. This may be due to structural hole changes and to the greater amount of time that the patient have to adapt to non-foveal fixation.

References

1. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013;120:2611–9.
2. Ezra E. Idiopathic full thickness macular hole: natural history and pathogenesis. Br J Ophthalmol. 2001;85:102–8.
3. Ali FS, Stein JD, Blachley TS, et al. Incidence of and risk factors for developing idiopathic macular hole among a diverse group of patients throughout the united states. JAMA Ophthalmol. 2017;135:299–305.
4. Steel DH, Lotery AJ. Idiopathic vitreomacular traction and macular hole: a comprehensive review of pathophysiology, diagnosis, and treatment. Eye (Lond). 2013;27:S1–21.
5. La Cour M, Friis J. Macular holes: classification, epidemiology, natural history and treatment. Acta Ophthalmol Scand. 2002;80:579–87.
6. Johnson RW, Gass JD. Idiopathic macular hole. Observations, stages of formation, and implications for surgical intervention. Ophthalmology. 1988;95:917–24.
7. Reese AB, Jones IS, Cooper WC. Vitreomacular traction syndrome confirmed histologically. Am J Ophthalmol. 1970;69:975–7.
8. Oh H. Idiopathic macular hole. Dev Ophthalmol. 2014;54:150–8.
9. Pang CE, Spaide RF, Freund KB. Comparing functional and morphologic characteristics of lamellar macular holes with and without lamellar hole-associated epiretinal proliferation. Retina. 2015;35:720–6.
10. Haouchine B, Massin P, Tadayoni R, et al. Diagnosis of macular pseudoholes and lamellar macular holes by optical coherence tomography. Am J Ophthalmol. 2004;138:732–9.
11. Chhablani J, Kumar K, Ali TR, et al. Spectral-domain optical coherence tomography features in fellow eyes of patients with idiopathic macular hole. Eur J Ophthalmol. 2014;24:382–6.
12. Madi HA, Masri I, Steel DH. Optimal management of idiopathic macular holes. Clin Ophthalmol. 2016;10:97–116.
13. García-Layana A, García-Arumí J, Ruiz-Moreno JM, et al. A review of current management of vitreomacular traction and macular hole. J Ophthalmol. 2015;2015:809640.
14. Lanzetta P, Polito A, Del Borrello M, et al. Idiopathic macular hole surgery with low-concentration infracyanine green-assisted peeling of the internal limiting membrane. Am J Ophthalmol. 2006;142:771–6.
15. Parravano M, Giansanti F, Eandi CM, et al. Vitrectomy for idiopathic macular hole. Cochrane Database Syst Rev. 2015;5:CD009080.
16. Bhavsar AR, Gomez J, Kelly NE, et al. Macular hole surgery: a review of past, present and latest treatments for macular hole. Exp Rev Ophthalmol. 2014;9:443–53.
17. Khan MA, Haller JA. Ocriplasmin for treatment of vitreomacular traction: an update. Ophthalmol Therapy. 2016;5:147–59.
18. Huang J, Liu X, Wu Z, et al. Classification of full-thickness traumatic macular holes by optical coherence tomography. Retina. 2009;29:340–8.
19. Miller JB, Yonekawa Y, Eliott D, et al. A review of traumatic macular hole: diagnosis and treatment. Int Ophthalmol Clin. 2013;53:59–67.

Myopic Foveoschisis and Macular Hole Retinal Detachment

4

Kazunari Hirota and Akito Hirakata

4.1 Introduction

Myopic foveoschisis (MF), also known as myopic traction maculopathy (MTM), was first described by Phillips as a localized retinal detachment in highly myopic eyes with a posterior staphyloma and without a macular hole (MH) [1]. Takano and Kishi were the first to use time-domain optical coherence tomographic (OCT) images to describe the morphological characteristics of MF, and they reported it to be a retinoschisis with or without a retinal detachment in the macular area (Fig. 4.1) [2].

More recent OCT studies have shown that MF is a schisis-like thickening of the inner and/or outer retina in highly myopic eyes with a posterior staphyloma. It has been suggested that the schisis-like thickening is due to fluid accumulation caused by traction on the retina rather than a true schisis [3].

It has been reported that MF can progress to a full-thickness MH and subsequent macular hole retinal detachment (MHRD) that is mainly located in the posterior pole but can extend beyond vascular arcade. The MHs in non-myopic eyes are mainly caused by anteroposterior traction by a posterior vitreous detachment, whereas the MHs in highly myopic eyes are caused by multiple anteroposterior and tangential tractional components which induce local or extensive rhegmatogenous retinal detachments. These eyes are difficult to treat because of their multiple and complicated pathogenesis.

MHRDs account for 0.5–21% of all retinal detachments [4, 5], and they are one of the most refractory retinal detachments with high rates of non-closure or reopening of the MHs. Recurrences of the retinal detachment often occur in spite of multiple surgical interventions. The retinal reattachment rate of MHRD has been reported to range from 50% to over 90% [6–8].

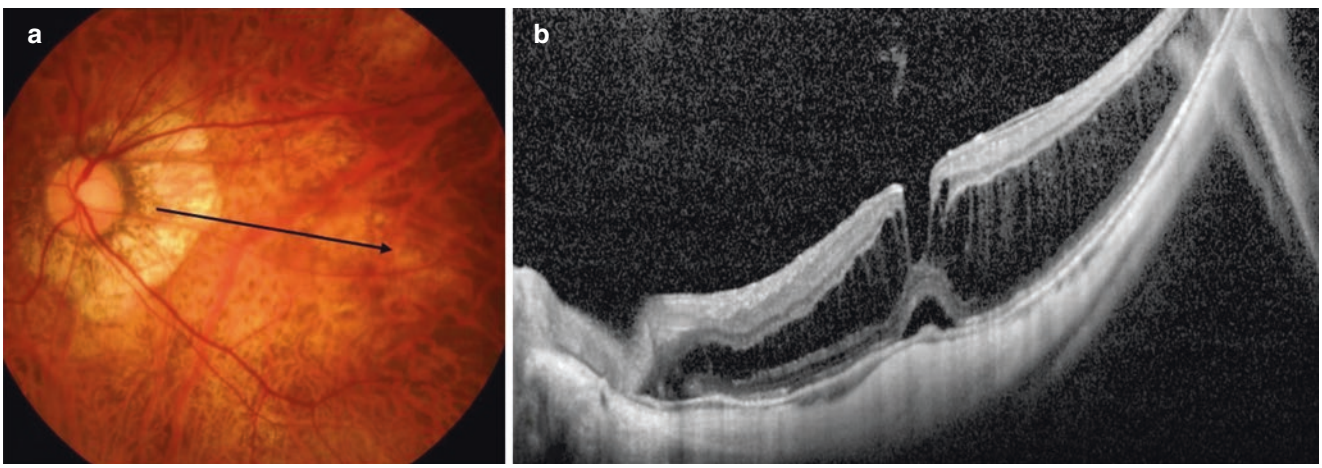

Fig. 4.1 (**a**) Fundus photograph and (**b**) corresponding spectral-domain optical coherence tomographic (SD-OCT) image of a myopic foveoschisis (MF) with macular retinoschisis and foveal retinal detachment. The black line in the fundus photograph is the direction of the SD-OCT scan. The patient was a 61-year-old woman whose decimal best-corrected visual acuity (BCVA) was 0.8

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4.2 Etiopathogenesis

Previous histopathological and OCT studies have shown that multiple tractional components were associated with the pathogenesis of MFs, MHs, and MHRDs in highly myopic eyes. The factors associated with the pathogenesis are preretinal, intraretinal, and subretinal factors. The major preretinal factors are the presence of an epiretinal membrane (ERM) and a partial or non-detached posterior hyaloid membrane which can cause anteroposterior or tangential traction on the retina. An electron microscopic study of the tractional components on the retinal surface of an eye with MHRD showed the presence of vitreous cortex, cellular elements of the ERMs, and the internal limiting membrane (ILM) in the biopsied specimen [9].

The intraretinal factors exerting traction on the retina are a stiffening of the ILM and the retinal vessels which prevent the retina from expanding in the anterior-posterior direction in highly myopic eyes. Bando and associates reported that collagen fibers and glial cells were present in 70% of the ILMs removed during vitrectomy from eyes with MF, and none of these elements were present in the control group consisting of eyes with an idiopathic macular hole. They concluded that the migration of glial cell and synthesis of collagen fibers on the inner surface of ILM contributed to the development of the MF [10].

The subretinal factors associated with MF are posterior staphylomas which are posterior ectasias causing an abnormal contour of the eye wall caused by an elongation of the axial length of highly myopic eyes. This can lead to a centrifugal traction on the retina and contribute to the development of MF. Chorioretinal atrophy is another subretinal factor that can contribute to the development of MF by reducing the attachment between the retina and the pigment epithelium or between the different retinal layers.

The prevalence of pathologic myopia among adolescents and children is less than 0.2% [11, 12], whereas it is 0.9–3.1% among middle-aged and elderly adults in Asian populations [13, 14] and 1.2% in a non-Asian adult population [15]. However, there has not been a study determining the prevalence of MF in a large, non-hospital-based population. Takano and Kishi reported that 11 of 32 highly myopic eyes with posterior staphylomas (34%) had MF [2], and Baba et al. reported that 7 of 78 eyes (9%) with high myopia and a posterior staphyloma had MF [16]. Thus, the incidence of MF is between 9% and 34% in highly myopic eyes of adults.

4.3 Clinical Features

Most of the patients with MF are asymptomatic, and the main complaint of a small number of patients is metamorphopsia. When a foveal retinal detachment and/or MH develop, the complaint is blurred vision. The characteristic biomicroscopic fundus finding in highly myopic eyes with MF is a microcystic appearance or shallow retinal detachment in the macular area.

OCT examinations are more reliable in detecting MFs. The common OCT findings in eyes with MF can be divided into four types that are presented in the order of progression.

- *Retinoschisis*. A retinoschisis is a splitting of the inner or outer retina with bridging columns without a foveal retinal detachment (Fig. 4.2).
- *Retinoschisis with a foveal retinal detachment* (Fig. 4.3).
- *Retinoschisis with a macular hole* (Fig. 4.4).
- *Macular hole retinal detachment* (Fig. 4.5).

The other OCT findings related to the pathogenesis of MFs are a detached ILM (Fig. 4.6), presence of preretinal structures (an ERM, a posterior vitreous membrane; Fig. 4.7), a MH in the inner retinal layer or outer retinal layer (Figs. 4.6 and 4.7), retinal vessel microfolds (Fig. 4.8),

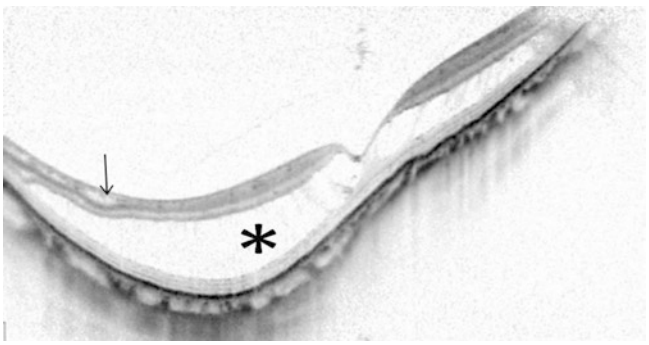

Fig. 4.2 Optical coherence tomographic (OCT) image of an eye with MF showing retinoschisis of the inner (arrow) and outer (asterisk) retinal layer without a foveal detachment. This condition is considered to be the initial stage of MF. The patient was a 70-year-old woman with a decimal BCVA of 0.5

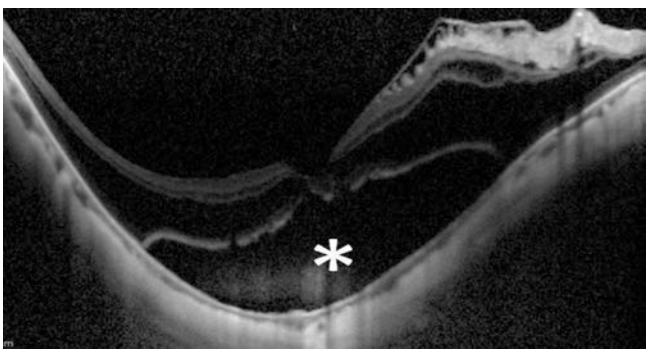

Fig. 4.3 OCT image of an eye with MF which has a foveal retinal detachment (asterisk). The patient was a 63-year-old woman with a decimal BCVA of 0.2

and paravascular microholes (Fig. 4.9). The OCT findings of a detached ILM, presence of preretinal structures on an elevated retina, retinal vessel microfolds, and perivascular microholes indicate an underlying traction of a stiffened ILM, preretinal structures, and retinal vasculature. The MHs in the inner retinal layer and outer retinal layer are caused by a stretching of the retina by various tractional elements and are considered to be precursors to a full-thickness MH.

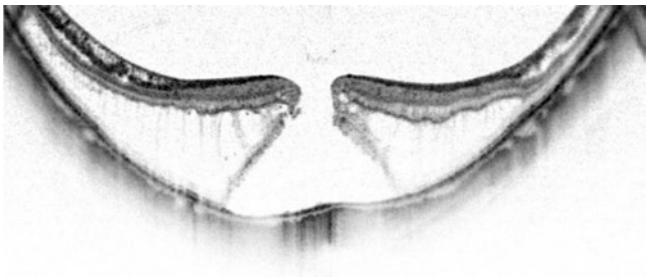

Fig. 4.4 OCT image of an eye with MF with a MH. The MH develops when the roof of a foveal detachment is separated by traction by antero-posterior or tangential components. The patient was a 74-year-old woman with a decimal BCVA of 0.1

4.4 Management

4.4.1 Observation Alone

An MF can remain stable for many years without affecting the vison. However, there are only a few studies on the natural course of MF (Table 4.1) which makes it difficult for surgeons to determine whether the case should be treated or just followed. Shimada et al. performed a longitudinal study of more than 2 years on eight eyes with MF. They reported that two eyes developed a MH and another two developed a foveal retinal detachment [17]. Gaucher et al. reported that 20 of 29 eyes with MF had a

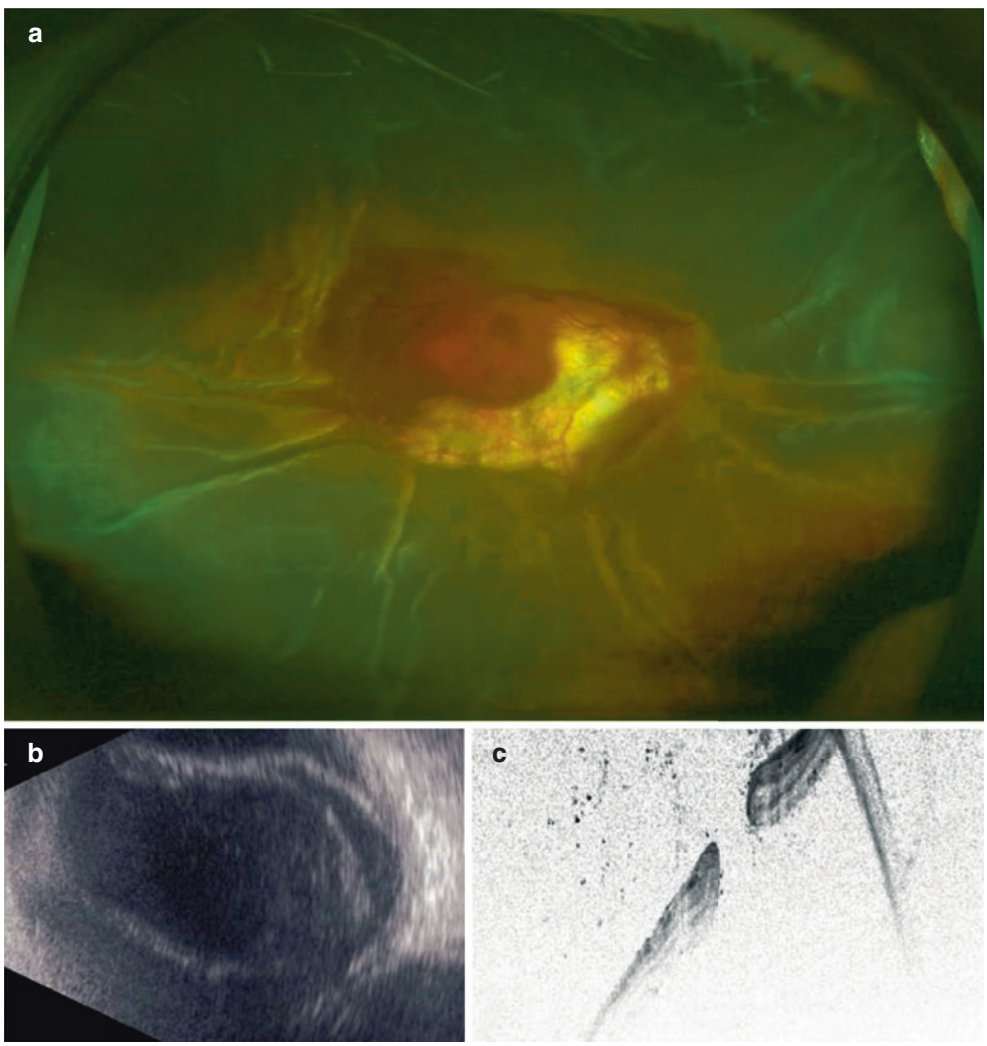

Fig. 4.5 Extensive MHRD following MH formation in an eye with MF. (**a**, **b**) Total retinal detachment associated with choroidal detachment can be seen. (**c**) OCT image showing full-thickness MH. Tangenital tractional components, an ERM, ILM, and retinal vessels, around the MH in the presence of a posterior staphyloma led to this condition. The patient was a 58-year-old woman with a decimal BCVA of 0.03. Intraocular pressure was as low as 5 mmHg with a choroidal detachment

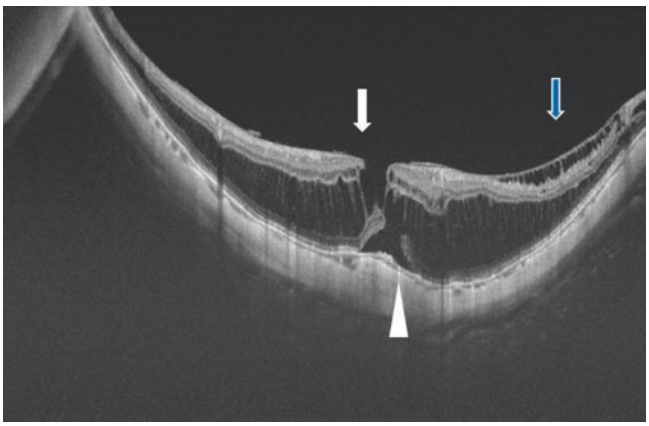

Fig. 4.6 OCT image showing a MH in the inner layer (white arrow), MH in the outer layer (arrowhead), and detached ILM (blue arrow)

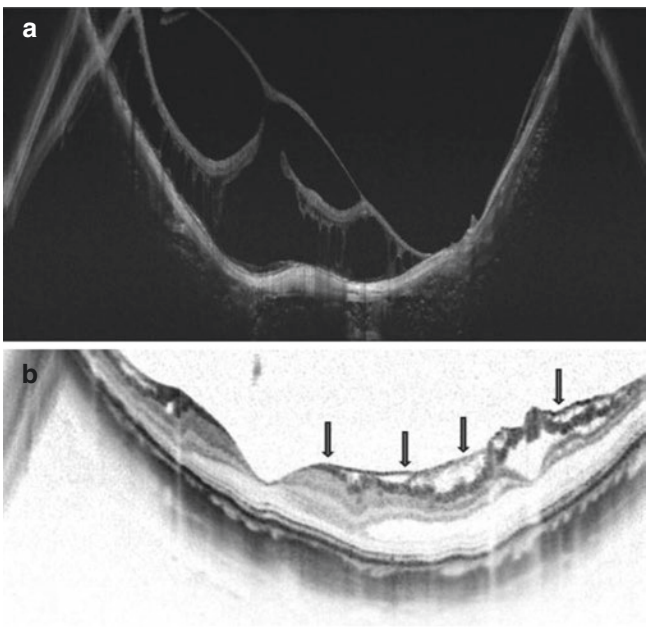

Fig. 4.7 OCT images showing preretinal structures in two eyes with MF. (**a**) Membranous structure which is probably the posterior vitreous membrane exerts traction on the retinal surface in the anteroposterior direction resulting in an outer layer retinoschisis and inner layer MH. (**b**) ERM on retinal surface exerting traction resulting in retinal folds and outer layer retinoschisis (arrow)

decrease of the visual acuity during a 31-month natural course study. They concluded that eyes with MF and the presence of premacular structures have a higher risk of progressing to a reduction in the visual acuity. In addition, those with a foveal detachment develop MHs more frequently whether or not surgery is performed. However, most of the cases without these findings remained stable during the 31-month follow-up period [18]. The results of these studies might suggest that many MF cases can progress to a more severe stage.

However, there have been other reports on a spontaneous resolution or none progression for several years of MFs (Fig. 4.10). Shimada et al. reported that only 11.6% of MF cases progressed which is much more stable than previously reported [19]. In addition, a spontaneous resolution of the MF with release of posterior vitreous traction has been reported [20], and a spontaneous resolution of four cases of MF with a release of posterior vitreous traction and reduced tangenital traction with ILM dehiscence have been reported [21]. Thus, the optimal time for surgery has not been definitively determined in eyes with MF. Many surgeons have reported that a progressive visual reduction and/or the presence of metamorphopsia are indications for surgery. This is because MF cases without foveal retinal detachment, traction by preretinal structure, or decreased vision may not require immediate surgical intervention. However, surgery is indicated for most cases that develop a MH or a MHRD.

4.4.2 Vitreoretinal Surgery

In the majority of earlier studies, the primary treatment for eyes with MF was vitrectomy with or without ILM peeling and with or without a gas tamponade. Some surgeons preferred macular buckling or scleral imbrication alone or in combination with vitrectomy. Ikuno et al. reported on 44 eyes with MF including 11 eyes with a full-thickness MH that underwent vitrectomy, ILM peeling, and gas tamponade. They reported that the retinoschisis with or without foveal retinal detachment was resolved in all of the eyes, the MH was closed in 4 of 11 eyes, and the visual acuity improved mostly in eyes with foveal retinal detachment [22].

The major postoperative complication of vitrectomy for MF without a MH is the formation of a MH and subsequent MHRD. Gaucher et al. suggested that when MF is combined with foveal retinal detachment, a MH develops more frequently whether surgery is performed or not performed [18].

The use of ILM peeling is still controversial. Taniuchi et al. reviewed 71 eyes of 64 patients with MF who underwent vitrectomy with or without ILM peeling, and they concluded that a recurrence of MF developed more frequently in eyes without ILM peeling [23]. Peeling a rigid ILM reduces tangential traction on the retina and promotes retinal reattachment. However, it can increase the risk of causing an iatrogenic MH on a thin retina of highly myopic eyes, and there are cases not requiring ILM removal for retinal reattachment (Fig. 4.11). To reduce the risk of postoperative MH formation in eyes that undergo ILM peeling, Shimada et al. compared the effects of fovea-sparing ILM peeling to complete ILM peeling on 45 consecutive eyes that underwent vitrectomy for MF. They reported that a

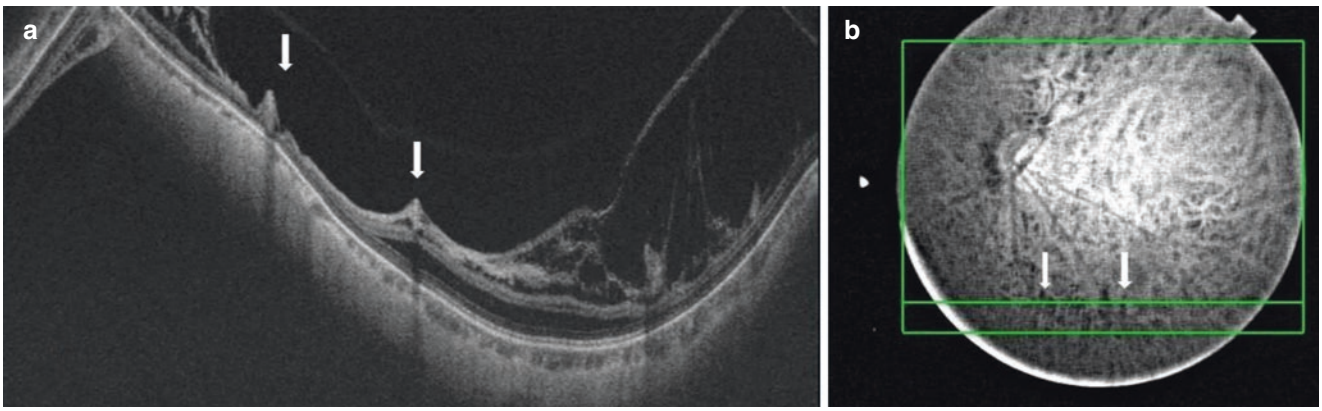

Fig. 4.8 (**a**) OCT image and (**b**) fundus photograph of retinal vascular microfolds. Tentlike elevations in the inner retina in the OCT image are located along the retinal vessels in the fundus photograph (arrows). These findings indicate an inward traction by the retinal vessels in an eye with a posterior staphyloma

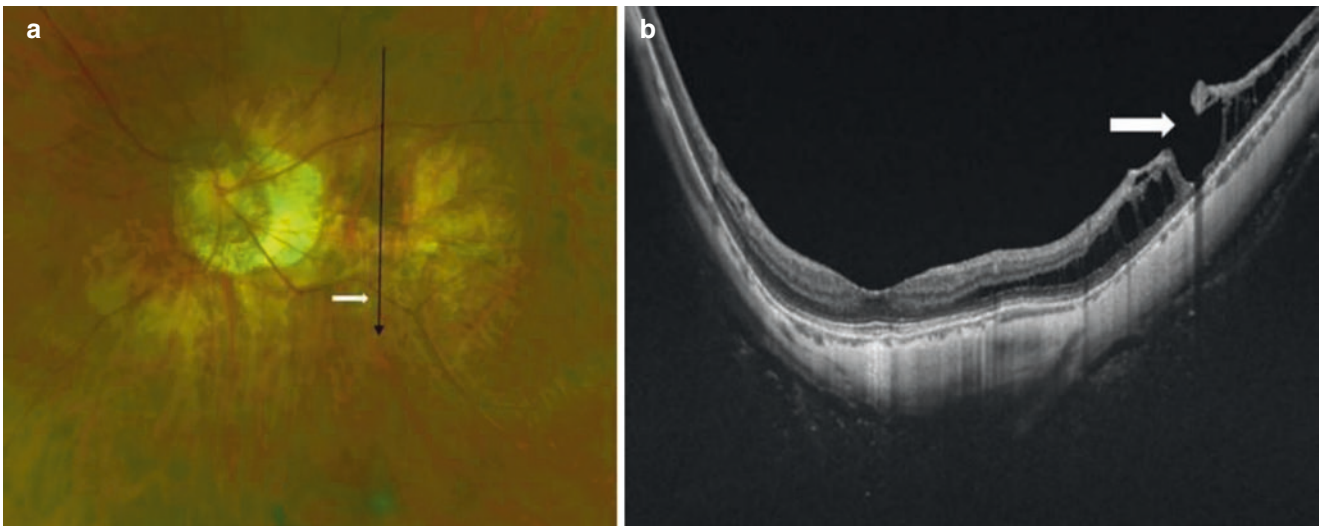

Fig. 4.9 (**a**) Fundus photograph and (**b**) OCT image of the same highly myopic eye. OCT image shows a perivascular microhole (white arrow) caused by an inward traction of a retinal vessel

Table 4.1 Major studies on the natural course of myopic foveoschisis (MF)

	Follow-up period	Progressed	Stable	Improved
Shimada et al. [17]	More than 2 years	4/8(50%)	4/8(50%)	0/8(0%)
Gaucher et al [18]	Mean 31.2 months	20/29(69%)	9/29(31%)	0/29(0%)
Shimada et al. [19]	More than 2 years	24/207(11.6%)	173/207(85.1%)	8/207(3.6%)

The latest report in 2013 shows a more stable natural course than the earlier two reports

MH developed in 5 of 30 eyes (16.7%) in the complete ILM peeled group and none of the 15 eyes in the fovea-sparing ILM peeling group [24] (Fig. 4.12).

In eyes with a full-thickness MH or a MHRD which is considered the end stage of MF, vitrectomy in combination with ILM peeling with gas or silicone oil tamponade, macular buckling with or without vitrectomy, and scleral imbrication with vitrectomy have been performed. Michalewska et al. introduced an inverted ILM flap technique for large MHs [25]. Since then, some investigators have used this technique for MH and MHRD in highly myopic eyes (Figs. 4.13 and 4.14). They have reported higher MH closure rates than only ILM peeling and favorable retinal reattachment rates. Baba et al. compared the efficacy of vitrectomy with or without the inverted ILM flap technique in 21 highly myopic eyes with a MHRD. They reported that the MH

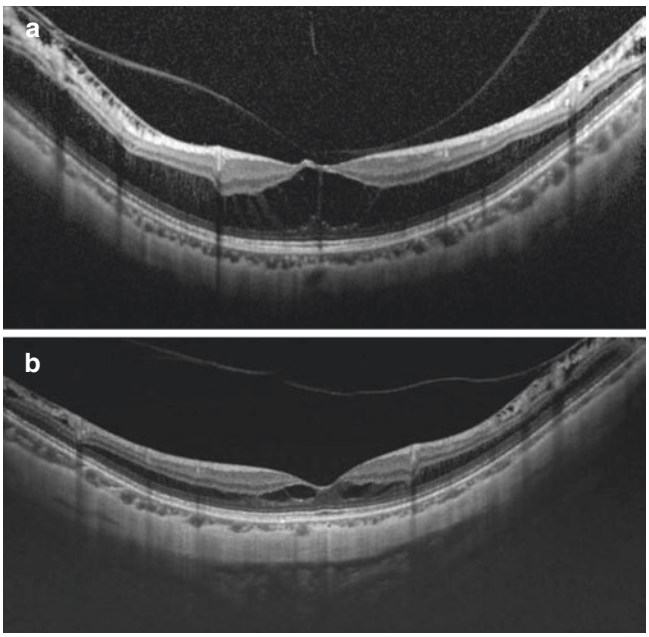

Fig. 4.10 (**a**) 69-year-old woman presented with metamorphopsia with decreased BCVA (0.3). OCT image shows retinoschisis with perifoveal posterior vitreous detachment (PVD). (**b**) After 12 months without intervention, the BCVA has improved to 0.8, and OCT shows a resolution of MF with progression of the PVD

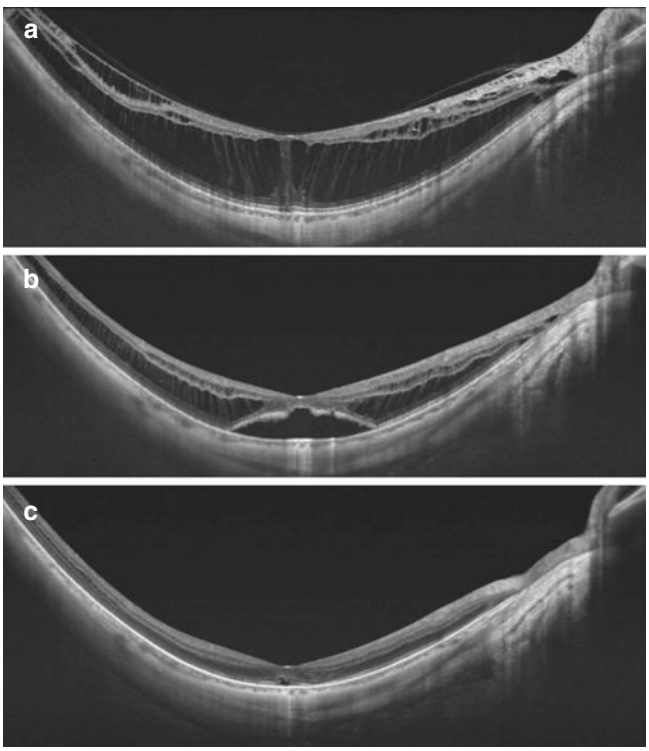

Fig. 4.11 OCT image of an eye with MF that underwent vitrectomy without ILM peeling. (**a**) In the preoperative OCT image, preretinal structures are not seen except for a shallow PVD, and the deformation of the inner retinal surface was slight. (**b**) One month after surgery, a decrease of the retinoschisis and development of foveal retinal detachment can be seen. (**c**) Two years after surgery, retina is almost completely reattached without retinoschisis. The creation of a PVD without ILM peeling was sufficient for retinal reattachment in this case. The patient was a 49-year-old man whose decimal BCVA improved from 0.3 to 0.4

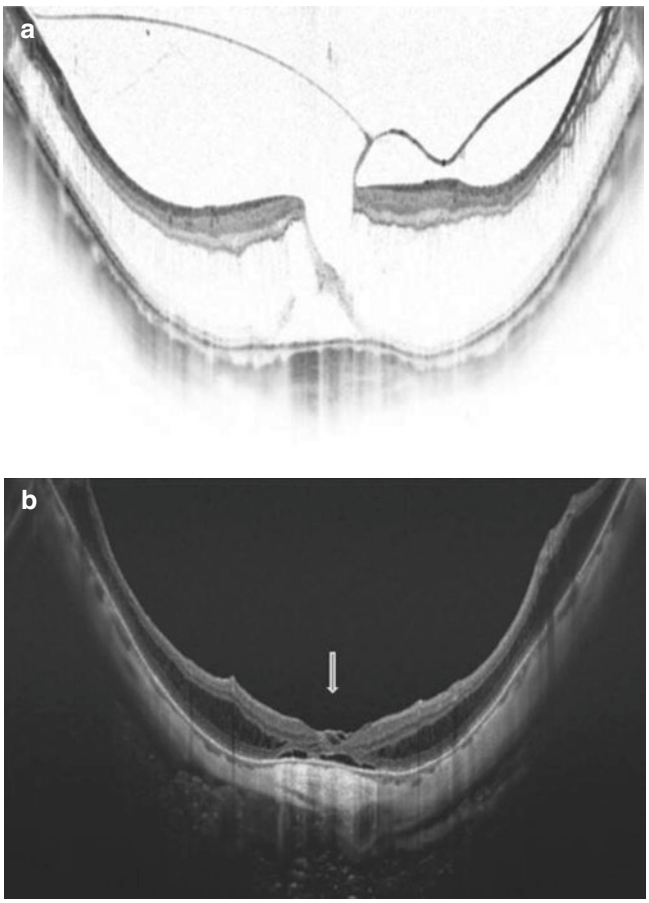

Fig. 4.12 (**a**) OCT images of an eye with MF accompanied by a MH passing through the inner and outer retinal layers. The risk of developing a postoperative full-thickness MH was high. (**b**) After vitrectomy with fovea-sparing ILM peeling, the MF was significantly reduced without a full-thickness MH. Note the remnant of the ILM in the postoperative OCT image (arrow). The patient was a 75-year-old woman whose decimal BCVA improved from 0.4 to 0.7

closure rate was 80% in ILM flap group which was significantly higher than that of complete ILM peeling (36%). The retinal reattachment rate was 100% in the ILM flap group and 91% in the ILM peeling group, and this difference was not statistically significant [26].

Macular buckling with silicone sponge or macular plombe is used alone or in combination with vitrectomy for complicated cases as an initial treatment for highly myopic eyes with MHs. Ando et al. compared the surgical outcomes of macular buckling alone to that of vitrectomy alone as the primary procedure for MHRDs in highly myopic eyes. They reported that the initial reattachment rate was 93.3% in the macular buckling group and 50% in the vitrectomy group [27]. By shortening the axial length of the eye and altering the shape of a posterior staphyloma, macular buckling reduced the anteroposterior and tangential vitreoretinal traction thus promoting macular attachment and MH closure (Fig. 4.15). However, due to technical difficulties and possible complications such as subretinal hemorrhage which

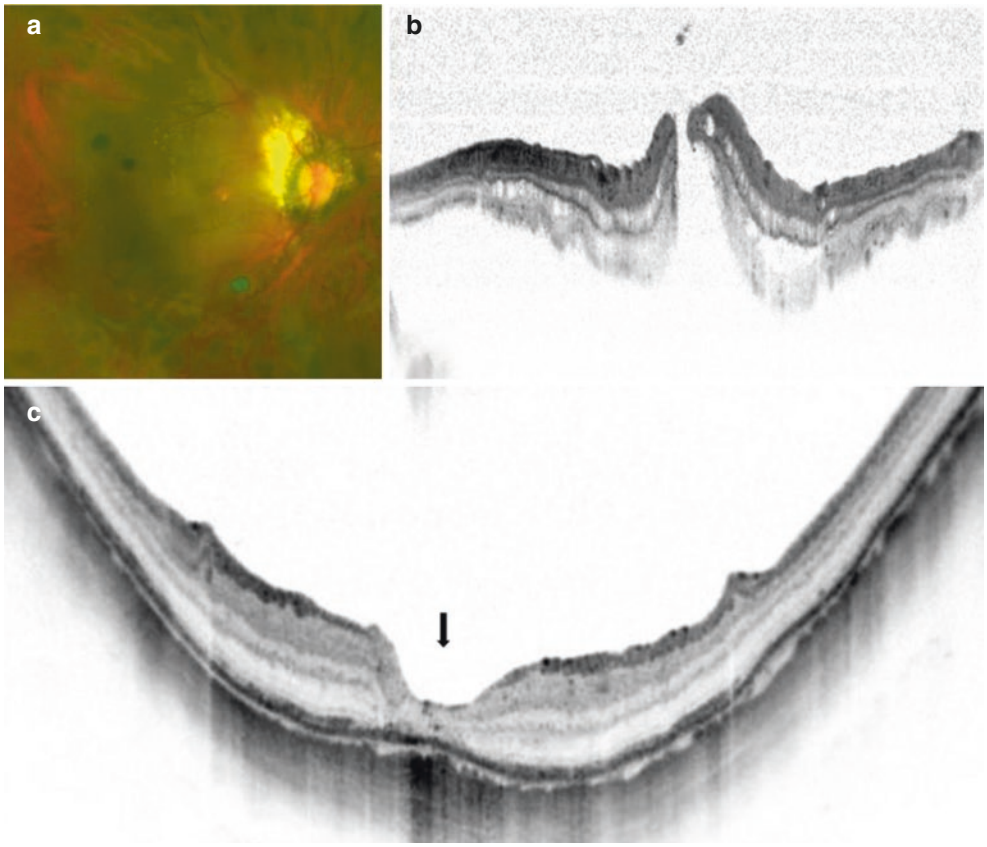

Fig. 4.13 Fundus photographs and SD-OCT images of the retina after vitrectomy with the inverted ILM technique. (**a**, **b**) The MHRD can be seen to extend beyond the vascular arcade. (**c**) The MH is closed with glial tissue substituting for foveal sensory retina, and the EZ is not seen (white arrow). The patient was a 62-year-old woman whose decimal BCVA improved from 0.04 to 0.2

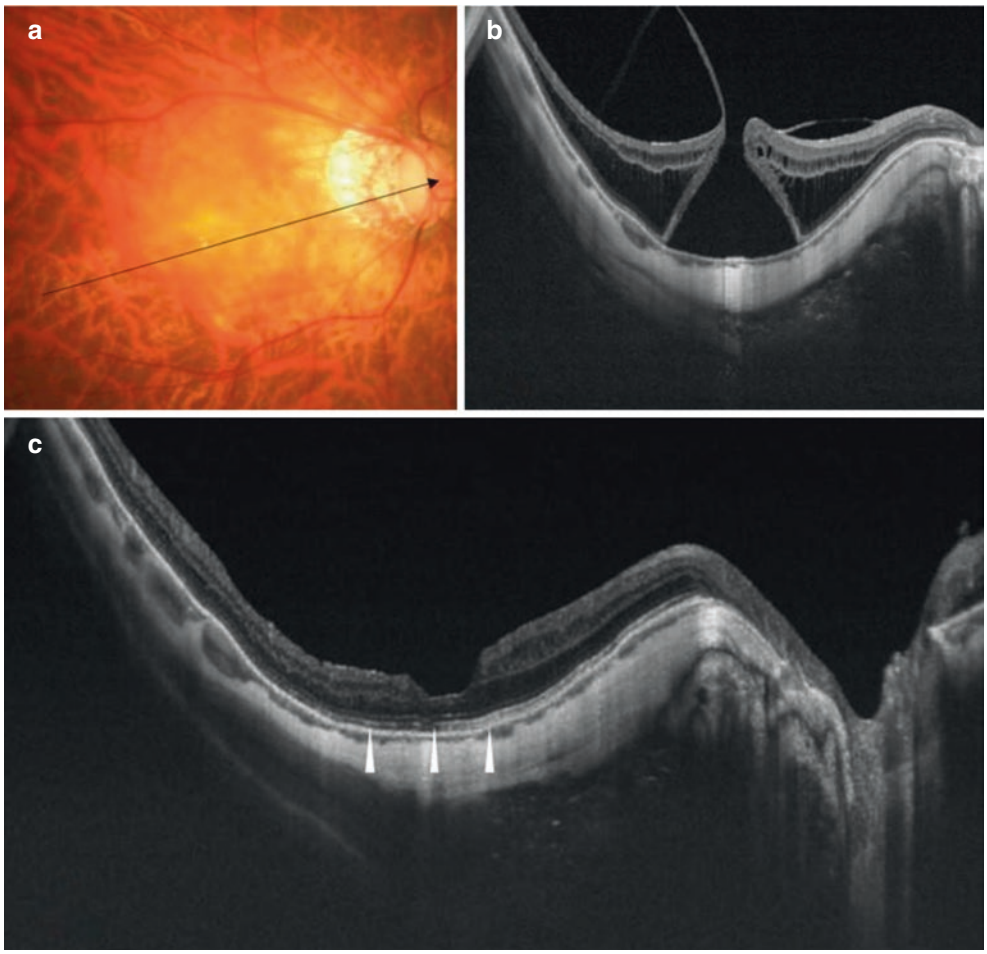

Fig. 4.14 Fundus photographs and SD-OCT images of the retina after vitrectomy with the inverted ILM technique. The images show different patterns of MH closure compared to the case shown in Fig. 4.13. (**a**, **b**) MF with full-thickness MH can be seen. (**c**) The MH is closed with a preservation of the EZ and the sensory retina (arrowhead). The patient was a 67-year-old woman whose BCVA improved from 0.2 to 0.7

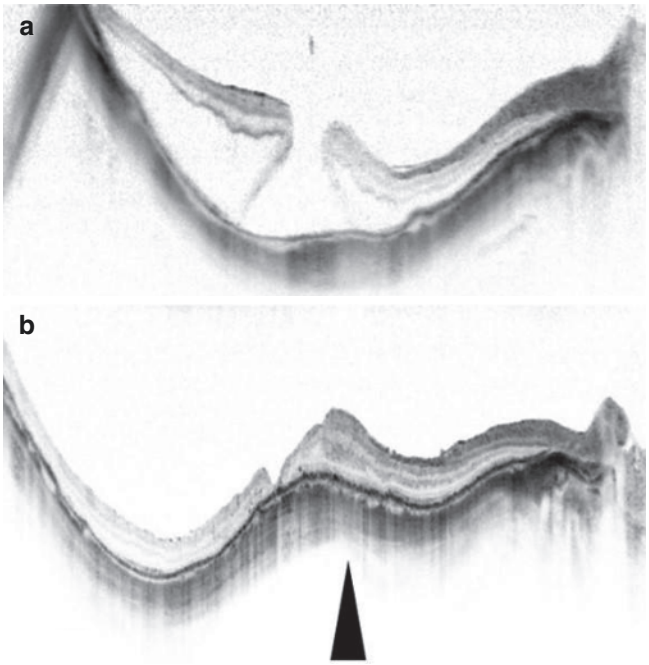

Fig. 4.15 Pre- and postoperative OCT images of two eyes that underwent vitrectomy with macular Ando plombe. (**a**) MF with full-thickness MH is seen in the OCT image. (**b**) Postoperative OCT image showing an indentation by the macular Ando plombe which changed the shape of the posterior staphyloma markedly leading to MH closure (arrowhead). The patient was a 68-year-old woman whose decimal BCVA improved from 0.1 to 0.5

can lead to chorioretinal atrophy and progression of myopic choroidal neovascularization, this technique tends to be used only in difficult cases in which vitrectomy alone is insufficient for retinal reattachment.

Scleral imbrication is also used in combination with vitrectomy to treat highly myopic eyes with MHs, and favorable results have been reported. Fujikawa et al. reported on eight highly myopic eyes with a MHRD that underwent vitrectomy combined with scleral imbrication. The retina was reattached in all eyes, and the MH was closed in six eyes (75%) [28]. The therapeutic mechanism for this procedure is a shortening of the axial length and alteration of the shape of the posterior staphyloma which is similar to that of macular buckling. Ando et al. reported on 17 eyes that underwent vitrectomy with scleral imbrication for MF or MHRD. They reported a decrease in the axial length and changes in the curvature of the posterior staphyloma at 1 month after surgery on 17 eyes that underwent vitrectomy with scleral imbrication for MF or MHRD. However, the change in the scleral curvature of the posterior staphyloma regressed at 3 and 6 months postoperatively [29]. This technique may have an advantage because the surgeon can avoid complications related to direct macular indentation although its impact on the axial length and shape of a posterior staphyloma may be less than that of macular buckling (Fig. 4.15). In addition, the effects of the surgery may reduce over years (Fig. 4.16).

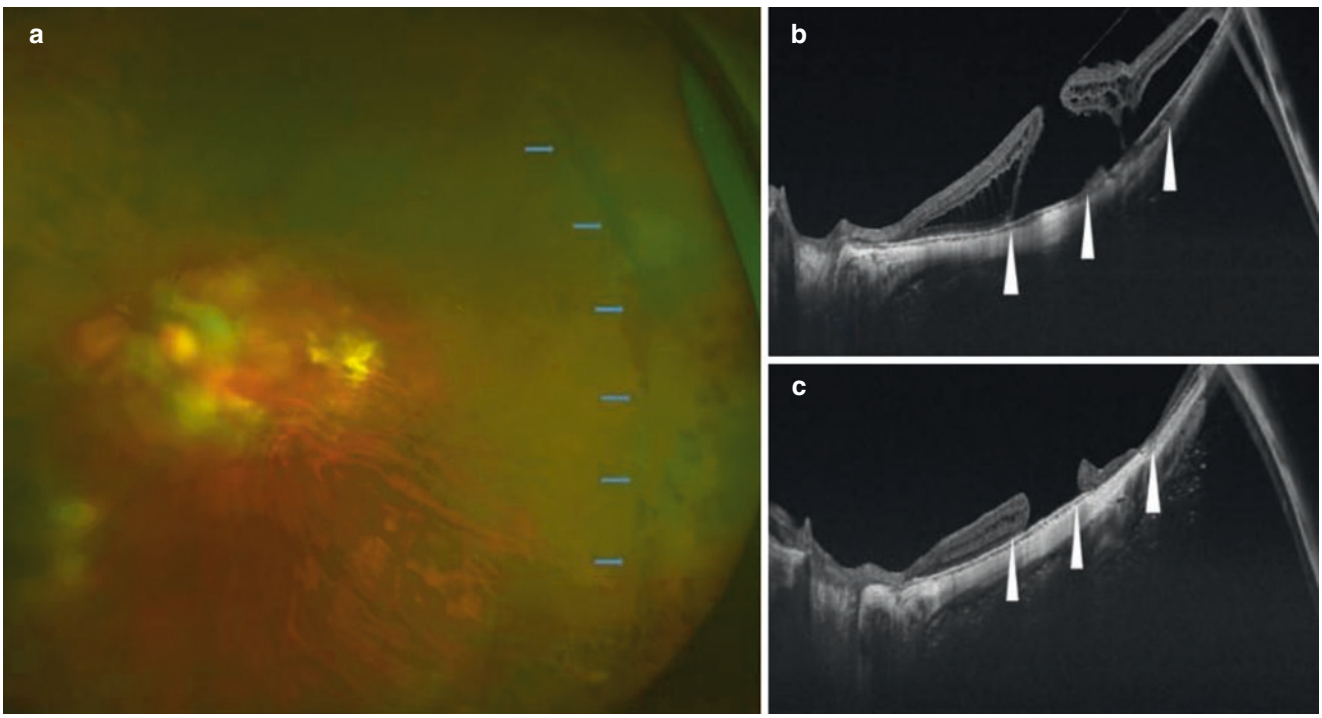

Fig. 4.16 Wide-field fundus photograph and OCT image of an eye that underwent vitrectomy with scleral imbrication. (**a**) Fundus photograph shows a protrusion created by the scleral imbrication (arrows). (**b**) Preoperative OCT image shows MF with full-thickness MH. (**c**) After vitrectomy with scleral imbrication, the change in curvature of posterior eye wall can be seen in the OCT image (arrowhead), but the MH remains opened. The patient was a 61-year-old woman whose BCVA improved from 0.1 to 0.2

4.5 Conclusions

A myopic foveoschisis (MF), also known as myopic traction maculopathy (MTM), is a tractional macular retinal thickening in patients with high myopia and posterior staphyloma with or without a macular hole. OCT is the main diagnostic method to detect MFs and determine the morphology of vitreoretinal interface which are difficult to detect by standard ophthalmoscopy. Although there exist many cases of MF without symptoms, a worsening of the BCVA, or the OCT findings, some cases can progress to a more severe stage. In such cases, surgery including vitrectomy in combination with other procedures is recommended. However, the best time to perform the surgery has not been determined because of a possibility of a spontaneous resolution or non-progression of the MF and possible postoperative complications. At present, careful OCT examinations and monitoring the changes of the BCVA are recommended. These findings should lead to a better understanding of the pathogenesis, pathology, and treatment of MF.

References

1. Phillips CI. Retinal detachment at the posterior pole. Br J Ophthalmol. 1958;42(12):749–53.
2. Takano M, Kishi S. Foveal retinoschisis and retinal detachment in severely myopic eyes with posterior staphyloma. Am J Ophthalmol. 1999;128(4):472–6.
3. Panozzo G, Mercanti A. Vitrectomy for myopic traction maculopathy. Arch Ophthalmol. 2007;125(6):767–72.
4. Margheria RR, Schepens CL. Macular breaks. 1. Diagnosis, etiology, and observations. Am J Ophthalmol. 1972;74(2):219–32.
5. Zhang CF, Hu C. High incidence of retinal detachment secondary to macular hole in a Chinese population. Am J Ophthalmol. 1982;94(6):817–9.
6. Chen YP, Chen TL, Yang KR, Lee WH, Kuo YH, Chao AN, Wu WC, Chen KJ, Lai CC. Treatment of retinal detachment resulting from posterior staphyloma-associated macular hole in highly myopic eyes. Retina. 2006;26(1):25–31.
7. Kadonosono K, Yazama F, Itoh N, Uchio E, Nakamura S, Akura J, Sawada H, Ohno S. Treatment of retinal detachment resulting from myopic macular hole with internal limiting membrane removal. Am J Ophthalmol. 2001;131(2):203–7.
8. Uemoto R, Yamamoto S, Tsukahara I, Takeuchi S. Efficacy of internal limiting membrane removal for retinal detachments resulting from a myopic macular hole. Retina. 2004;24(4):560–6.
9. Sakaguchi H, Ikuno Y, Choi JS, Ohji M, Tano T. Multiple components of epiretinal tissues detected by triamcinolone and indocyanine green in macular hole and retinal detachment as a result of high myopia. Am J Ophthalmol. 2004;138(6):1079–81.
10. Bando H, Ikuno Y, Choi JS, Tano Y, Yamanaka I, Ishibashi T. Ultrastructure of internal limiting membrane in myopic foveoschisis. Am J Ophthalmol. 2005;139(1):197–9.
11. Pi LH, Chen L, Liu Q, Ke N, Fang J, Zhang S, Xiao J, Ye WJ, Xiong Y, Shi H, Zhou XY, Yin ZQ. Prevalence of eye diseases and causes of visual impairment in school-aged children in Western China. J Epidemiol. 2012;22(1):37–44.
12. Samarawickrama C, Mitchell P, Tong L, Gazzard G, Lim L, Wong TY, Saw SM. Myopia-related optic disc and retinal changes in adolescent children from singapore. Ophthalmology. 2011;118(10):2050–7.
13. Gao LQ, Liu W, Liang YB, Zhang F, Wang JJ, Peng Y, Wong TY, Wang NL, Mitchell P, Friedman DS. Prevalence and characteristics of myopic retinopathy in a rural Chinese adult population: the Handan Eye Study. Arch Ophthalmol. 2011;129(9):1199–204.
14. Liu HH, Xu L, Wang YX, Wang S, You QS, Jonas JB. Prevalence and progression of myopic retinopathy in Chinese adults: the Beijing Eye Study. Ophthalmology. 2010;117(9):1763–8.
15. Vongphanit J, Mitchell P, Wang JJ. Prevalence and progression of myopic retinopathy in an older population. Ophthalmology. 2002;109(4):704–11.
16. Baba T, Ohno-Matsui K, Futagami S, Yoshida T, Yasuzumi K, Kojima A, Tokoro T, Mochizuki M. Prevalence and characteristics of foveal retinal detachment without macular hole in high myopia. Am J Ophthalmol. 2003;135(3):338–42.
17. Shimada N, Ohno-Matsui K, Baba T, Futagami S, Tokoro T, Mochizuki M. Natural course of macular retinoschisis in highly myopic eyes without macular hole or retinal detachment. Am J Ophthalmol. 2006;142(3):497–500.
18. Gaucher D, Haouchine B, Tadayoni R, Massin P, Erginay A, Benhamou N, Gaudric A. A Long-term follow-up of high myopic foveoschisis: natural course and surgical outcome. Am J Ophthalmol. 2007;143(3):455–62.
19. Shimada N, Tanaka Y, Tokoro T, Ohno-Matsui K. Natural course of myopic traction maculopathy and factors associated with progression or resolution. Am J Ophthalmol. 2013;156(5):948–57.
20. Polito A, Lanzetta P, Del Borrello M, Bandello F. Spontaneous resolution of a shallow detachment of the macula in a highly myopic eye. Am J Ophthalmol. 2003;135(4):546–7.
21. Hirota K, Hirakata A, Inoue M. Dehiscence of detached internal limiting membrane in eyes with myopic traction maculopathy with spontaneous resolution. BMC Ophthalmol. 2014;14:39.
22. Ikuno Y, Sayanagi K, Soga K, Oshima Y, Ohji M, Tano Y. Foveal anatomical status and surgical results in vitrectomy for myopic foveoschisis. Jpn J Ophthalmol. 2008;52(4):269–76.
23. Taniuchi S, Hirakata A, Itoh Y, Hirota K, Inoue M. Vitrectomy with or without internal limiting membrane peeling for each stage of myopic traction maculopathy. Retina. 2013;33(10):2018–25.
24. Shimada N, Sugamoto Y, Ogawa M, Takase H, Ohno-Matsui K. Fovea-sparing internal limiting membrane peeling for myopic traction maculopathy. Am J Ophthalmol. 2012;154(4):693–701.
25. Michalewska Z, Michalewski J, Adelman RA, Nawrocki J. Inverted internal limiting membrane flap technique for large macular holes. Ophthalmology. 2010;117(10):2018–25.
26. Baba R, Wakabayashi Y, Umazume K, Ishikawa T, Yagi H, Muramatsu D, Goto H. Efficacy of the inverted internal limiting membrane flap technique with vitrectomy for retinal detachment associated with myopic macular holes. Retina. 2017;37(3):466–71.
27. Ando F, Ohba N, Touura K, Hirose H. Anatomical and visual outcomes after episcleral macular buckling compared with those after pars plana vitrectomy for retinal detachment caused by macular hole in highly myopic eyes. Retina. 2007;27(1):37–44.
28. Fujikawa M, Kawamura H, Kakinoki M, Sawada O, Sawada T, Saishin Y, Ohji M. Scleral imbrication combined with vitrectomy and gas tamponade for refractory macular hole retinal detachment associated with high myopia. Retina. 2014;34(12):2451–7.
29. Ando Y, Hirakata A, Ohara A, Yokota R, Orihara T, Hirota K, Koto T, Inoue M. Vitrectomy and scleral imbrication in patients with myopic traction maculopathy and macular hole retinal detachment. Graefes Arch Clin Exp Ophthalmol. 2017;255(4):673–80.

Diabetic Retinopathy: Surgical Aspects

5

Xuejing Chen and Michelle C. Liang

5.1 Introduction

Vision loss due to diabetic retinopathy can be devastating and results from numerous complications, including macular edema, retinal and choroidal ischemia, vitreous hemorrhage, tractional retinal detachments, epiretinal membranes (with or without vitreoretinal traction), and papillopathy [1, 2]. The Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) showed that proper blood pressure and blood glucose control can delay the progression of diabetic retinopathy [3–5]. Additionally, local therapies such as focal macular laser, panretinal photocoagulation, intravitreal anti-vascular endothelial growth factor (VEGF), and intravitreal steroids can delay progression of retinopathy and treat associated vision-threatening complications [6]. Nevertheless, some patients continue to progress and require surgical intervention with pars plana vitrectomy (PPV) for optimal vision [6]. An estimated 5% of patients with proliferative diabetic retinopathy required PPV despite laser treatment and good glycemic and hypertensive control in the Early Treatment Diabetic Retinopathy Study (ETDRS) cohort [7].

Traditional indications for surgery include vitreous hemorrhage, macula-involving or macula-threatening tractional retinal detachment, combined tractional and rhegmatogenous retinal detachment, and diabetic macular edema with or without epiretinal membrane or traction [2, 6].

The goals of diabetic vitrectomy are to clear media opacities such as vitreous hemorrhage, to restore normal retinal anatomy, and to seal any retinal breaks. The latter two goals are accomplished by releasing anterior-posterior and tangential traction on the retina through removal or segmentation of tractional fibrovascular proliferation and epiretinal membranes [2]. The status of the posterior hyaloid is an important factor in the severity of fibrovascular proliferation which can use the adherent vitreous cortex as a scaffold for neovascular expansion. With continued growth, tight tractional membranes form and subsequently contract, promoting vitreous hemorrhage and tractional retinal detachments [8–10]. The removal of the posterior hyaloid face eliminates the scaffolding for subsequent neovascularization, decreasing future tractional forces on the retina. Relief of traction on retinal vessels can also improve blood flow within vessels and reduce leakage [11].

However, even with anatomically successful results after surgery, a patient's vision may ultimately be limited by ischemia from chronic microvascular disease or atrophy secondary to prolonged anatomic abnormalities [12]. Eyes in patients with diabetes typically also have an inherently abnormal vitreoretinal interface which increases the risks of intraoperative bleeding and iatrogenic breaks. Thus, the decision for surgical intervention in this patient population always requires a careful weighing of risks and benefits prior to proceeding.

5.2 Indications for Surgery

5.2.1 Vitreous Hemorrhage

Vitreous hemorrhage is a common cause of vision loss from proliferative diabetic retinopathy [2]. Hemorrhage can occur from leakage from active neovascularization or traction caused by fibrovascular proliferation on weak vessels (Fig. 5.1). The first successful PPV was performed by

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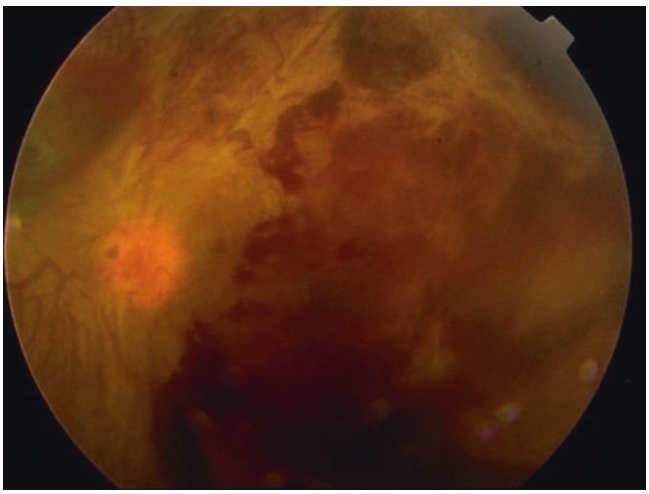

Fig. 5.1 This patient has proliferative diabetic retinopathy with extensive neovascularization radiating from the optic nerve head as well as subhyaloid and vitreous hemorrhage

Machemer in an eye with diabetic vitreous hemorrhage [13]. Historically, ophthalmologists would wait 6–12 months before considering surgery for diabetic vitreous hemorrhage [11]; however, the landmark Diabetic Retinopathy Vitrectomy Study (DRVS) concluded that vitreous hemorrhage in patients with type 1 diabetes benefited from earlier vitrectomy compared to those with type 2 diabetes as these patients tended to develop more aggressive fibrovascular proliferation [14–17]. This study looked at a large cohort of patients with vitreous hemorrhage for at least 1 month and vision 5/200 or worse who were randomized to early vitrectomy within 6 months or observation. The DRVS showed a clear benefit for early surgery in patients with type 1 diabetes, where a delay in surgical intervention more often led to aggressive fibrovascular proliferation and tractional retinal detachment. In this study, 25% of patients undergoing early PPV had a visual acuity of 20/40 or better as opposed to 15% of patients who underwent conventional therapy (observation unless there was a macula-off retinal detachment or NCVH >1 year) [14]. A more recent study showed that at least 87% of patients have an improvement of three lines or greater with a vitrectomy [18].

Commonly, vitreous hemorrhage will settle inferiorly out of the visual axis, or clear spontaneously through the zonules via aqueous outflow. In light of the DRVS results, many clinicians elect to operate after 1 month for type 1 diabetics and 3 months for type 2 diabetics. This, however, is a loose guideline as many other factors are considered prior to surgery: presenting vision, the vision and status of the fellow eye, previous panretinal photocoagulation, history of recurrent vitreous hemorrhage, the patient's daily visual demands, and coexisting conditions such as macula-involving or macula-threatening tractional retinal detachment or ghost cell glaucoma. In the latter scenarios, waiting for surgery may cause irreversible damage. Additionally, earlier surgery may be warranted for subhyaloid hemorrhage as these hemorrhages tend to be blocked from clearance via the anterior segment. The presence of anterior chamber neovascularization or long-standing vitreous hemorrhage with vitreous base fibrosis blocking the pathway for spontaneous drainage are other indications for early vitrectomy [19].

5.2.2 Tractional Retinal Detachment

Tractional retinal detachments (TRDs) occur from contraction of fibrovascular proliferation on the retina. These detachments tend to be slow growing or stable and can be monitored when they are outside the macula, especially if nasal [20] (Fig. 5.2). One study showed that only 14% of eyes with extramacular TRDs experienced a loss of vision within 1 year [21]. However, for TRDs that involve the macula or for progressively expanding TRDs that are threatening the macula, surgical intervention is usually warranted. A 2008 publication reported that in eyes with a TRD involving the macula, 57% achieved vision of 6/60 or better, whereas in eyes without a macular detachment, 84% could see 6/60 or better [22]. As expected, eyes with a recent history of foveal detachment had a better chance of visual recovery when compared to long-standing ones even if an equally good anatomical result was obtained [23].

Combined tractional and rhegmatogenous retinal detachments occur when the contracting force of the fibrovascular complexes create a retinal break. They can be more convex in configuration and extend further anteriorly [10]. Unlike purely tractional detachments, this kind of detachment can be rapidly progressive and prompt surgery is necessary. These surgeries tend to be complex as separating tightly adherent fibrotic tissue from mobile retina can be difficult and can have worse success rates than detachments without retinal breaks [24]. Despite this, postoperative vision in these patients may improve in up to 70% of eyes [20].

5.2.3 Diabetic Macular Edema

Diabetic macular edema (DME) is the leading cause of visual impairment in patients with diabetes [25, 26]. The role of the vitreous on the development of DME is unclear, but natural history studies have shown that macular edema is more likely to resolve with vitreomacular separation [27, 28]. Eyes with DME more commonly have an attached posterior hyaloid compared to eyes without DME [29]. Diabetic macular edema without clear traction is generally treated with anti-VEGF, intravitreal steroids, and/or focal laser (Fig. 5.3). However, some degree of vitreomacular traction is present in 12% of eyes with DME and up to 24% in eyes undergoing vitrectomy [30]. The subgroup of

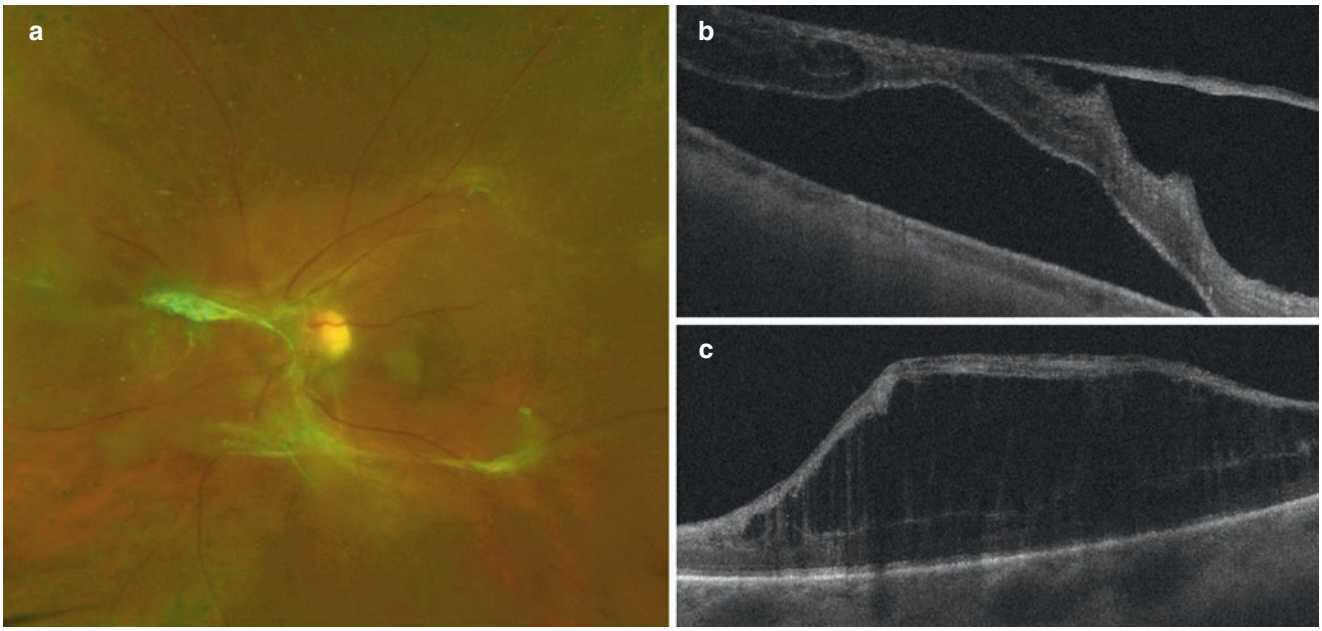

Fig. 5.2 A nasal tractional retinal detachment (**a**, **b**) and retinoschisis (**a**, **c**) in a patient with extensive preretinal fibrosis extending from the optic nerve head (**a**). The macula remained well attached without traction, and the patient had a visual acuity of 20/30, so surgery was deferred

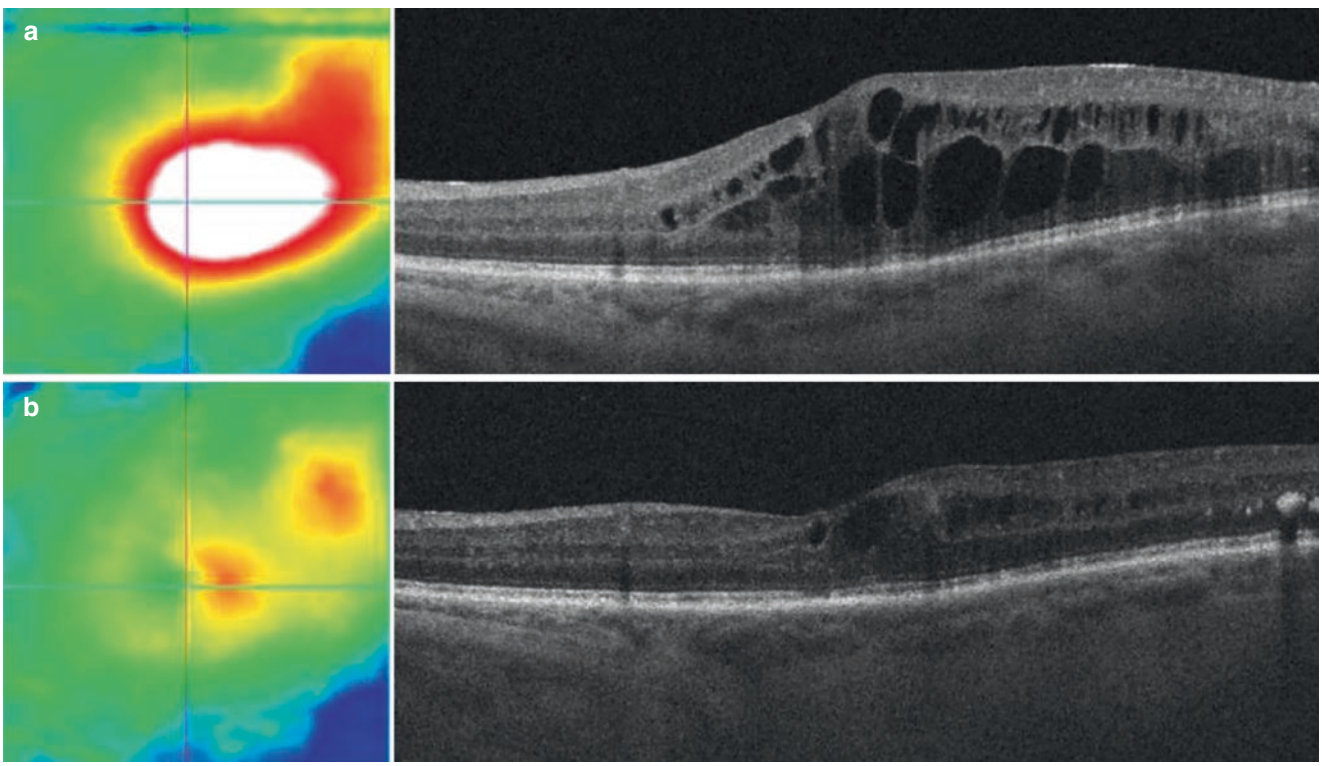

Fig. 5.3 This patient has center-involving diabetic macular edema without an epiretinal membrane (**a**). He underwent serial injections of intravitreal bevacizumab with anatomic and visual improvement (**b**)

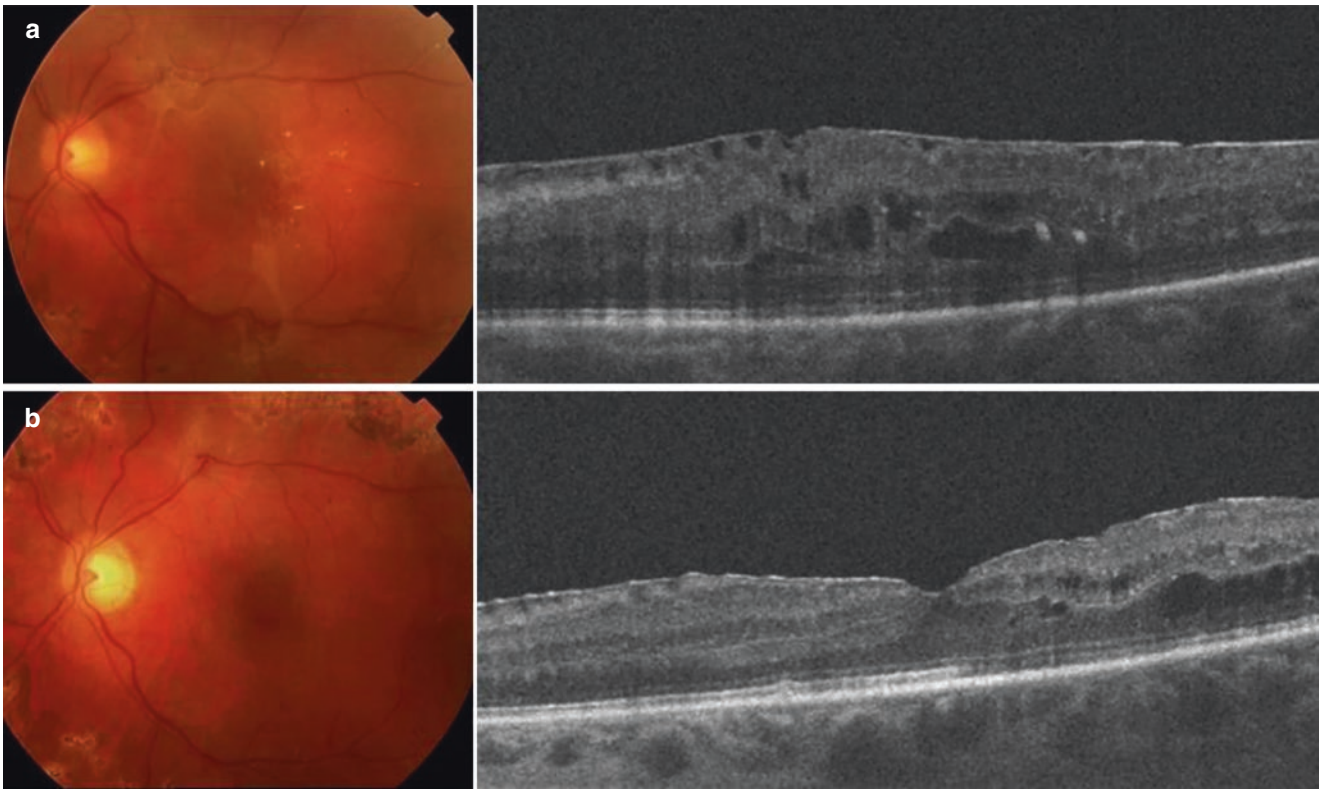

Fig. 5.4 This patient has center-involving diabetic macular edema with an epiretinal membrane (**a**). Her macular edema was refractory to multiple intravitreal injections of different anti-vascular endothelial growth factor (VEGF) agents, so she underwent vitrectomy with membrane peel. Subsequently, her vision improved from 20/80 to 20/50 (**b**). She continues to be treated with intravitreal anti-VEGF to maintain vision but has since developed a recurrent epiretinal membrane

eyes with a taut premacular posterior hyaloid or epiretinal membrane may benefit from vitrectomy [31] (Fig. 5.4). However, even in the absence of clear traction, vitrectomy may be helpful as removal of the vitreous can improve oxygenation and nutrition to the macula and reduce VEGF [32–35]. Vitreous viscosity is 300–2000 times greater than aqueous viscosity [36], which can allow intravitreal molecules such as VEGF to diffuse away from the macula more easily [37, 38]. Similarly, however, intravitreal drugs can also diffuse away from the retina reducing the effective half-life of these medications [39].

The anatomic and functional results of PPV for macular edema appear to vary. In a 2006 randomized controlled trial of PPV with internal limiting membrane (ILM) peeling versus treatment with focal laser, there was no difference in visual or anatomical results between the two treatment modalities [40]. On the other hand, a comparative study of vitrectomy with ILM peeling for diffuse clinically significant macular edema demonstrated structural improvement in foveal thickness and significant improvement in the macular volume but limited visual improvement 12 months postoperatively [41, 42]. Although not widely performed, the argument for ILM peeling for DME is to relieve tractional forces not visible biomicroscopically from preretinal vitreous or the ILM. As has been shown with previous studies, both functional and anatomic results have varied, with some studies showing benefit of ILM peel [43–47], while others did not [40–42, 48, 49].

A meta-analysis published in 2017 of all randomized clinical trials up to 2014 comparing PPV to focal macular laser or observation showed an improvement of approximately 100 μm in central macular thickness at 6 months for PPV compared to laser or observation; however, that gain was reversed by 12 months [25]. The same meta-analysis showed an insignificant two ETDRS letter vision gain for PPV over laser or observation [25].

Published data comparing macular laser with anti-VEGF treatment, which has become the gold standard for diabetic macular edema, showed an average gain of 6–7 letters at 6–12 months in favor of anti-VEGF therapy. Therefore, PPV does not appear to compare well to anti-VEGF based on historic data; however, it must be recognized that PPV is

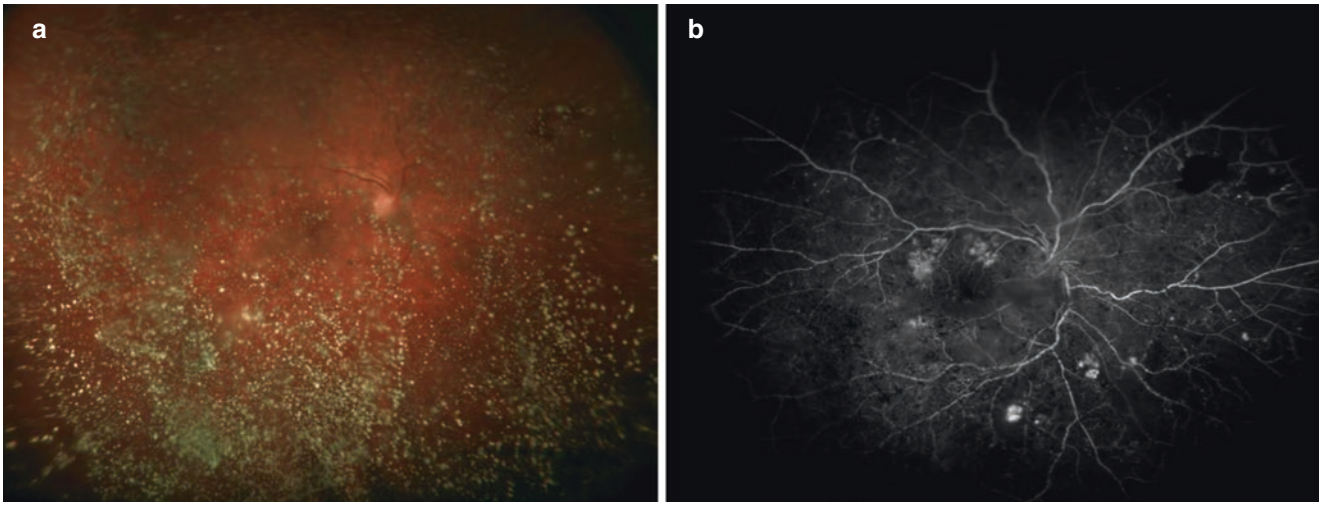

Fig. 5.5 This patient underwent vitrectomy in the right eye for asteroid hyalosis (**a**) that was limiting the view for retinal examination and adequate placement of in-office panretinal photocoagulation. Preoperative fluorescein angiography (**b**) confirmed multiple areas of neovascularization elsewhere

often reserved for patients who are refractive to injections or lasers. Further data comparing PPV with anti-VEGF therapy is needed to directly compare these treatment options.

5.2.4 Miscellaneous

5.2.4.1 Cataract

Patients with diabetes have a higher rate of cataract development than the average population [50]. It is not uncommon for the cataract and/or posterior synechiae from anterior segment neovascularization to limit examination of the retina and/or prevent adequate panretinal photocoagulation. In these situations, cataract surgery is needed. If there is significant posterior neovascularization, the rapid development of a posterior vitreous detachment that can happen with cataract surgery may sometimes lead to vitreous hemorrhage. Additionally, cataract surgery can worsen diabetic retinopathy. The presence of diabetic retinopathy should not be prohibitory to cataract surgery, but preoperative treatment with either laser and/or anti-VEGF medications may be warranted [50].

Combined cataract surgery and PPV can be done when the view to the retina is suboptimal from the dense cataract [51]. In these surgeries, it is particularly important to minimize phacoemulsification energy to keep the cornea as clear as possible for the retina surgery. Additionally, a more rigid three-piece intraocular lens and placing of a corneal suture at the main cataract incision can help keep the intraocular lens and globe stable during and following retinal surgery. There are varying views on the timing of intraocular lens—before vitrectomy or afterward. Placing the intraocular lens at the end of the procedure allows an improved view of the periphery through an aphakic eye and may be advantageous in anterior dissections [51].

5.2.4.2 Asteroid Hyalosis

Media opacities such as asteroid hyalosis may also limit or prevent adequate treatment of diabetic retinopathy (Fig. 5.5). In some instances, it may be necessary to perform a vitrectomy to improve the view in order to optimize treatment and attempt to preserve vision prior to the development of further complications.

5.3 Preoperative Considerations

5.3.1 Systemic Optimization

Patients with diabetic retinopathy requiring surgery are a difficult group to treat given they can be systemically unwell with multiple medical comorbidities. The 5-year survival of patients undergoing diabetic vitrectomy ranged from 68% to 86%, especially in the presence of coexisting heart and renal disease [52–57]. A more recent study showed that in this population, 39% have a history of stroke, 28% have a history myocardial infarction, and 43% have a history of renal failure [58]. In addition, many patients require anticoagulation and antiplatelet therapy, and the decision of whether to hold these

medications prior to surgery must be made in conjunction with the patient's primary care physician and/or cardiologist. Medical clearance by an internist and the anesthesiologist is recommended to ensure that the patient's health is optimized so they can more safely undergo surgery.

5.3.2 Ancillary Testing and Patient Expectation

In the case of media opacity such as vitreous hemorrhage, cataract, or hyphema, B-scan ultrasonography can be crucial to maximize preoperative clinical information to determine the surgical plan. The B-scan can reveal areas of traction, rhegmatogenous detachment, or anterior hyaloid fibrovascular proliferation [2] (Fig. 5.6).

In cases where there is a view, fluorescein angiography and, more recently, optical coherence tomography angiography can show macular ischemia which may limit ultimate vision despite anatomically successful surgery and the absence of macular edema. Structural optical coherence tomography showing integrity of the external limiting membrane and ellipsoid zone has also been shown to correlate well with postoperative best corrected visual acuity, while central foveal thickness and enlarged foveal avascular zone only exhibit a weak correlation [58].

Even with anatomically successful results, ultimate vision postoperatively may be limited by ischemia from chronic microvascular disease or atrophy from chronic anatomic abnormalities [6]. Patient expectations must be managed preoperatively. These various imaging modalities can often be helpful to establishing realistic patient expectations prior to going into surgery.

5.3.3 Preoperative Anti-VEGF

Prior to doing surgery, many providers will inject intravitreal anti-VEGF agents to minimize or eliminate progressive bleeding; however, in patients with underlying traction, the rapid regression of neovascular tissue can theoretically cause a "crunch phenomenon" [2], leading to new or worsening tractional detachments at a mean of 13 days following injection [59–63]. However, in the recently published DRCR.net protocol S trial, no patients were seen to experience the "crunch phenomenon" [64]. There is limited published evidence to guide the use of preoperative anti-VEGF, but expert opinion suggests limiting anti-VEGF to within 3 days of surgery and only in patients medically cleared for surgery [2, 6, 51, 65].

5.4 Surgical Techniques

In recent years, new preoperative and intraoperative instrumentation and surgical techniques have improved the manner in which retinal specialists treat diabetic retinopathy. The surgical goals for diabetic vitrectomy include removing any media opacities, relieving traction, removing or segmenting preretinal membranes, drainage of fluid through retinal holes or breaks when present, endolaser around breaks and for panretinal photocoagulation to decrease neovascular drive, and the placement of tamponade agents such as gas or silicone oil, if needed.

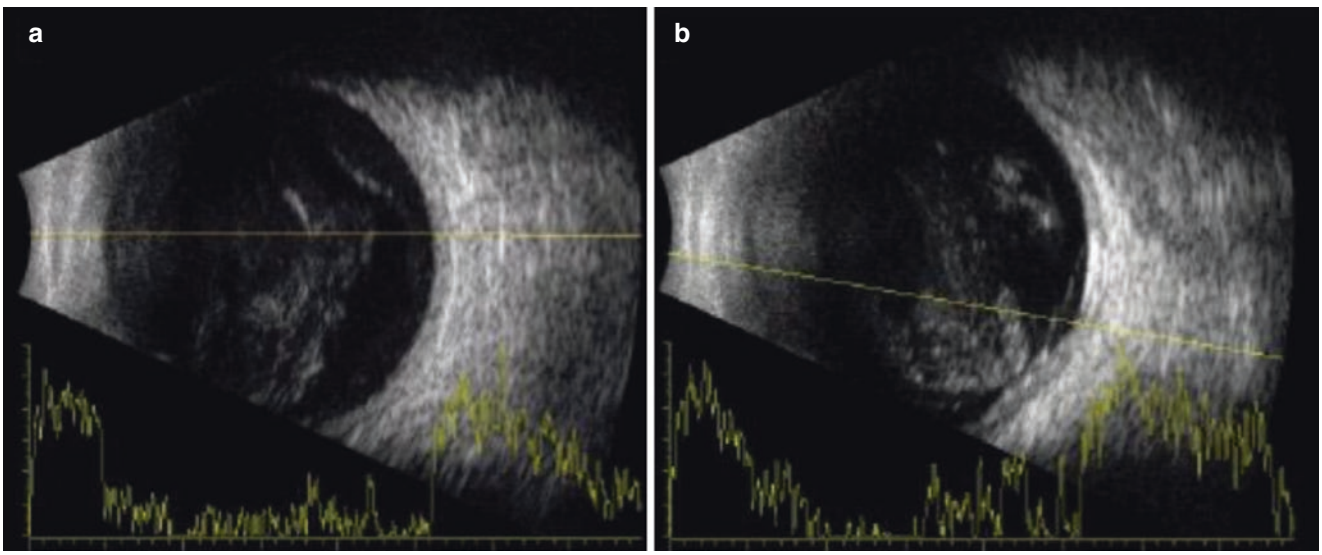

Fig. 5.6 This patient presented with a dense vitreous hemorrhage with no view to the posterior pole. B-scan ultrasonography showed a vitreous hemorrhage (**a**) with questionable area of traction inferotemporally (**b**)

A good vitrectomy is crucial in diabetic surgery. The typical diabetic vitreoretinal interface is abnormal. Triamcinolone acetonide can be used intraoperatively to better visualize the vitreous, especially in the case of vitreoschisis. Afterward, two general techniques are used to address fibrovascular membranes: segmentation and delamination.

1. *Segmentation* involves the vertical cutting of membranes between areas of retinal adherence into small segments either with the vitreous cutter or vertical scissors. The remaining fibrovascular stumps are then trimmed with the vitreous cutter leaving behind small, circumscribed remnants centered on neovascular pegs. Segmentation is necessary in situations where removal the fibrovascular membrane is impossible or too risky due to tight adherence or mobile retina. The disadvantage of segmentation is the residual islands of fibrovascular tissue that can reproliferate and bleed.
2. *Delamination* involves completely separating the vitreoretinal adhesions between the retina and fibrovascular proliferation either with peeling, horizontal scissors, a pick, or hydro-/viscodissection to gently remove the tissue from the retina. Diathermy may be needed in these cases to cauterize neovascular pegs to limit bleeding. The disadvantage of this technique is excessive hemorrhage and the risk of iatrogenic retinal tears if performed too aggressively [66]. Dyes such as indocyanine green, brilliant blue G, and trypan blue can be used to highlight preretinal membranes that cause traction.

Ultimately, endolaser photocoagulation is essential in the face of active neovascularization to decrease the neovascular drive and to circumscribe any areas of retinal breaks. In a prospective study of 174 consecutive vitrectomies, 39% of eyes were found to have a retinal break. In 27%, the breaks were posterior and occurred during membrane dissection, whereas 17% of eyes had entry site breaks [67].

Long-term tamponade such as gas or silicone oil can also be helpful in cases where there are multiple and/or large retinal defects, whether they were present preoperatively due to traction or created intraoperatively during retinal manipulation. In one study, 49% of eyes required internal tamponade, with air used in 8% of eyes, SF_6 gas in 24%, C_3F_8 gas in 10%, and silicone oil in 7% [22]. The use of silicone oil can also reduce the risk of postoperative phthisis in combined tractional-rhegmatogenous retinal detachments [20, 68]. Even in the absence of retinal breaks, the use of intraocular gas tamponade has been proposed to reduce postoperative hemorrhaging, albeit with variable results [69, 70]. In the case of silicone oil use, water-soluble growth factors can reach high concentrations in the thin fluid film between the retina and the silicone bubble, and consequently there can be an increased tendency for fibrovascular re-proliferation. Any sub-silicone oil fibrosis can be removed with silicone oil exchange or by direct peeling under silicone oil.

Modern vitrectomy machines have cut rates over 10,000 and a wide range of flow options [71]. High-cut rates with low aspiration allow for precise cutting in close proximity to the retina, resulting in reduced risk of retinal tear formation. The use of small gauge instrumentation with 25- or 27-gauge instruments can also provide precise segmentation and delamination of fibrovascular tissue without the use of multiple instruments [72]. With certain machines, the option of proportional reflux can be used for hydrodissection or viscodissection of preretinal fibrovascular plaques. Also, a bimanual technique, after placement of a chandelier or with use of lighted instruments, can be helpful, especially with strongly adherent fibrovascular tissue on a detached retina. A variety of instrumentation such as flex loops, retinal forceps, and retinal scissors are available for use offering numerous options for segmentation and delamination.

Mixed gauge surgery is also an option where 23- or 25-gauge trocars are used in conjunction with 23-/25- and 25-/27-gauge instrumentation. 27-gauge cutters can be advantageous in reaching tight spaces between preretinal membranes and retina and offer more precise maneuverability [2]. For more peripheral pathology or in situations where a stiffer instrument is needed, 23-/25-gauge instruments can still be used. Smaller gauge surgery with 27-gauge instrumentation has been shown to have lower intra- and postoperative complications with less bleeding, iatrogenic breaks, and hypotony [73].

Intraoperative OCT is a novel imaging technology that allows the surgeon to view real-time cross-sectional microstructure of the retina and vitreoretinal surface. The technology is still evolving but can be used in complex cases to help identify tissue planes, subclinical epiretinal- or internal-limiting membranes, subclinical detachments, and diagnosis of inadvertent macular hole formation [2, 6, 51, 74].

5.5 Surgical Complications

The first study on diabetic vitrectomy, DRVS, had a high complication rate with 20% of patients losing light perception vision [75]. The introduction of better visualization and illumination, diathermy, small gauge surgery, valved cannulas, and improved surgical techniques and instrumentation have drastically decreased the complication rate.

5.5.1 Intraoperative Complications

Maintaining hemostasis is an important concept in all of intraocular surgery; however, it is of particular importance in diabetic vitrectomy given the propensity for these eyes to

bleed given the fragile vessels and adherent fibrovascular tissue. Modern vitrectomy machines and packs include valved cannulas and the ability to control intraocular pressure, allowing hemostasis without using excessive diathermy. In addition, appropriately timed preoperative intravitreal anti-VEGF can also reduce the likelihood of intraocular bleeding from neovascularization [6].

In cases of dense vitreous hemorrhage where the chronic hemorrhage can be very thick, the vitreous can wrap around the vitrectomy cutter when passed through the cannulas. If this vitreous is not sufficiently removed before retracting the cutter, the extraneous vitreous can lock the cutter in the cannula, and any subsequent forceful pulling can dislodge the cannula with the vitrector causing significant traction leading to adjacent retinal tears [6]. Extra care must be taken to identify and treat any inadvertent tears that may be created during the surgery.

Similarly, the tight abnormal posterior hyaloid adhesion to the retina predisposes the retina to iatrogenic tears and retinal detachments, especially in maneuvers that emphasize anterior-posterior traction. The rate of iatrogenic tears has been reported to range from 20% to 41% [22, 24, 76, 77]. If found, traction adjacent to the retinal breaks should be relieved and the breaks then encircled with endolaser.

Loss of adequate visualization can make any PPV difficult. This is particularly important in diabetic vitrectomy given the challenging and sometimes lengthy nature of the surgery and the need to have intermittent intraocular pressure elevation to achieve hemostasis. Therefore, intraoperative corneal edema and osmotic cataract can be real concerns [78]. Occasionally, removal of the corneal epithelium is necessary to improve intraoperative view [79]. While corneal epithelium in healthy individuals regenerates within days, the epithelial defect in patients with diabetes can become a non-healing corneal abrasion requiring bandage contact lens placement and antibiotic care to prevent against discomfort and corneal ulcers, scars, and even melt [79, 80]. Adding 50% dextrose to the BSS infusion bottle can help prevent loss of view from the lens in phakic patients [81].

Prior to the advent of small incision vitrectomy, vitreous and retinal incarcerations at the site of large sclerotomy wounds were also possible. These large sclerotomies also allowed for fibrovascular ingrowth in extremely ischemic eyes, and manipulation without cannulas would induce vitreous traction and lead to subincisional retinal tears [73]. This, fortunately, is much less common with advances in modern vitrectomy.

5.5.2 Postoperative Complications

5.5.2.1 Vitreous Hemorrhage

Vitreous hemorrhage is a common postoperative complication, occurring in 5–63% of eyes, almost half presenting on the first postoperative day [22, 63, 82–87]. Immediate postoperative hemorrhage, often called "shake-out" hemorrhage, usually resolves spontaneously over a few weeks. Periodic ultrasonography in the case of no retinal view should be performed to exclude a retinal detachment, which would require prompt surgery given rapid progression in a post-vitrectomized eye. Early postoperative hemorrhage typically results from dispersion of difficult to remove blood from the peripheral vitreous skirt and from inadequately diathermized vessels and fibrovascular complexes, which can be further exacerbated by postoperative hypotony or changes in intraocular pressure during sclerotomy closure [87]. Causes of late postoperative hemorrhage include fibrovascular ingrowth into sclerotomies as noted above, more common prior to small gauge vitrectomy [88–91], and persistent neovascularization from residual fibrovascular tissue [85]. Variable evidence exists for whether preoperative anti-VEGF decreases the risk of postoperative bleeding with some studies supporting no benefit [63, 85] and some studies reporting a reduction in early postoperative bleeding [82].

5.5.2.2 Retinal Detachment

A rhegmatogenous retinal detachment (RRD) extending from the periphery is uncommon in the presence of existing panretinal photocoagulation and is more likely to be found posterior due to unrecognized retinal breaks. The rate of postoperative detachments has been found to range from 4.3% to 8.1% [76, 92, 93]. The risk of RRD following diabetic vitrectomy appears to be declining, probably due to the use of wide-angle viewing systems, which allow for more accurate examination of the peripheral retina [93].

5.5.2.3 Cornea

The incidence of corneal complications following a diabetic vitrectomy has been reported to be as high as 50% [94] and can be due to delayed epithelial regeneration and abnormal neurotrophic status [95]. Additionally, diabetics have been found to have structurally and functionally abnormal corneal endothelial cells that are susceptible to damage and this can translate to the health of the corneal epithelium which require the endothelial pump to remain healthy [96–98]. The use of silicone oil in complicated detachments can also lead to band keratopathy.

5.5.2.4 Miscellaneous

- Expedited cataract progression following diabetic vitrectomy is common and should be promptly treated not only for visual rehabilitation but also to allow adequate examinations of the retina.
- Postoperative epiretinal membranes in eyes with appropriate visual potential can undergo subsequent surgical management if they cause visually significant distortion or blurry vision.

– Elevated intraocular pressure can happen after any intraocular surgery either due to endotamponade agent or by obstruction of the ocular drainage system; however, diabetic optic nerve heads have also been found to have impaired flow autoregulation that makes them especially prone to changes in intraocular pressure [99].

References

1. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet. 2010;376:124–36. https://doi.org/10.1016/S0140-6736(09)62124-3.
2. Codenotti M, Iuliano L, Maestranzi G. Surgical management and techniques. Manag Diab Retinop. 2017;60:143–59. https://doi.org/10.1159/000459702.
3. Diabetes Control and Complications Trial Research Group. Progression of retinopathy with intensive versus conventional treatment in the diabetes control and complications trial. Ophthalmology. 1995;102:647–61. https://doi.org/10.1016/S0161-6420(95)30973-6.
4. Group BMJP. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998;317:703–13. https://doi.org/10.1136/bmj.317.7160.703.
5. Zoungas S, Arima H, Gerstein HC, et al. Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. Lancet Diabetes Endocrinol. 2017;5:431–7. https://doi.org/10.1016/S2213-8587(17)30104-3.
6. Oellers P, Mahmoud T. Surgery for proliferative diabetic retinopathy: new tips and tricks. J Ophthalmic Vis Res. 2016;11:93–7. https://doi.org/10.4103/2008-322X.180697.
7. Flynn HW, Chew EY, Simons BD, et al. Pars plana vitrectomy in the early treatment diabetic retinopathy study. ETDRS report number 17. The Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology. 1992;99:1351–7.
8. Akiba J, Arzabe CW, Trempe CL. Posterior vitreous detachment and neovascularization in diabetic retinopathy. Ophthalmology. 1990;97:889–91.
9. Ono R, Kakehashi A, Yamagami H, et al. Prospective assessment of proliferative diabetic retinopathy with observations of posterior vitreous detachment. Int Ophthalmol. 2005;26:15–9. https://doi.org/10.1007/s10792-005-5389-2.
10. Rami El H, Barham R, Sun JK, Silva PS. Evidence-based treatment of diabetic retinopathy. Semin Ophthalmol. 2017;32:67–74. https://doi.org/10.1080/08820538.2016.1228397.
11. Helbig H, Sutter FKP. Surgical treatment of diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol. 2004;242:704–9. https://doi.org/10.1007/s00417-004-0977-9.
12. Huang C-H, Hsieh Y-T, Yang C-M. Vitrectomy for complications of proliferative diabetic retinopathy in young adults: clinical features and surgical outcomes. Graefes Arch Clin Exp Ophthalmol. 2017;255:863–71. https://doi.org/10.1007/s00417-016-3579-4.
13. Machemer R, Buettner H, Norton EW, Parel JM. Vitrectomy: a pars plana approach. Trans Am Acad Ophthalmol Otolaryngol. 1971;75:813–20.
14. Two-year course of visual acuity in severe proliferative diabetic retinopathy with conventional management. Diabetic Retinopathy Vitrectomy Study (DRVS) report #1. Ophthalmology. 1985;92:492–502.
15. Early vitrectomy for severe proliferative diabetic retinopathy in eyes with useful vision. Clinical application of results of a randomized trial--diabetic retinopathy vitrectomy study report 4. The Diabetic Retinopathy Vitrectomy Study Research Group. Ophthalmology. 1988a;95:1321–34.
16. Early vitrectomy for severe vitreous hemorrhage in diabetic retinopathy. Four-year results of a randomized trial: diabetic Retinopathy Vitrectomy Study Report 5. Arch Ophthalmol. 1990;108:958–64.
17. Early vitrectomy for severe proliferative diabetic retinopathy in eyes with useful vision. Results of a randomized trial--diabetic retinopathy vitrectomy study report 3. The Diabetic Retinopathy Vitrectomy Study Research Group. Ophthalmology. 1988b;95:1307–20.
18. Gupta B, Sivaprasad S, Wong R, et al. Visual and anatomical outcomes following vitrectomy for complications of diabetic retinopathy: the DRIVE UK Study. Eye. 2012;26:510–6. https://doi.org/10.1038/eye.2011.321.
19. Landers MB, Perraki AD. Management of post-vitrectomy persistent vitreous hemorrhage in pseudophakic eyes. Am J Ophthalmol. 2003;136:989–93. https://doi.org/10.1016/S0002-9394(03)00718-9.
20. Yang C-M, Su P-Y, Yeh P-T, Chen M-S. Combined rhegmatogenous and traction retinal detachment in proliferative diabetic retinopathy: clinical manifestations and surgical outcome. Can J Ophthalmol. 2008;43:192–8. https://doi.org/10.3129/i08-007.
21. Charles S, Flinn CE. The natural history of diabetic extramacular traction retinal detachment. Arch Ophthalmol. 1981;99:66–8. https://doi.org/10.1001/archopht.1981.03930010068003.
22. Yorston D, Wickham L, Benson S, et al. Predictive clinical features and outcomes of vitrectomy for proliferative diabetic retinopathy. Br J Ophthalmol. 2008;92:365–8. https://doi.org/10.1136/bjo.2007.124495.
23. Cohen HB, McMeel JW, Franks EP. Diabetic traction detachment. Arch Ophthalmol. 1979;97:1268–72. https://doi.org/10.1001/archopht.1979.01020020010002.
24. Ramezani A, Ahmadieh H, Rozegar A, et al. Predictors and outcomes of vitrectomy and silicone oil injection in advanced diabetic retinopathy. Korean J Ophthalmol. 2017;31:217–29. https://doi.org/10.3341/kjo.2016.0018.
25. Jackson TL, Nicod E, Angelis A, et al. Pars plana vitrectomy for diabetic macular edema: a systematic review, meta-analysis, and synthesis of safety literature. Retina. 2017;37:886–95. https://doi.org/10.1097/IAE.0000000000001280.
26. Klein R, Klein BE, Moss SE, et al. The Wisconsin epidemiologic study of diabetic retinopathy. IV. Diabetic macular edema. Ophthalmology. 1984;91:1464–74.
27. Hikichi T, Fujio N, Akiba J, et al. Association between the short-term natural history of diabetic macular edema and the vitreomacular relationship in type II diabetes mellitus. Ophthalmology. 1997;104:473–8. https://doi.org/10.1016/S0161-6420(97)30289-9.
28. Nasrallah FP, Jalkh AE, Van Coppenolle F, et al. The role of the vitreous in diabetic macular edema. Ophthalmology. 1988;95:1335–9.
29. Sivaprasad S, Ockrim Z, Massaoutis P, et al. Posterior hyaloid changes following intravitreal triamcinolone and macular laser for diffuse diabetic macular edema. Retina. 2008;28:1435–42. https://doi.org/10.1097/IAE.0b013e31817f2dae.
30. Jackson TL, Nicod E, Angelis A, et al. Vitreous attachment in age-related macular degeneration, diabetic macular edema, and retinal vein occlusion: a systematic review and meta-analysis. Retina. 2013;33:1099–108. https://doi.org/10.1097/IAE.0b013e31828991d6.
31. Pendergast SD, Hassan TS, Williams GA, et al. Vitrectomy for diffuse diabetic macular edema associated with a taut premacular posterior hyaloid. Am J Ophthalmol. 2000;130:178–86. https://doi.org/10.1016/S0002-9394(00)00472-4.
32. Simpson ARH, Dowell NG, Jackson TL, et al. Measuring the effect of pars plana vitrectomy on vitreous oxygenation using magnetic resonance imaging. Invest Ophthalmol Vis Sci. 2013;54:2028–34. https://doi.org/10.1167/iovs.12-11258.

33. Stefansson E, Landers MB, Wolbarsht ML. Increased retinal oxygen supply following pan-retinal photocoagulation and vitrectomy and lensectomy. Trans Am Ophthalmol Soc. 1981;79:307–34.
34. Stefansson E, Landers MB, Wolbarsht ML. Vitrectomy, lensectomy, and ocular oxygenation. Retina. 1982;2:159–66.
35. Stefansson E, Novack RL, Hatchell DL. Vitrectomy prevents retinal hypoxia in branch retinal vein occlusion. Invest Ophthalmol Vis Sci. 1990;31:284–9.
36. Lee B, Litt M, Buchsbaum G. Rheology of the vitreous body: Part 2. Viscoelasticity of bovine and porcine vitreous. Biorheology. 2017;31:327–38. https://doi.org/10.3233/BIR-1994-31403.
37. Lee SS, Ghosn C, Yu Z, et al. Vitreous VEGF clearance is increased after vitrectomy. Invest Ophthalmol Vis Sci. 2010;51:2135–8. https://doi.org/10.1167/iovs.09-3582.
38. Stefánsson E. Physiology of vitreous surgery. Graefes Arch Clin Exp Ophthalmol. 2008;247:147–63. https://doi.org/10.1007/s00417-008-0980-7.
39. Beer PM, Bakri SJ, Singh RJ, et al. Intraocular concentration and pharmacokinetics of triamcinolone acetonide after a single intravitreal injection. Ophthalmology. 2003;110:681–6. https://doi.org/10.1016/S0161-6420(02)01969-3.
40. Kumar A, Sinha S, Azad R, et al. Comparative evaluation of vitrectomy and dye-enhanced ILM peel with grid laser in diffuse diabetic macular edema. Graefes Arch Clin Exp Ophthalmol. 2006;245:360–8. https://doi.org/10.1007/s00417-006-0456-6.
41. Patel JI, Hykin PG, Schadt M, et al. Pars plana vitrectomy with and without peeling of the inner limiting membrane for diabetic macular edema. Retina. 2006a;26:5–13. https://doi.org/10.1097/00006982-200601000-00002.
42. Patel JI, Hykin PG, Schadt M, et al. Diabetic macular oedema: pilot randomised trial of pars plana vitrectomy vs macular argon photocoagulation. Eye. 2006b;20:873–81. https://doi.org/10.1038/sj.eye.6702012.
43. Bahadir M, Ertan A, Mertoğlu O. Visual acuity comparison of vitrectomy with and without internal limiting membrane removal in the treatment of diabetic macular edema. Int Ophthalmol. 2005;26:3–8. https://doi.org/10.1007/s10792-006-0008-4.
44. Bardak Y, Cekiç O, Tiğ SU. Comparison of ICG-assisted ILM peeling and triamcinolone-assisted posterior vitreous removal in diffuse diabetic macular oedema. Eye. 2006;20:1357–9. https://doi.org/10.1038/sj.eye.6702152.
45. Doi N, Sakamoto T, Sonoda Y, et al. Comparative study of vitrectomy versus intravitreous triamcinolone for diabetic macular edema on randomized paired-eyes. Graefes Arch Clin Exp Ophthalmol. 2012;250:71–8. https://doi.org/10.1007/s00417-011-1777-7.
46. Thomas D, Bunce C, Moorman C, Laidlaw DAH. A randomised controlled feasibility trial of vitrectomy versus laser for diabetic macular oedema. Br J Ophthalmol. 2005;89:81–6. https://doi.org/10.1136/bjo.2004.044966.
47. Ulrich JN. Pars plana vitrectomy with internal limiting membrane peeling for nontractional diabetic macular edema. Open Ophthalmol J. 2017;11:5–10. https://doi.org/10.2174/1874364101711010005.
48. Figueroa MS, Contreras I, Noval S. Surgical and anatomical outcomes of pars plana vitrectomy for diffuse nontractional diabetic macular edema. Retina. 2008;28:420–6. https://doi.org/10.1097/IAE.0b013e318159e7d2.
49. Hoerauf H, Brüggemann A, Muecke M, et al. Pars plana vitrectomy for diabetic macular edema. Internal limiting membrane delamination vs posterior hyaloid removal. A prospective randomized trial. Graefes Arch Clin Exp Ophthalmol. 2011;249:997–1008. https://doi.org/10.1007/s00417-010-1610-8.
50. Pollreisz A, Schmidt-Erfurth U. Diabetic cataract-pathogenesis, epidemiology and treatment. J Ophthalmol. 2010;2010:608751–8. https://doi.org/10.1155/2010/608751.
51. Berrocal MH, Acaba LA, Acaba A. Surgery for diabetic eye complications. Curr Diab Rep. 2016;16:99. https://doi.org/10.1007/s11892-016-0787-6.
52. Banerjee PJ, Moya R, Bunce C, et al. Long-term survival rates of patients undergoing vitrectomy for proliferative diabetic retinopathy. Ophthalmic Epidemiol. 2016;23:94–8. https://doi.org/10.3109/09286586.2015.1089578.
53. Gollamudi SR, Smiddy WE, Schachat AP, et al. Long-term survival rate after vitreous surgery for complications of diabetic retinopathy. Ophthalmology. 1991;98:18–22.
54. Helbig H, Kellner U, Bornfeld N, Foerster MH. Life expectancy of diabetic patients undergoing vitreous surgery. Br J Ophthalmol. 1996;80:640–3.
55. Lux A, Ostri C, Dyrberg E, et al. Survival rates after diabetic vitrectomy compared with standard diabetes and general populations. Acta Ophthalmol (Oxf). 2012;90:e650–2. https://doi.org/10.1111/j.1755-3768.2012.02404.x.
56. Summanen P, Karhunen U, Laatikainen L. Characteristics and survival of diabetic patients undergoing vitreous surgery. Acta Ophthalmol (Oxf). 1987;65:197–202.
57. Uchio E, Inamura M, Ohno S, et al. Survival rate after vitreous surgery in patients with diabetic retinopathy. Ophthalmologica. 1993;206:83–8.
58. Shah VA, Brown JS, Mahmoud TH. Correlation of outer retinal microstucture and foveal thickness with visual acuity after pars plana vitrectomy for complications of proliferative diabetic retinopathy. Retina. 2012;32:1775–80. https://doi.org/10.1097/IAE.0b013e318255068a.
59. Arevalo JF, Maia M, Flynn HW, et al. Tractional retinal detachment following intravitreal bevacizumab (Avastin) in patients with severe proliferative diabetic retinopathy. Br J Ophthalmol. 2008;92:213–6. https://doi.org/10.1136/bjo.2007.127142.
60. Arevalo JF, Wu L, Sanchez JG, et al. Intravitreal bevacizumab (Avastin) for proliferative diabetic retinopathy: 6-months follow-up. Eye. 2009;23:117–23. https://doi.org/10.1038/sj.eye.6702980.
61. Mitamura Y, Ogata K, Oshitari T, et al. Retinal detachment with macular hole following intravitreal bevacizumab in patient with severe proliferative diabetic retinopathy. Br J Ophthalmol. 2008;92:717–8. https://doi.org/10.1136/bjo.2008.139378.
62. Moradian S, Ahmadieh H, Malihi M, et al. Intravitreal bevacizumab in active progressive proliferative diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol. 2008;246:1699–705. https://doi.org/10.1007/s00417-008-0914-4.
63. Oshima Y, Shima C, Wakabayashi T, et al. Microincision vitrectomy surgery and intravitreal bevacizumab as a surgical adjunct to treat diabetic traction retinal detachment. Ophthalmology. 2009;116:927–38. https://doi.org/10.1016/j.ophtha.2008.11.005.
64. Writing Committee for the Diabetic Retinopathy Clinical Research Network, Gross JG, Glassman AR, et al. Panretinal photocoagulation vs intravitreous ranibizumab for proliferative diabetic retinopathy. JAMA. 2015;314:2137–46. https://doi.org/10.1001/jama.2015.15217.
65. Sharma T, Fong A, Lai TY, et al. Surgical treatment for diabetic vitreoretinal diseases: a review. Clin Experiment Ophthalmol. 2016;44:340–54. https://doi.org/10.1111/ceo.12752.
66. Jackson TL, Johnston RL, Donachie PHJ, et al. The Royal College of Ophthalmologists' National ophthalmology database study of vitreoretinal surgery: report 6, diabetic vitrectomy. JAMA Ophthalmol. 2016;134:79–85. quiz 120. https://doi.org/10.1001/jamaophthalmol.2015.4587.
67. Sima P, Zoran T. Long-term results of vitreous surgery for proliferative diabetic retinopathy. Doc Ophthalmol. 1994;87:223–32.

68. Douglas MJ, Scott IU, Flynn HW. Pars plana lensectomy, pars plana vitrectomy, and silicone oil tamponade as initial management of cataract and combined traction/rhegmatogenous retinal detachment involving the macula associated with severe proliferative diabetic retinopathy. Ophthalmic Surg Lasers Imaging. 2003;34:270–8.
69. Balakrishnan D, Jain B, Nayaka A, et al. Role of tamponade in vitrectomy for proliferative diabetic retinopathy with vitreous hemorrhage. Semin Ophthalmol. 2017;32:488–91. https://doi.org/10.3109/08820538.2015.1120757.
70. Yang C-M, Yeh P-T, Yang C-H. Intravitreal long-acting gas in the prevention of early postoperative vitreous hemorrhage in diabetic vitrectomy. Ophthalmology. 2007;114:710–5. https://doi.org/10.1016/j.ophtha.2006.07.047.
71. Hubschman J-P, Gupta A, Bourla DH, et al. 20-, 23-, and 25-gauge vitreous cutters: performance and characteristics evaluation. Retina. 2008;28:249–57. https://doi.org/10.1097/IAE.0b013e31815ec2b3.
72. Mikhail M, Ali-Ridha A, Chorfi S, Kapusta MA. Long-term outcomes of sutureless 25-G+ pars-plana vitrectomy for the management of diabetic tractional retinal detachment. Graefes Arch Clin Exp Ophthalmol. 2017;255:255–61. https://doi.org/10.1007/s00417-016-3442-7.
73. Berrocal MH. All-probe vitrectomy dissection techniques for diabetic tractional retinal detachments: lift and shave. Retina. 2017;38:s2. https://doi.org/10.1097/IAE.0000000000001884.
74. Falkner-Radler CI, Glittenberg C, Gabriel M, Binder S. Intrasurgical microscope-integrated spectral domain optical coherence tomography-assisted membrane peeling. Retina. 2015;35:2100–6. https://doi.org/10.1097/IAE.0000000000000596.
75. Charles S. Diabetic retinopathy vitrectomy study. Arch Ophthalmol. 1986;104:486–8.
76. Kamura Y, Sato Y, Deguchi Y, Yagi F. Iatrogenic retinal breaks during 20-gauge vitrectomy for proliferative diabetic retinopathy. Clin Ophthalmol. 2012;7:29. https://doi.org/10.2147/OPTH.S38784.
77. Kharrat W, Turki K, Ben Amor H, et al. Use of silicone oil in vitreal hemorrhage complicating proliferated diabetic retinopathy. J Fr Ophtalmol. 2009;32:98–103. https://doi.org/10.1016/j.jfo.2009.01.002.
78. Gupta V. Surgical management of diabetic retinopathy. Middle East Afr J Ophthalmol. 2013;20:283. https://doi.org/10.4103/0974-9233.120003.
79. Chen W-L, Lin C-T, Ko P-S, et al. In vivo confocal microscopic findings of corneal wound healing after corneal epithelial debridement in diabetic vitrectomy. Ophthalmology. 2009;116:1038–47. https://doi.org/10.1016/j.ophtha.2009.01.002.
80. Chen H-F, Yeung L, Yang K-J, Sun C-C. Persistent corneal epithelial defect after pars plana vitrectomy. Retina. 2016;36:148–55. https://doi.org/10.1097/IAE.0000000000000657.
81. Haimann MH, Abrams GW. Prevention of lens opacification during diabetic vitrectomy. Ophthalmology. 1984;91:116–21.
82. Ahmadieh H, Shoeibi N, Entezari M, Monshizadeh R. Intravitreal bevacizumab for prevention of early postvitrectomy hemorrhage in diabetic patients: a randomized clinical trial. Ophthalmology. 2009;116:1943–8. https://doi.org/10.1016/j.ophtha.2009.07.001.
83. Khuthaila MK, Hsu J, Chiang A, et al. Postoperative vitreous hemorrhage after diabetic 23-gauge pars plana vitrectomy. Am J Ophthalmol. 2013;155:757–63– 763.e1–2. https://doi.org/10.1016/j.ajo.2012.11.004.
84. Lee BJ, Yu HG. Vitreous hemorrhage after the 25-gauge transconjunctival sutureless vitrectomy for proliferative diabetic retinopathy. Retina. 2010;30:1671–7. https://doi.org/10.1097/IAE.0b013e3181dcfb79.
85. Lo WR, Kim SJ, Aaberg TM, et al. Visual outcomes and incidence of recurrent vitreous hemorrhage after vitrectomy in diabetic eyes pretreated with bevacizumab (avastin). Retina. 2009;29:926–31. https://doi.org/10.1097/IAE.0b013e3181a8eb88.
86. Sato T, Morita S-I, Bando H, et al. Early vitreous hemorrhage after vitrectomy with preoperative intravitreal bevacizumab for proliferative diabetic retinopathy. Middle East Afr J Ophthalmol. 2013;20:51–5. https://doi.org/10.4103/0974-9233.106387.
87. Sato T, Tsuboi K, Nakashima H, Emi K. Characteristics of cases with postoperative vitreous hemorrhage after 25-gauge vitrectomy for repair of proliferative diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol. 2017;255:665–71. https://doi.org/10.1007/s00417-016-3522-8.
88. Bhende M, Agraharam SG, Gopal L, et al. Ultrasound biomicroscopy of sclerotomy sites after pars plana vitrectomy for diabetic vitreous hemorrhage. Ophthalmology. 2000;107:1729–36.
89. Hershberger VS, Augsburger JJ, HUTCHINS RK, et al. Fibrovascular ingrowth at sclerotomy sites in vitrectomized diabetic eyes with recurrent vitreous hemorrhage: ultrasound biomicroscopy findings. Ophthalmology. 2004;111:1215–21. https://doi.org/10.1016/j.ophtha.2003.08.043.
90. Krieger AE. The pars plana incision: experimental studies, pathologic observations, and clinical experience. Trans Am Ophthalmol Soc. 1991;89:549–621.
91. Rezende FA, Qian CX, Robert M-C. Fibrovascular ingrowth after 25-gauge transconjunctival vitrectomy in proliferative diabetic retinopathy. Ophthal Surg Lasers Imag Retina. 2013;44:405–8. https://doi.org/10.3928/23258160-20130604-03.
92. Hsu Y-J, Hsieh Y-T, Yeh P-T, et al. Combined tractional and rhegmatogenous retinal detachment in proliferative diabetic retinopathy in the anti-VEGF era. J Ophthalmol. 2014;2014:917375–11. https://doi.org/10.1155/2014/917375.
93. Schrey S, Krepler K, Wedrich A. Incidence of rhegmatogenous retinal detachment after vitrectomy in eyes of diabetic patients. Retina. 2006;26:149–52.
94. Hiraoka M, Amano S, Oshika T, et al. Factors contributing to corneal complications after vitrectomy in diabetic patients. Jpn J Ophthalmol. 2001;45:492–5.
95. Chiang W-Y, Lee J-J, Kuo H-K, et al. Factors associated with corneal epithelial defects after pars plana vitrectomy. Int Ophthalmol. 2017;116:1038–6. https://doi.org/10.1007/s10792-016-0429-7.
96. Larsson LI, Bourne WM, Pach JM, Brubaker RF. Structure and function of the corneal endothelium in diabetes mellitus type I and type II. Arch Ophthalmol. 1996;114:9–14.
97. Módis L, Szalai E, Kertész K, et al. Evaluation of the corneal endothelium in patients with diabetes mellitus type I and II. Histol Histopathol. 2010;25:1531–7. https://doi.org/10.14670/HH-25.1531.
98. Roszkowska AM, Tringali CG, Colosi P, et al. Corneal endothelium evaluation in type I and type II diabetes mellitus. Ophthalmologica. 1999;213:258–61.
99. Hashimoto R, Sugiyama T, Masahara H, et al. Impaired autoregulation of blood flow at the optic nerve head during vitrectomy in patients with type 2 diabetes. Am J Ophthalmol. 2017;181:125–33. https://doi.org/10.1016/j.ajo.2017.06.021.

Retinal Detachment and PVR

6

Peiquan Zhao

6.1 Introduction

Retinal detachment refers to a separation of the neurosensory retina from the underlying retinal pigment epithelium (RPE). Based on the underlying cause, retinal detachment can be categorized into three types, rhegmatogenous retinal detachment (RRD), traction retinal detachment, and exudative retinal detachment. Combined subtypes of retinal detachment can sometimes occur. RRD often causes severe visual loss [1, 2].

Proliferative vitreoretinopathy (PVR) was identified as an independent clinical entity in 1983 by the Retina Society Terminology Committee [3]. PVR is complicated in 5–12% eyes with RRD and is listed as a prognostic factor failure of retinal detachment repair. Further, PVR remains the major complication after retinal detachment surgery [3, 4].

This chapter discusses RRD and PVR with regard to etiopathogenesis, clinical features, and management.

6.2 Etiopathogenesis

RRD may be associated with three factors: (1) full-thickness retinal break in the neurosensory retina, (2) the existence of tractional forces on the edges of the tear, (3) and vitreous fluid entering the subretinal space [5].

The development of PVR involves cellular migration and proliferation, which in turn leads to fibrocellular membrane contraction [6, 7].

6.3 PVR Classification and Retinal Detachment (Figs. 6.1, 6.2, and 6.3)

There are mainly three classification systems of PVR among which the updated Retina Society Classification has been mostly cited in the literature [3, 4]. Severity, location, and morphological type are factors in the classification system [4, 8] (Table 6.1).

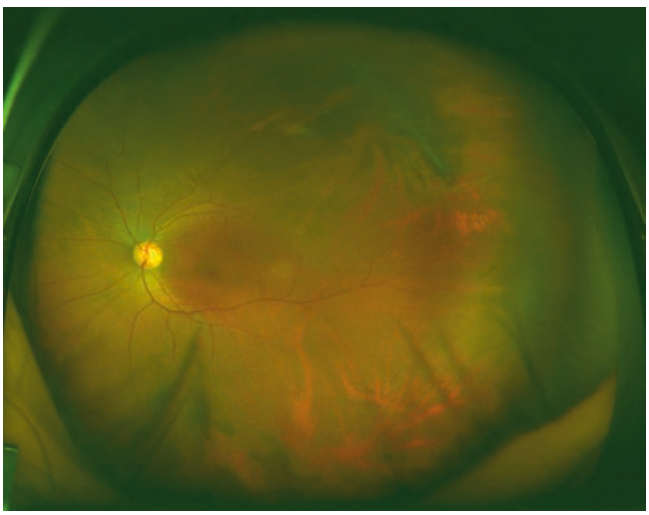

Fig. 6.1 Fundus photograph by Optos shows a horseshoe tear in the temporal periphery with peripheral local retinal detachment and PVR A

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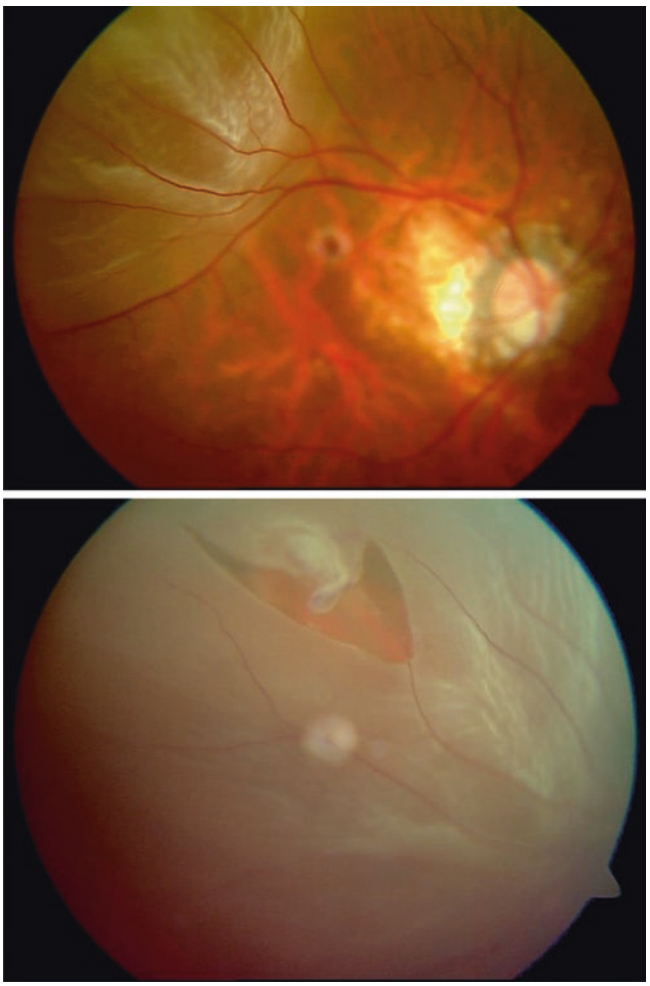

Fig. 6.2 Fundus photographs show retinal detachment in the temporal periphery (upper figure) with a 3 disc diameter (DD) horseshoe tear. PVR B is graded concerning the wrinkling of inner retinal surface and rolled and irregular edge of retinal break (lower figure)

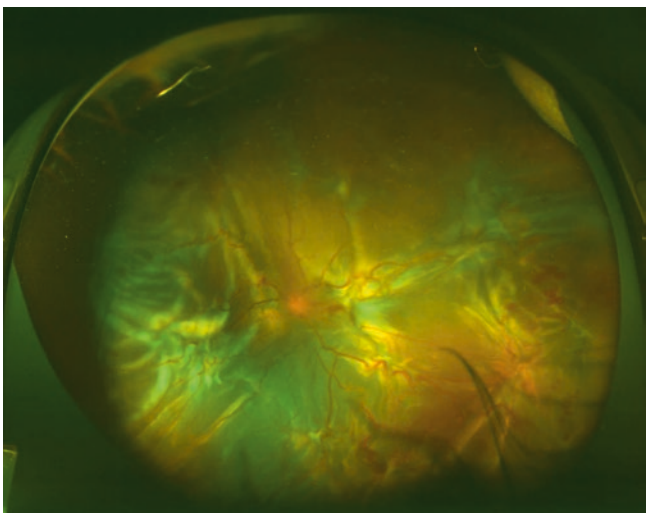

Fig. 6.3 Fundus photograph by Optos shows total retinal detachment. PVR C (A and P) is graded concerning the full-thickness retinal folds

Table 6.1 The updated Retina Society Classification of PVR

Grade and type	Clinical signs
A	Vitreous haze and pigment clumps
B	Wrinkling of inner retinal surface, retinal stiffness, vessel tortuosity, rolled and irregular edge of retinal break, and decreased mobility of vitreous
CP (posterior)	Full-thickness retinal folds or subretinal strands posterior to equator (1–12 clock hours involvement)
(1) Type:	
(a) Focal	(1) Starfolds posterior to vitreous base
(b) Diffuse	(2) Confluent starfolds posterior to vitreous base; optic disc that may not be visible
(c) Subretinal	(3) Proliferation under the retina; annular strand near disc; linear strands; moth-eaten-appearing sheets
CA (anterior)	Full-thickness retinal folds or subretinal strands anterior to equator (1–12 clock hours involvement), anterior displacement, and condensed vitreous strands
(1) Type:	
(a) Circumferential	(1) Retina contraction inward at the posterior edge of the vitreous base; with central displacement of the retina; peripheral retina stretched; posterior retina in radial folds
(b) Anterior	(2) Anterior contraction on the retina at the vitreous base; ciliary body detachment and epiciliary membrane; iris retraction

6.4 Subtypes of RRD and Management

RRD can be classified into subtypes based on course, location, onset age, status of lens, etc. Herein, we describe several special subtypes of RRD in our clinical scenarios.

6.4.1 Macular-ON (Fig. 6.4) Versus Macular-OFF RRD (Fig. 6.5)

The major determinant for functional outcome after successful surgical repair for RRD is whether the macula was involved (macula-OFF) [9]. In an ideal situation, retinal detachment surgery should be scheduled before macular involvement. Floaters seem to be a good early warning signal for retinal detachment, especially for macula-ON RRD patients [10].

Scleral buckling may be more beneficial for macula-ON RRD, while primary pars plana vitrectomy repair results in a good final visual outcome for patients with primary macular-ON RRD [11]. Persistent subfoveolar fluid (PSF) as seen on optical coherence tomography (OCT) is a recognized

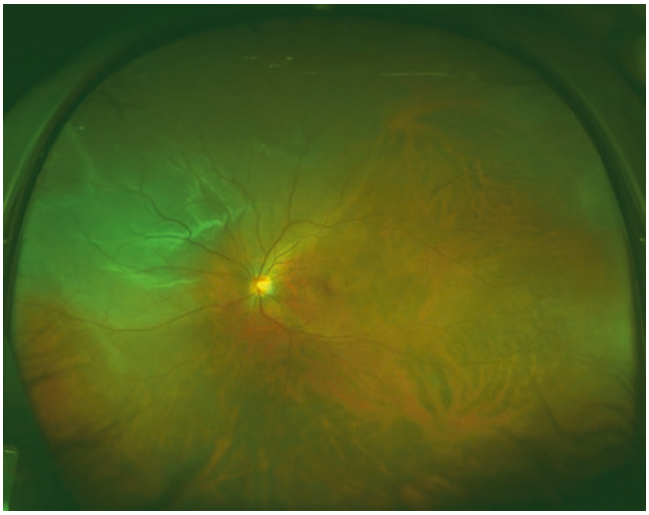

Fig. 6.4 Fundus photograph by Optos shows nasal retinal detachment with macular on PVR B is graded

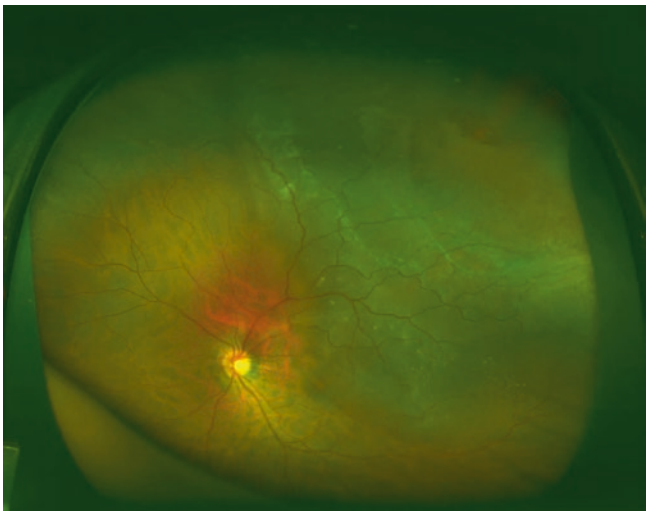

Fig. 6.5 Fundus photograph by Optos shows retinal detachment with a tear in the superotemporal periphery. Macula is detached and PVR B is graded

complication of otherwise anatomically successful scleral buckling for macular-OFF RRD, with reported prevalence between 0% and 94% [12]. Main microstructural changes after PSF include lesion in the photoreceptor layer, disrupted inner segment/outer segment (IS/OS) junction, discontinued external limiting membrane, and hyper-reflective spots in the outer nuclear layer [13] (Figs. 6.6 and 6.7).

6.4.2 Giant Tear RRD

Giant retinal tears (GRTs) are defined as full-thickness circumferential tears of more than 90° of the retina [14, 15]. Although GRTs can occur spontaneously, they are often associated with a number of conditions including ocular trauma, high myopia, aphakia, pseudophakia, genetic mutations involving collagen, and young age. Common techniques used to treat GRTs include fluid-air exchange, pneumatic retinopexy, scleral buckling, primary vitrectomy with gas, or silicone oil tamponade [16] (Fig. 6.7).

6.4.3 Chronic RRD

Chronic RRD is characterized by a history of symptoms of at least 3-month, with a prevalence between 4.5% and 29% [17]. Typical clinical presentations include a pigmented demarcation line, intraretinal cysts, retinal thinning, a smooth surface on the detached retina, and an inferior retinal break. Although scleral buckling procedures can be used for most patients, primary pars plana vitrectomy (PPV) is a widely accepted and effective surgical procedure for the management of chronic RRD (Fig. 6.8).

6.4.4 RRD Complicated by Choroidal Detachment (CD)

The prognosis for RRD complicated by CD, marked hypotony, and intraocular inflammation is rather unfavorable. Such a condition is predisposed to high redetachment rates [18]. It has been reported that administration of topical or oral steroids before surgical repair in eyes with the disorder improves reattachment rates [19, 20] (Fig. 6.9).

6.4.5 RRD in Young Patients

Rhegmatogenous retinal detachment (RRD) in young population has different clinical features compared with the elder patients. It often presents with a longer duration of detachment, PVR, and a macular-OFF RRD. It also has some predisposing factors, such as trauma, developmental abnormalities, myopia, x-linked juvenile schisis, preceding uveitis, atopic dermatitis, and previous intraocular surgery [21, 22]. In Asian countries, there is a high incidence of familial exudative vitreoretinopathy (FEVR), accounting for 13–20% of pediatric RRD [23] (Figs. 6.10, 6.11, and 6.12).

In cases in which a retinal break was precisely localized, scleral buckling is the primary choice for RRD in young patients. It is often difficult to perform a complete removal of the cortical vitreous on the detached retina, as there is stronger vitreoretinal adhesion in pediatric RRD patients.

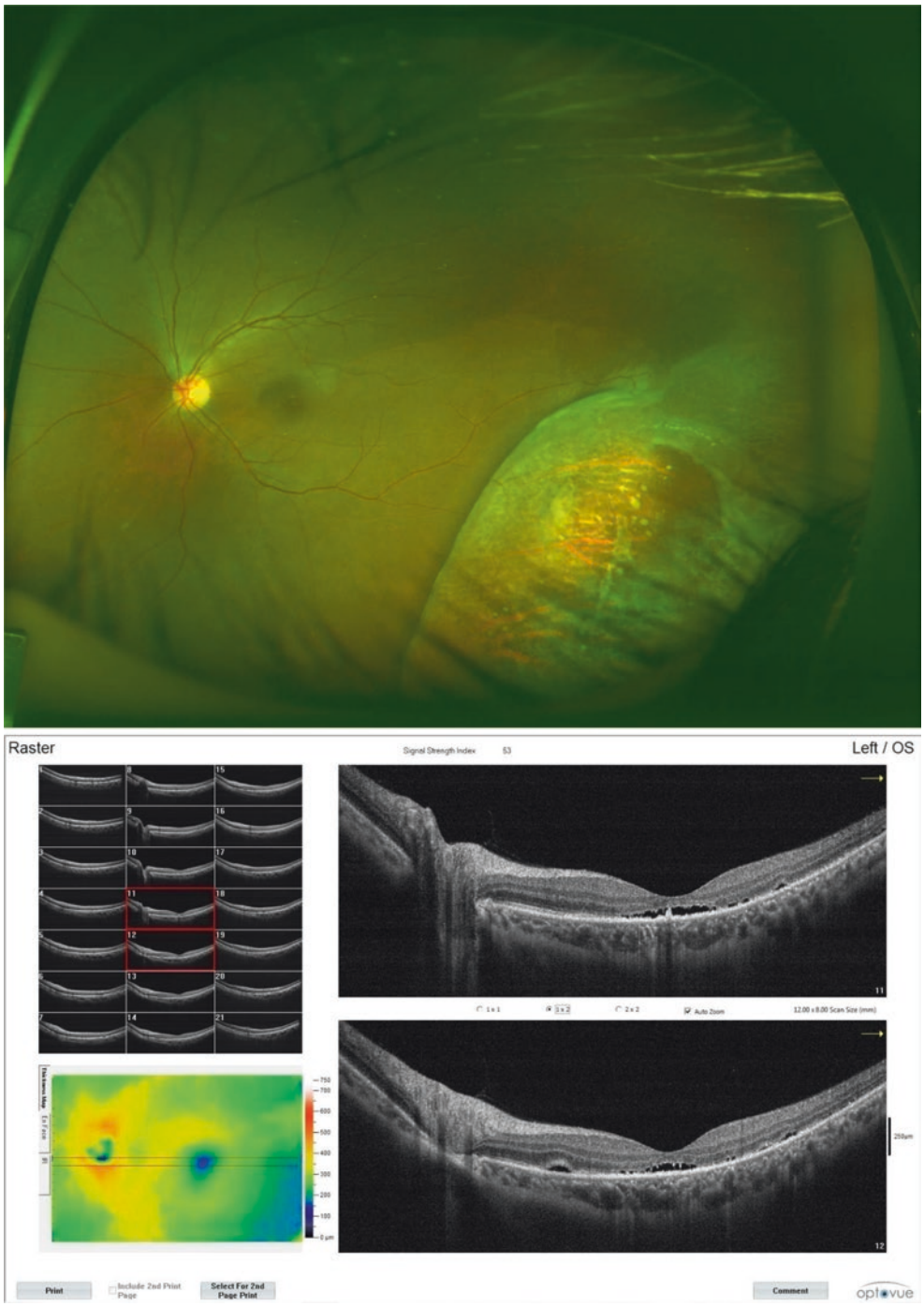

Fig. 6.6 Fundus photograph by Optos (upper figure) and optical coherence tomography (lower figure) show that a Macular-off retinal detachment has reattachment 20 days after sclera buckling in the inferotemporal periphery. Macula is involved with subretinal fluid and microstructure changes of the outer retina

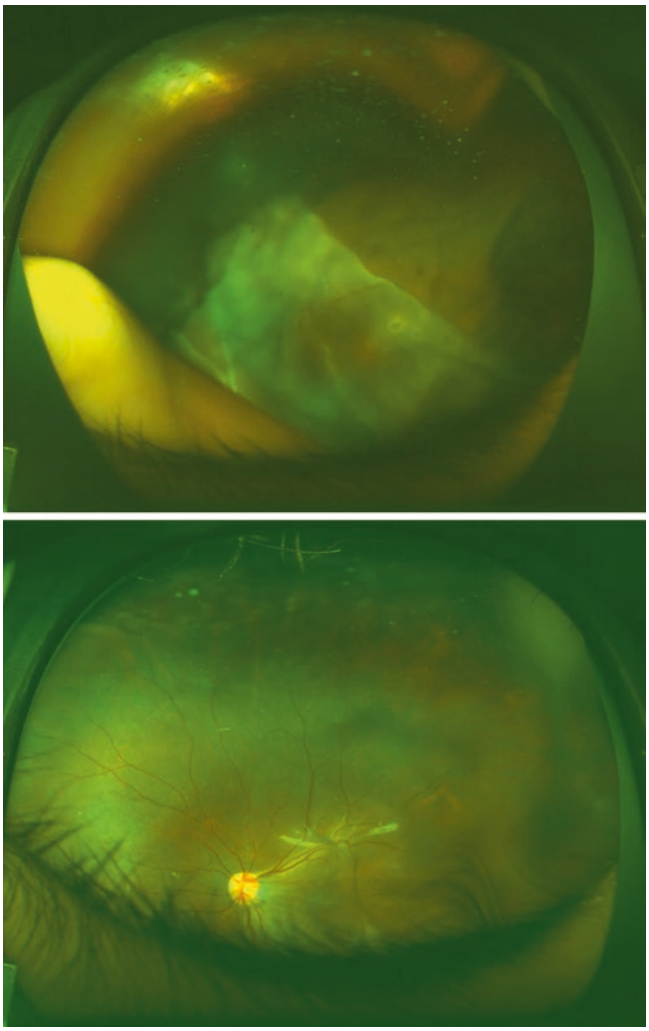

Fig. 6.7 Fundus photograph by Optos shows that a total retinal detachment induced by a giant retinal tear in the upper part. PVR C is graded (upper figure). After vitrectomy and silicone oil tamponade, the retina is now reattached (lower figure)

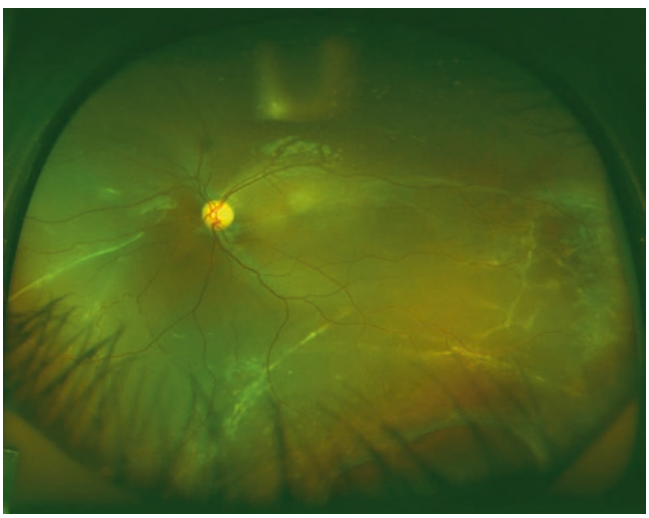

Fig. 6.8 Fundus photograph by Optos shows chronic retinal detachment with a large tear in the inferior periphery. Typical presentations include a pigmented demarcation line and subretinal string. PVR C is graded

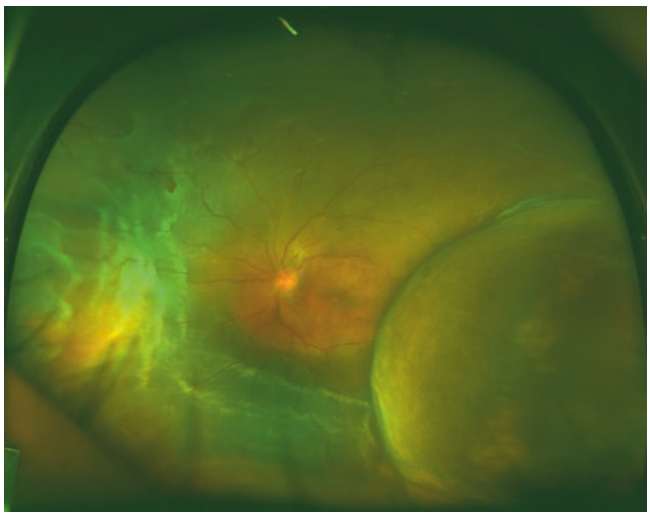

Fig. 6.9 Fundus photograph by Optos shows retinal detachment complicated by choroidal detachment. PVR C is graded

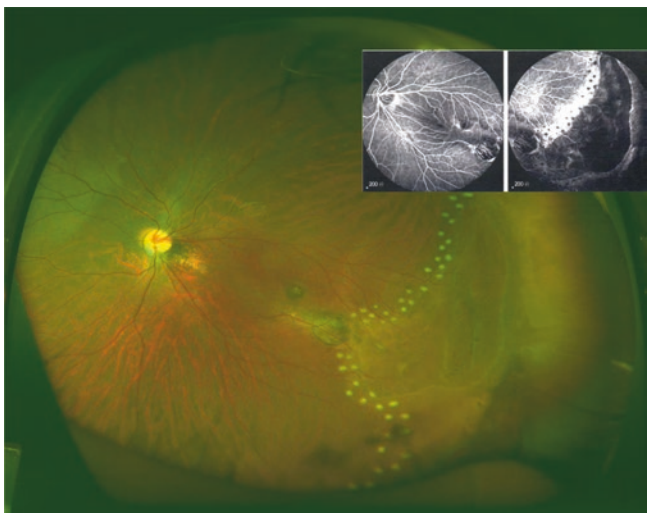

Fig. 6.10 Fundus photograph by Optos and fundus angiography (right upper) show retinal detachment complicated with FEVR. A retinal break was observed in the inferotemporal avascular retina. Laser photocoagulation was administered posterior to the avascular retina before surgery. PVR B is graded

Fig. 6.11 Fundus photograph by Optos (upper figure) and OCT (lower figure) show retinal detachment complicated with x-linked juvenile schisis in the right eye. PVR B is graded

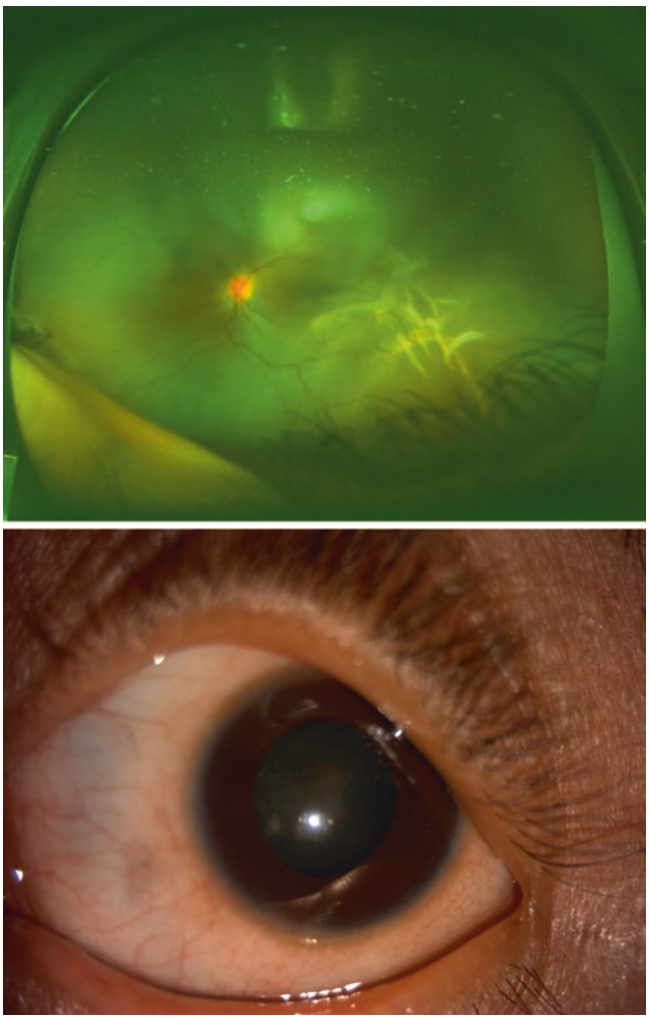

Fig. 6.12 Fundus photograph by Optos (upper figure) and photograph of lid (lower figure) show retinal detachment complicated with atopic dermatitis. PVR CP is graded

6.5 Surgical Techniques for RRD and PVR

Conventional treatments of RRD include scleral buckling, pars plana vitrectomy, and pneumatic retinopexy. In the recent years, we have performed several modified surgical repair techniques for RRD.

6.5.1 Scleral Buckling

Scleral buckling has evolved from segmental scleral sponge exoplant surgery reported first by Custodis [24], followed by Schepens et al. [25] describing an encircling scleral buckle (SB) procedure.

Transscleral cryotherapy is currently the most popular method used to create a chorioretinal adhesion during scleral buckling. Minimizing cryotherapy from conventional scleral buckling surgery may improve visual recovery by reducing the rate of macular pucker, postoperative uveitis, and cystoid macular edema, and it may ultimately reduce the incidence of PVR [26]. Laser photocoagulation to the lesion after retinal reattachment surgery can be an additional treatment when minimum amount of transscleral cryotherapy was done.

6.5.2 Segmental Scleral Bucking

Minimal segmental buckling by a sponge without drainage of subretinal fluid, introduced by Schepens [25] and Custodis [24] and subsequently refined by Lincoff and Kreissig, remains a common surgical procedure in the management of RRD [27, 28]. Limbal peritomy, usually over one quadrant combined with two radial incisions through the conjunctiva and Tenon's capsule, is routinely performed in segmental buckling surgery. In the recent years, we performed a modification of minimal segmental bucking through a small in situ conjunctival incision with minimal surgical trauma to the anterior conjunctiva Tenon's capsule and extraocular muscles [29] (Fig. 6.13).

6.5.3 Combined Scleral Buckle-Vitrectomies

Scleral buckle-vitrectomies have been historically used in RRD complicated with severe PVR. With the refinement of vitreoretinal surgical techniques, scleral buckling is seldom required to release circumferential tractional force in peripheral retina. A modified combination pattern can be done during sclera buckling surgery when dry vitrectomy with a small gauge cutter enters the globe and removes local tractional components.

6.5.4 Combined Scleral Buckle-Phacoemulsification

RRD is occasionally complicated with cataract and surgical options may include phacovitrectomy or combined scleral buckle-phacoemulsification. We have performed phacoemulsification combined with scleral buckle in several patients to treat RRD and cataract. Phacoemulsification for cataract removal is firstly done followed by a conventional scleral buckling. Implantation of intraocular lens can be performed as the last step of the combined surgery, or in several days when biological measurement can be accurately provided after resolution of submacular fluid.

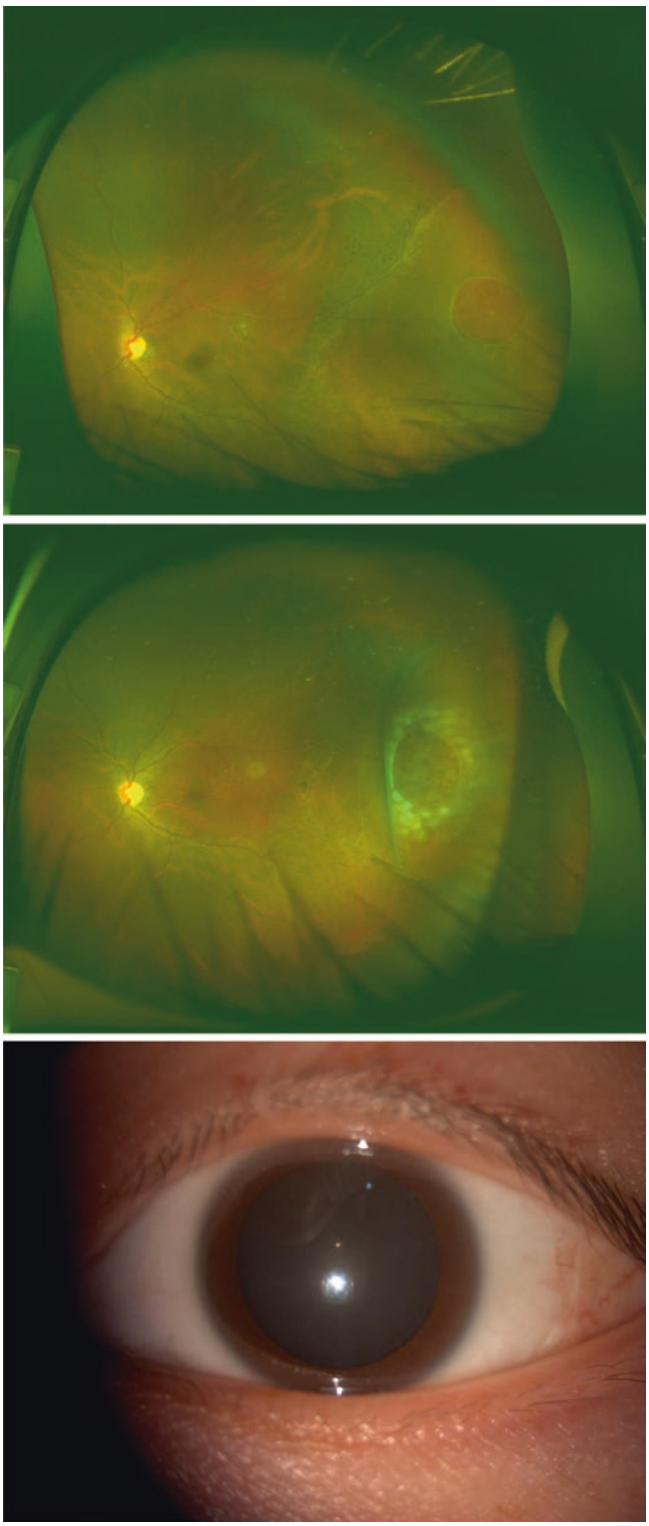

Fig. 6.13 Fundus photographs by Optos show retinal detachment in the temporal periphery. PVR A is graded (upper figure). The retina is reattached after segmental scleral buckling followed by laser photocoagulation (middle figure). The modification of minimal segmental bucking through a small in situ conjunctival incision posed little trauma to the ocular surface (lower figure)

6.6 Tamponade

Tamponade substances during vitrectomy for RRD mainly comprise of long-standing gas and silicone oil. Pars plana vitrectomy with postoperative perfluoro-n-octane retention or with heavy oil has been used for inferior retinal detachment repair or severe PVR.

6.7 Prognosis for RRD

Choroidal detachment, significant hypotony, grade C-1 PVR, detached quadrants, and large or giant retinal breaks are independent explanatory variables of retinal detachment repair failure [29].

References

1. Kuhn F, Aylward B. Rhegmatogenous retinal detachment: a reappraisal of its pathophysiology and treatment. Ophthalmic Res. 2014;51:15–31.
2. Theodossiadis PG, Georgalas IG, Emfietzoglou J, et al. Optical coherence tomography findings in the macula after treatment of rhegmatogenous retinal detachments with spared macula preoperatively. Retina. 2003;23(1):69–75.
3. Hilton G, Machemer R, Michels R, et al. The classification of retinal detachment with proliferative vitreoretinopathy. Ophthalmology. 1983;90(2):121–5.
4. Di Lauro S, Kadhim MR, Charteris DG, et al. Classifications for proliferative vitreoretinopathy (PVR): an analysis of their use in publications over the last 15 years. J Ophthalmol. 2016;2016:7807596. https://doi.org/10.1155/2016/7807596. Epub 2016 Jun 27.
5. Figueroa MS, Corte MD, Sbordone S, et al. Scleral buckling technique without retinopexy for treatment of rhegmatogeneous: a pilot study. Retina. 2002;22(3):288–93.
6. Pastor JC. Proliferative vitreoretinopathy: an overview. Surv Ophthalmol. 1998;43(1):3–18.
7. Lean JS, Stern WH, Irvine AR, et al. Classification of proliferative vitrereotinopathy used in the silicone study. Ophthalmology. 1989;96(6):765–71.
8. Machemer R, Aaberg TM, Freeman HM, et al. An updated classification of retinal detachment with proliferative vitreoretinopathy. Am J Ophthalmol. 1991;112(2):159–65.
9. Salicone A, Smiddy WE, Venkatraman A, et al. Visual recovery after sclera buckling procedure for retinal detachment. Ophthalmology. 2006;113:1734–42.
10. Eijk ES, Busschbach JJ, Timman R, et al. What made you wait so long? Delays in presentation of retinal detachment: knowledge is related to an attached macula. Acta Ophthalmol. 2016;94(5):434–40.
11. Kim JD, Pham HH, Lai MM, et al. Effect of symptom duration on outcomes following vitrectomy repair of primary macula-off retinal detachments. Retina. 2013;33(9):1931–7.
12. Tee JJ, Veckeneer M, Laidlaw DA. Persistent subfoveolar fluid following retinal detachment surgery: an SD-OCT guided study on the incidence, aetiological associations, and natural history. Eye (Lond). 2016;30(3):481–7.

13. Delolme MP, Dugas B, Nicot F, et al. Anatomical and functional macular changes after rhegmatogenous retinal detachment with macula off. Am J Ophthalmol. 2012;153(1):128–36.
14. Ang GS, Townend J, Lois N. Epidemiology of giant retinal tears in the United Kingdom: the British giant retinal tear epidemiology eye study (BGEES). Retina. 2010;51:4781–7.
15. Ghosh YK, Banerjee S, Savant V, et al. Surgical treatment and outcome of patients with giant retinal tears. Eye (Lond). 2004;18:996–1000.
16. Berrocal MH, Chenworth ML, Acaba LA. Management of giant retinal tear detachments. J Ophthalmic Vis Res. 2017;12(1):93–7.
17. Sayman Muslubas I, Hocaoglu M, Ersoz MG, et al. Choroidal thickness in chronic rhegmatogenous retinal detachment before and after surgery, and comparison with acute cases. Int Ophthalmol. 2017; https://doi.org/10.1007/s10792-017-0556-9. [Epub ahead of print].
18. Alibet Y, Levytska G, Umanets N, et al. Ciliary body thickness changes after preoperative anti-inflammatory treatment in rhegmatogenous retinal detachment complicated by choroidal detachment. Graefes Arch Clin Exp Ophthalmol. 2017; https://doi.org/10.1007/s00417-017-3673-2. [Epub ahead of print].
19. Sharma T, Gopal L, Reddy RK, et al. Primary vitrectomy for combined rhegmatogenous retinal detachment and choroidal detachment with or without oral corticosteroids: a pilot study. Retina. 2005;25(2):152–7.
20. Wei Y, Wang N, Chen F, Wang H, Bi C, Zu Z, Yang X. Vitrectomy combined with periocular/intravitreal injection of steroids for rhegmatogenous retinal detachment associated with choroidal detachment. Retina. 2014;34(1):136–41. https://doi.org/10.1097/IAE.0b013e3182923463.
21. Soheilian M, Ramezani A, Malihi M, et al. Clinical features and surgical outcomes of pediatric rhegmatogenous retinal detachment. Retina. 2009;29(4):545–51. https://doi.org/10.1097/IAE.0b013e318194fd1a.
22. Oono Y, Uehara K, Haruta M, et al. Characteristics and surgical outcomes of pediatric rhegmatogenous retinal detachment. Clin Ophthalmol. 2012;6:939–43. https://doi.org/10.2147/OPTH.S31765.
23. Ranchod TM, Ho LY, Drenser KY, et al. Clinical presentation of familial exudative vitreoretionpathy. Ophthalmology. 2011;118(10):2070–5.
24. Custodis E. Treatment of retinal detachment by circumscribed diathermal coagulation and by scleral depression in the area of tear caused by imbedding of a plastic implant. Klin Monbl Augenheilkd Augenarztl Fortbild. 1956;129(4):476–95.
25. Schepens CL, Okamura ID, Brockhurst RJ. The scleral buckling procedures. I. Surgical techniques and management. AMA Arch Ophthalmol. 1957;58(6):797–811.
26. Mahdizadeh M, Masoumpour M, Ashraf H. Anatomical retinal reattachment after scleral buckling with and without retinopexy: a pilot study. Acta Ophthalmol. 2008;86(3):297–301.
27. Lincoff H, Baras I, McLean J. Modifications to the Custodis procedure for retinal detachment. Arch Ophthalmol. 1965;73:160–3.
28. Lincoff H, Kreissig I. The treatment of retinal detachment without drainage of subretinal fluid (modifications of the Custodis procedure, Part VI). Trans Am Acad Ophthalmol Otolaryngol. 1972;76(5):1221–32.
29. Adelman RA, Parnes AJ, Michalewska Z, European Vitreo-Retinal Society (EVRS) Retinal Detachment Study Group, et al. Clinical variables associated with failure of retinal detachment repair: the European vitreo-retinal society retinal detachment study report number 4. Ophthalmology. 2014;121(9):1715–9.

Cavitary Optic Disc Maculopathy

7

Nieraj Jain and Mark W. Johnson

7.1 Introduction

Serous maculopathy associated with optic pits and related optic disc malformations represents a unique but well-recognized entity that has long confounded ophthalmologists. The source and pathophysiology of macular fluid in such cases has been an ongoing subject of discussion that has spanned generations [1, 2]. In recent years, this condition has spawned a variety of treatment approaches, both with conventional vitreoretinal surgical maneuvers and more novel approaches. Yet attempts at repair are often met with persistent or recurrent submacular fluid, and there remains a lack of consensus regarding the optimal treatment approach.

7.2 Classification and Clinical Features

Cavitary optic disc maculopathy may occur in eyes with a range of related congenital cavitary malformations of the optic disc, including typical coloboma, optic disc pit and other atypical colobomas, and morning glory disc anomaly (Fig. 7.1) [3]. Typical coloboma of the optic disc is a large and inferonasally located excavation of the optic disc that may be associated with a juxtapapillary chorioretinal coloboma. This lesion may result in an isolated serous maculopathy or in a more extensive rhegmatogenous retinal detachment, particularly in the setting of a large chorioretinal coloboma. Optic disc pits, a form of atypical disc coloboma, tend to be small, grayish cavitations along the temporal or inferotemporal aspect of the disc. They account for the majority of cases of cavitary disc maculopathy. Morning glory disc anomaly is a unilateral markedly enlarged optic papilla with funnel-shaped excavation and radially oriented retinal vessels emanating from the optic disc. Affected patients tend to have poor vision and may have associated intracranial abnormalities warranting neuroimaging.

Several lines of evidence suggest that these entities share in common a faulty closure of the fetal fissure during embryogenesis. Histopathologic studies demonstrate similar structural abnormalities within these lesions, which are typically comprised of dysplastic retinal tissue herniated into a lamina cribrosa or scleral defect [4]. In some individuals, optic pit or morning glory has been seen in association with typical coloboma in the same or contralateral eye [5]. Furthermore, in one family with a five-generation pedigree with autosomal dominant inheritance of cavitary disc anomalies, individuals manifested a spectrum of phenotypes including disc coloboma, morning glory disc anomaly, and optic pit [6].

In a subset of patients, estimated at 50% in cases of optic disc pit, cavitary disc malformations involve a congenital defect in the fluid barrier that is normally present where the retina abuts the optic disc [7]. The resulting serous maculopathy, when involving the fovea, represents a treatable cause of vision loss and is often the presenting sign in patients with previously unrecognized disc anomalies. Some authors have postulated that acquired defects in the lamina cribrosa, as seen in advanced glaucoma, may occasionally result in a similar maculopathy [8].

The serous maculopathy typically develops in a two-step process. In most cases, fluid initially migrates from the optic disc cavitation into the retinal stroma, most commonly at the level of the outer nuclear or Henle's fiber layer (Fig. 7.2). The fluid may ultimately percolate into the subretinal space, sometimes through an outer layer break that is visible clinically [9]. In a minority of cases, the fluid tract extends from the disc directly into the subretinal space. Although typically confined to the posterior pole, detachment can be more extensive, particularly in the setting of a large associated chorioretinal coloboma.

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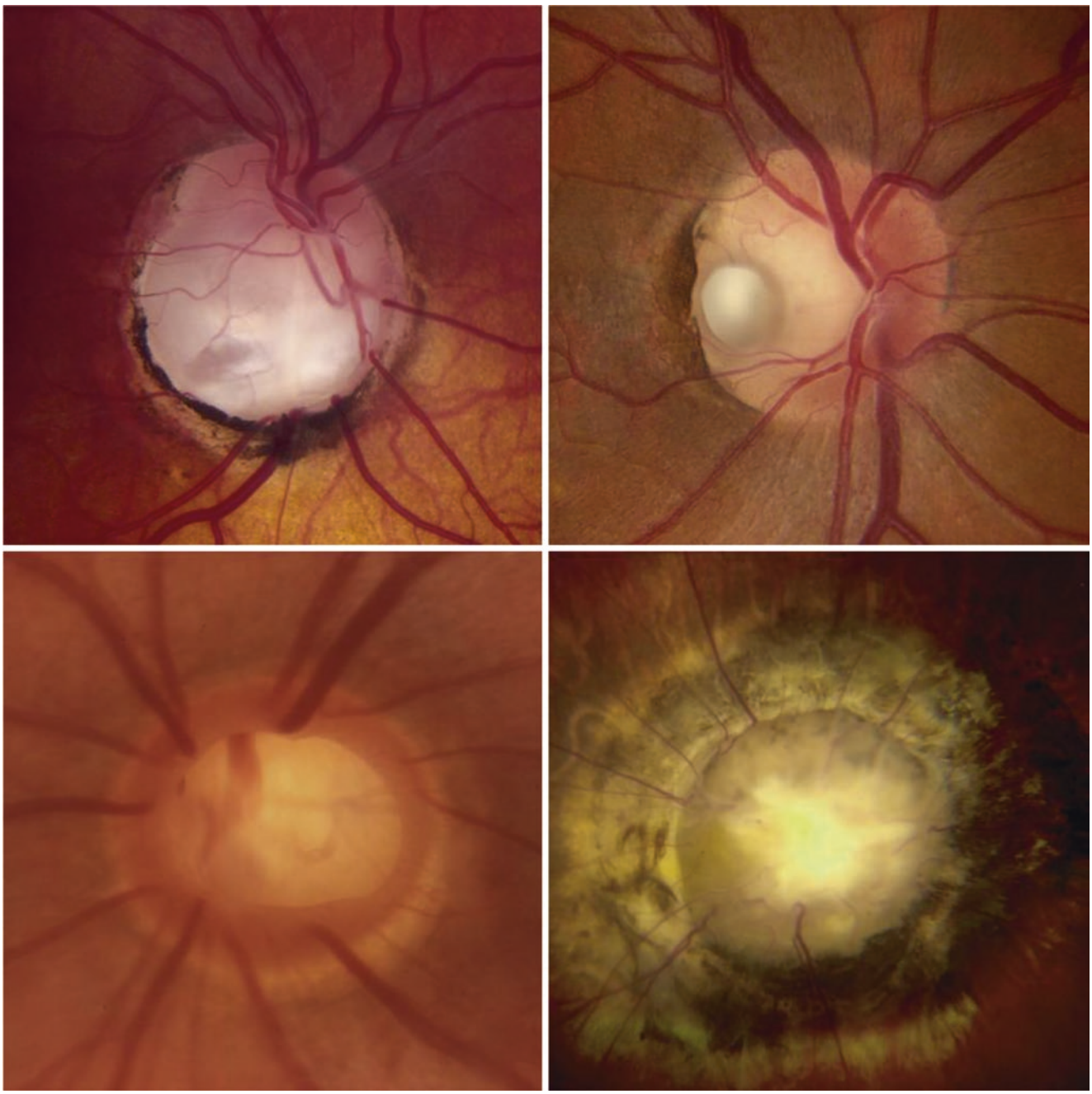

Fig. 7.1 Fundus photographs showing the spectrum of cavitary disc anomalies: (top left) typical coloboma, (top right) classic optic pit, (bottom left) centrally located atypical coloboma, and (bottom right) morning glory anomaly. Reprinted from *Am J Ophthalmol* 2014;158(3): 423–435, Jain and Johnson, Pathogenesis and treatment of maculopathy associated with cavitary optic disc anomalies; copyright 2014, with permission from Elsevier

7.3 Pathogenesis

The unifying anatomic theme of cavitary disc anomalies is a defect in the eye wall involving the lamina cribrosa and/or juxtapapillary sclera. These tissues, in normal eyes, form a pressure- and water-tight barrier between the intraocular and extraocular spaces, while allowing for the axons of the retinal nerve fiber layer to converge and exit the globe as the optic nerve. As a result of the congenital defect, the vitreous, subretinal, and subarachnoid spaces may be variably interconnected through the relatively compliant and porous tissue comprising the cavitary anomaly. This defect thus allows the translaminar pressure gradient to act upon intraocular and extraocular fluids, inducing movement of these fluids into the juxtapapillary retina (Fig. 7.3) [2].

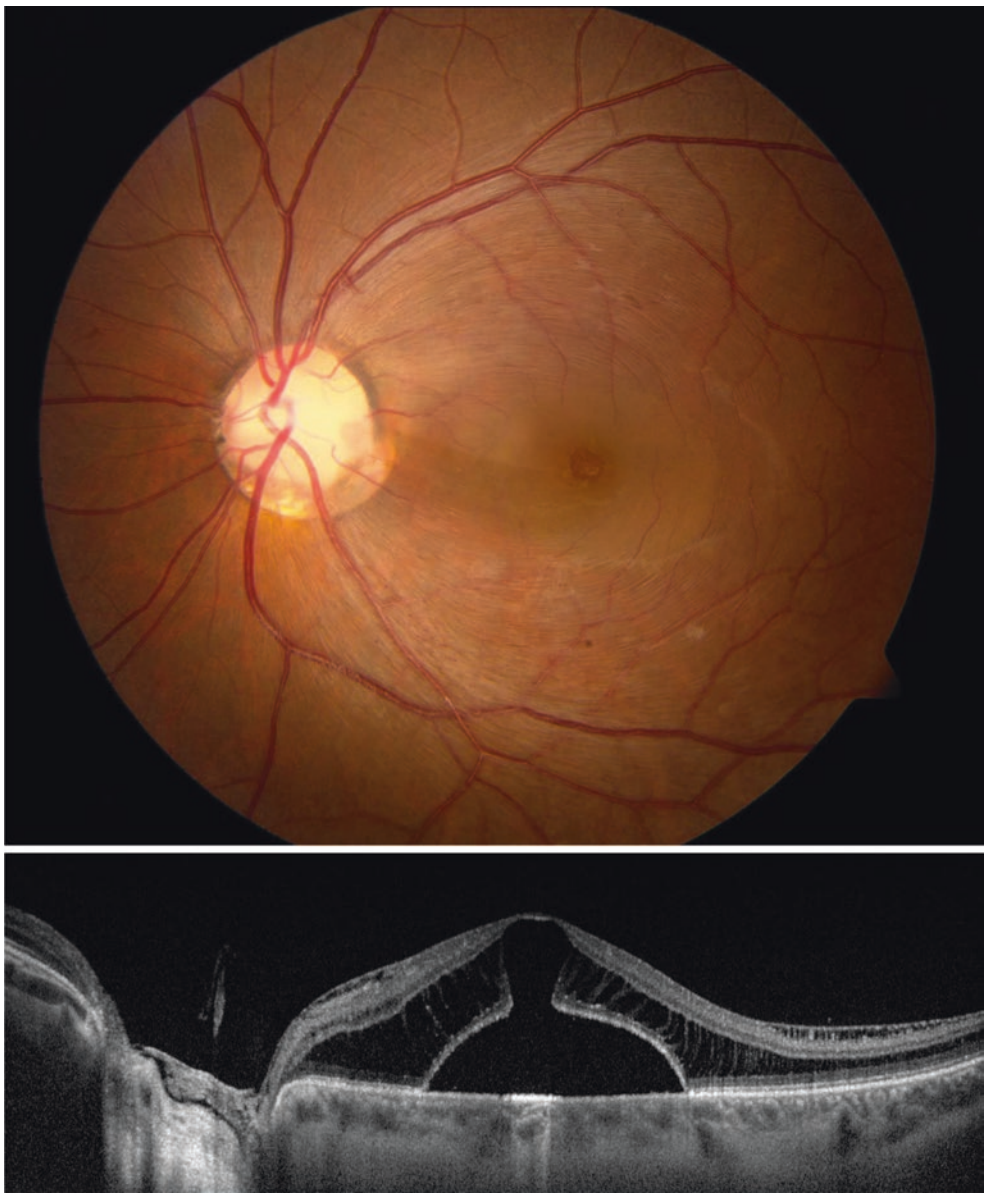

Fig. 7.2 Images showing typical fluid pathways in cavitary disc maculopathy. (Top) Color fundus photograph of left eye shows a subtle optic pit, diffuse macular thickening, and an outer lamellar macular hole surrounded by localized submacular fluid. (Bottom) Spectral-domain optical coherence tomography image shows that the intraretinal fluid emerges from the optic pit and enters the subretinal space through an outer lamellar foveal dehiscence

The dynamic translaminar pressure gradient acts upon both intra- and extraocular spaces, and it follows that the macular fluid may derive in a given eye from either the vitreous or subarachnoid space, or possibly both. The pathways for flow are most clearly demonstrated by the intraoperative and postoperative passage of vitreous substitutes, including gas and silicone oil, across the cavitary anomaly and into either the subretinal or subarachnoid space [2]. Efforts at intraoperative sampling to characterize the fluid directly are limited by the small quantities obtained and potential for contamination yet have shown fluid composition resembling both vitreous and CSF in different cases [10, 11].

While the fluctuating trans-scleral or trans-laminar pressure gradient appears to be the primary driver of macular fluid accumulation, the pathogenic role of vitreous traction in cavitary disc maculopathy remains unclear. Some authors have suggested a role for vitreous traction based on the observations that the maculopathy has resolved spontaneously following posterior vitreous detachment in isolated cases [12, 13] and that vitrectomy alone leads to resolution of macular fluid in many cases [14].

However, cavitary disc maculopathy is clearly distinct from true traction maculopathies, such as vitreomacular traction syndrome, idiopathic macular hole, and myopic traction maculopathy. Notably, cavitary disc maculopathy usually develops long before the early stages of posterior vitreous detachment, including in very young children. All disorders that are widely accepted to be caused by vitreous traction are associated with partial PVD states, in which partially detached hyaloid exerts traction at points of

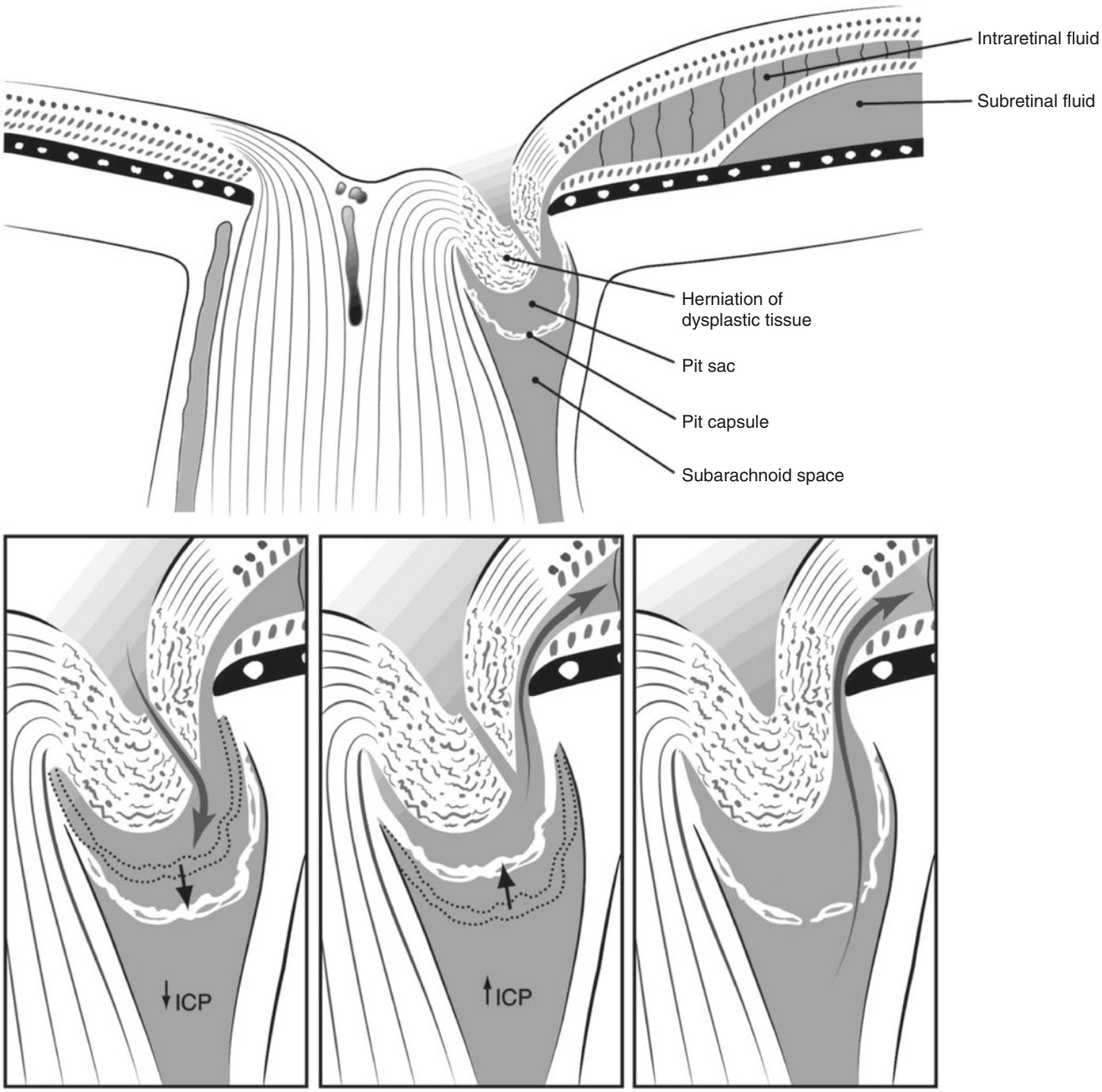

Fig. 7.3 Schematic illustration showing the anatomic features of an optic pit and the associated maculopathy. (Top) The herniated dysplastic tissue and pit capsule likely vary in permeability from one eye to another. In eyes with an impermeable capsule, the pit functions like a bulb syringe, (bottom left) "sucking" vitreous fluid into the pit sac during a drop in intracranial pressure (ICP) and then, (bottom center) during a rise in pressure, expelling it from the sac. (Bottom right) In eyes with a permeable capsule, fluctuations in ICP are transmitted to the pit by cerebrospinal fluid migration across the capsule. (Reprinted with permission from: Johnson TM, Johnson MW. Pathogenic implications of subretinal gas migration through pits and atypical colobomas of the optic nerve. Reproduced with permission from *Arch Ophthalmol* 2004;122(12):1793–1800. Copyright © 2004 American Medical Association. All rights reserved)

persistent vitreoretinal adhesion. This is typically evidenced by characteristic findings on OCT imaging, where retina is tented anteriorly with sharp angulations at sites of vitreoretinal adherence. This characteristic traction profile is almost never seen in either the macula or optic disc in cases of cavitary disc maculopathy. Furthermore, the vitreous traction hypothesis cannot account for the development of cavitary disc maculopathy in eyes with complete posterior vitreous detachment nor for the persistence or recurrence of maculopathy in eyes that have undergone vitrectomy with posterior hyaloid removal [15].

It is possible that vitreous gel plays a secondary or facilitating role in the development of cavitary disc maculopathy in select eyes. This could be mediated by an unidentifiable

traction force along the insertion of the posterior hyaloid at the optic disc margin, by the presence of incarcerated vitreous gel maintaining patency of a fluid channel, by modulation of translaminar pressure gradients, or possibly by contributing to a one-way valve within the cavitary anomaly. One or more of such theoretical mechanisms may help explain the apparent beneficial role of vitrectomy alone in a subset of eyes with this disorder.

7.4 Management

Cavitary disc maculopathy remains one of a small handful of causes of macular thickening that does not respond to pharmacologic therapy. Vitreoretinal surgeons have employed a full spectrum of therapeutic strategies, including observation, laser photocoagulation, pharmacologic approaches, and vitreoretinal surgery. In many instances, these interventions are met with persistent or recurrent macular fluid.

Affected patients present with a range of macular involvement, and it is not always clear whether intervention is warranted. Due to the rarity of the condition and preference for intervention in current practice, there is limited natural history data available to guide therapy. In 1980, Brown and co-authors estimated the incidence of serous maculopathy at approximately 50% in eyes with optic disc pit [7]. Their study from the pre-OCT era likely underrepresents mild cases of maculopathy. In a study published in 1990, 80% of 15 untreated subjects with submacular fluid lost vision to a level of 20/200 over a mean observation period of 9 years [16]. Again, it is likely that selection bias in this pre-OCT study resulted in a particularly advanced subset of patients.

For patients with foveal involvement and clinically significant vision loss, the decision about whether to intervene may be complex. As with any elective surgical procedure, decision-making should account for a number of factors, including extent and severity of the maculopathy, chronicity and rate of progression, age and health of the patient, and status of the fellow eye. As spontaneous resolution has been documented in a small minority of cases, it is reasonable to observe affected eyes for a short period of time to better understand the trajectory and functional impact of the maculopathy. However, lengthy delay may lead to atrophic changes in the retina and retinal pigment epithelium. Furthermore, there is some evidence that the extent of macular fluid is associated with final anatomic outcomes, which may justify earlier intervention in progressive cases [17].

7.4.1 Vitrectomy with Juxtapapillary Laser Photocoagulation

Effective interventions for cavitary optic disc maculopathy should be rooted in a basic understanding of its underlying pathomechanism. Ample evidence suggests that either CSF or vitreous fluid may be driven into the retina by the dynamic translaminar pressure gradient, based on the unique congenital disc malformation of each particular patient. We have demonstrated that formation of a laser-induced intraretinal fluid barrier may block the final common pathway for all varieties of cavitary disc maculopathy (Fig. 7.4).

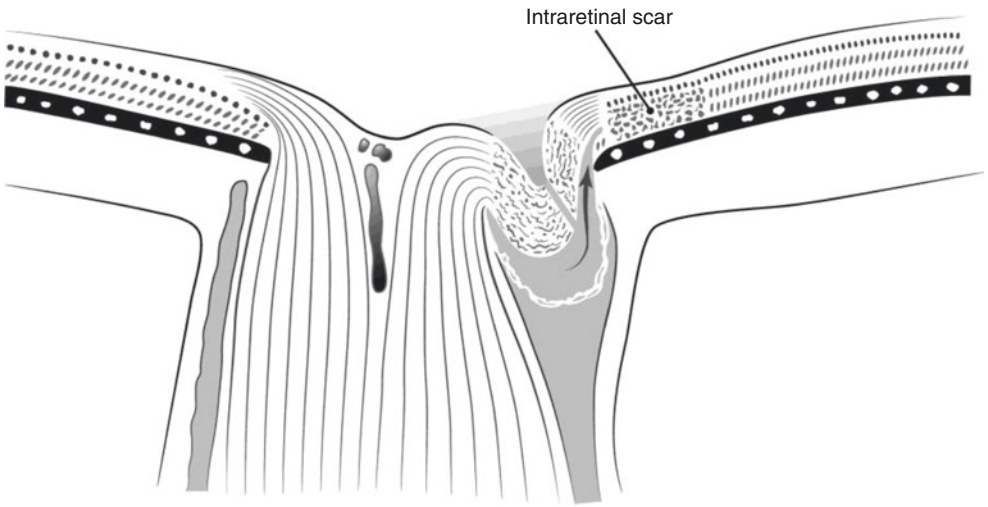

Fig. 7.4 Schematic illustration showing a juxtapapillary fluid barrier. Laser-induced intraretinal and subretinal scarring blocks fluid flow (arrow) out of the optic pit. The scarring spares the nerve fiber layer to avoid central visual field loss. Intraretinal and subretinal fluid in the macula gradually resolve after the barrier is established. Reprinted from *Am J Ophthalmol* 2014;158(3):423–435, Jain and Johnson, Pathogenesis and treatment of maculopathy associated with cavitary optic disc anomalies; copyright 2014, with permission from Elsevier

Our current approach is to perform titrated, OCT-guided laser photocoagulation of the juxtapapillary retina at the slit lamp followed immediately by vitrectomy with gas tamponade [18]. Preoperative OCT imaging reveals the location of intraretinal and/or subretinal fluid emanating from the optic disc, thereby guiding the circumferential extent of the laser treatment. We use red laser energy for deeper tissue penetration and to avoid laser uptake by retinal vessels in the inner retina. With slit-lamp delivery and a high-magnification fundus contact lens for optimal visualization, we carefully titrate the laser treatment for moderate whitening of the outer retina and thermal spread to middle retinal layers. We initiate the treatment approximately one laser width (200 μM) from the temporal disc margin and apply 4–5 confluent curvilinear rows to cover the circumferential extent of the fluid tract (Fig. 7.5). Subsequently, we perform a standard three-port pars plana vitrectomy, inducing posterior vitreous detachment with the vitreous cutter, followed by gas tamponade. We typically attempt gentle aspiration of macular fluid through the cavitary disc lesion. The primary purpose of the vitrectomy, however, is to allow for the placement of a large vitreous cavity gas bubble to dry and compress the juxtapapillary retina, allowing formation of an intraretinal laser-induced scar. We advise the patient to position face down for 7–10 days to achieve maximal drying of the intraretinal fluid and optimize the creation of an intraretinal barrier.

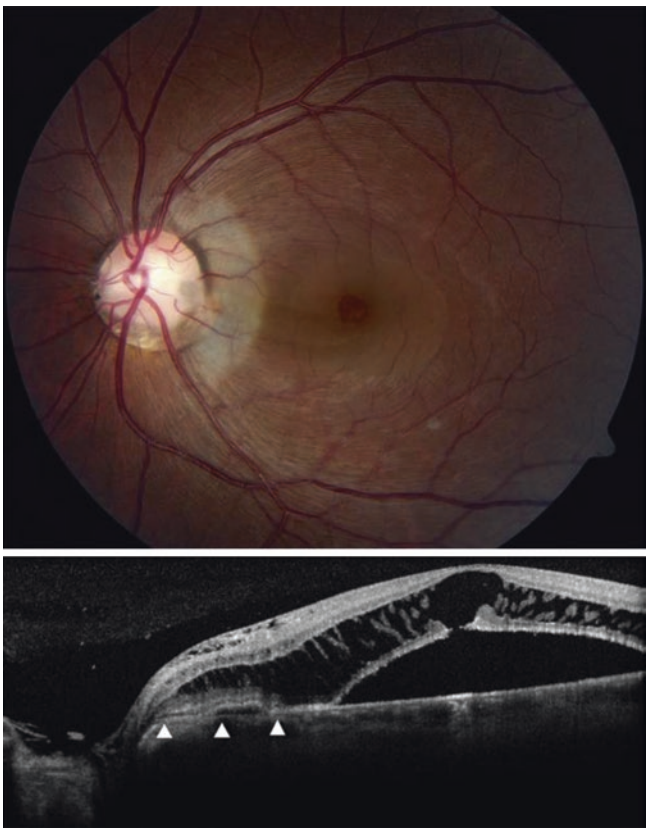

Fig. 7.5 Color fundus photograph and optical coherence tomography (OCT) image taken immediately after carefully titrated slit-lamp delivery of red wavelength juxtapapillary laser photocoagulation for optic disc pit maculopathy. (Top) There is moderate whitening of the outer and middle retinal layers, sparing the inner retina. The acute thermal injury (arrowheads) visible on the OCT image (bottom) involves the outer to middle retinal layers but spares the inner retina. Laser treatment was immediately followed by vitrectomy with gas tamponade to facilitate formation of an intraretinal and subretinal scar. Reprinted from *Am J Ophthalmol* 2017;173:34–44, Kiang and Johnson, Formation of an intraretinal fluid barrier in cavitary optic disc maculopathy; copyright 2017, with permission from Elsevier

The value of this barrier is nicely illustrated in Fig. 7.6, in an eye with fluid emanating from the cavitary lesion both nasal and temporal to the disc [18]. Laser was applied in a targeted fashion along the temporal margin of the optic disc, and the nasal aspect was left untreated. This eye ultimately had complete drying of macular fluid but persistence of intraretinal fluid nasal to the disc.

In a series of 11 consecutive eyes with maculopathy from a variety of cavitary disc anomalies, we achieved complete resolution of intra- and subretinal fluid in all eyes using juxtapapillary laser followed by vitrectomy and fluid-gas exchange [18]. Some of the patients in this series at our tertiary referral center had received multiple prior treatments, with refractory or recurrent maculopathy. Over a mean follow-up of 48 months after the final surgery, only 1 of 11 subjects had recurrent maculopathy. In this case, the patient had initially presented with a fluid tract extending directly from the disc lesion into the subretinal space, which may have hindered the successful creation of a laser-induced fluid barrier. Only one patient in this series, who had received multiple prior sessions of endolaser photocoagulation elsewhere, was thought to develop a laser-induced central scotoma.

It is reasonable in theory to consider prophylactic juxtapapillary laser photocoagulation prior to the accumulation of intra- or subretinal fluid in an attempt to create a barrier to the passage of fluid in eyes with cavitary disc lesions. However, in the absence of an intra- or subretinal fluid buffer, the papillomacular bundle has greater exposure to potential thermal injury in such eyes. We do not presently advocate such treatment. Further study into the natural history of cavitary disc lesions may reveal imaging biomarkers for progressive disease, possibly guiding decision-making regarding prophylactic therapy.

7.4.2 Vitrectomy Alone

Several authors have reported that many cases of cavitary maculopathy respond to vitrectomy alone without laser photocoagulation. The durability of the response to this intervention remains unclear, given variable follow-up in these

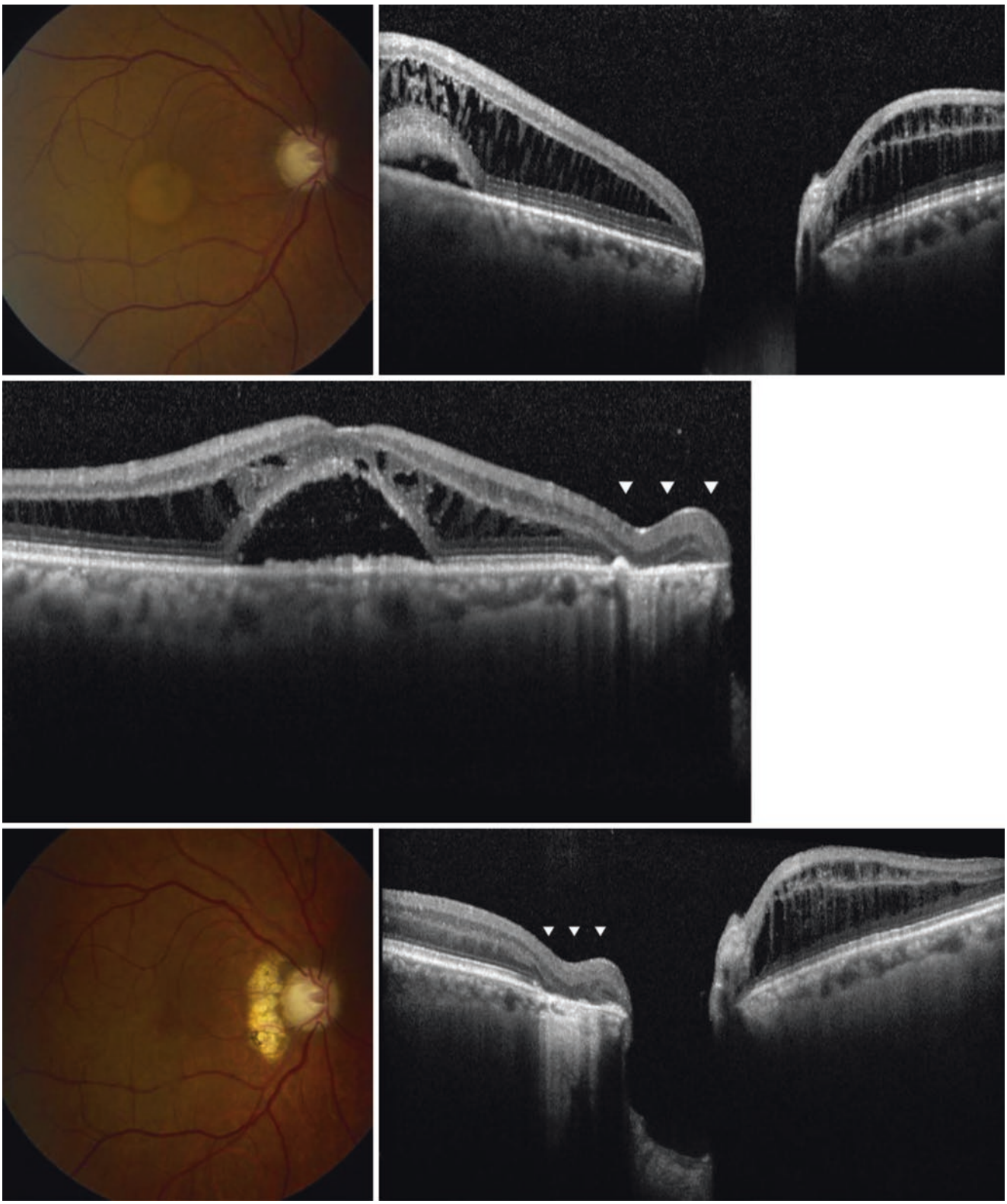

Fig. 7.6 Imaging before and after surgery for cavitary disc maculopathy. Color photograph (top left) and optical coherence tomography (OCT) image (top right) of the right eye preoperatively show schisis-like intraretinal fluid throughout the macula and papillomacular bundle, as well as nasal to the disc. There is subretinal fluid with vitelliform material in the macular center. (Middle) OCT image taken 6 weeks postoperatively shows a dry, compact laser scar (arrowheads) with decreasing intraretinal fluid and persistent chronic subretinal fluid. Color photograph (bottom left) and OCT image (bottom right) taken 18 months postoperatively show a temporal juxtapapillary laser scar (arrowheads) with a dry macula but persistent intraretinal fluid nasal to the disc where there is no laser barrier. Reprinted from *Am J Ophthalmol* 2017;173:34–44, Kiang and Johnson, Formation of an intraretinal fluid barrier in cavitary optic disc maculopathy; copyright 2017, with permission from Elsevier

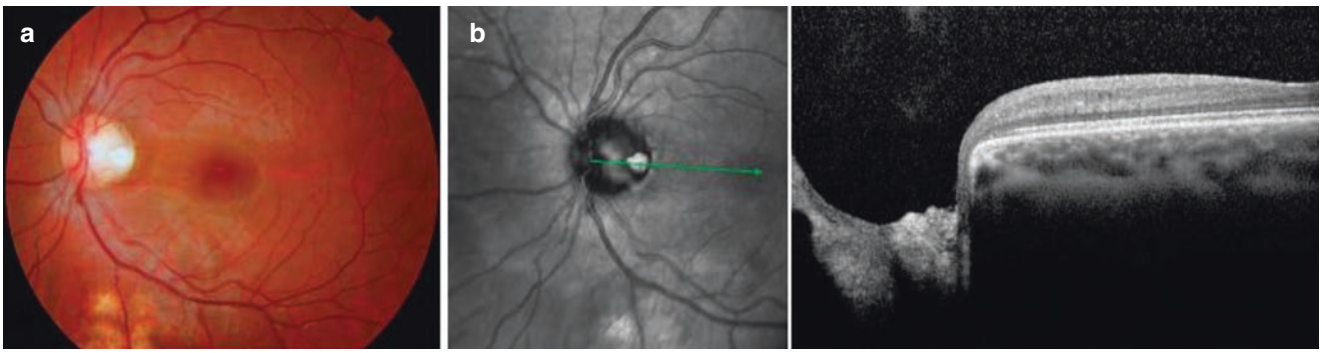

Fig. 7.7 Color fundus photo (**a**) and optical coherence tomography image (**b**) demonstrating position of a scleral flap at the base of an optic pit. This technique was employed after failure of an initial vitrectomy approach for optic pit maculopathy in a 15-year-old boy with best corrected visual acuity (BCVA) of 20/200. These images demonstrate resolution of serous maculopathy 7 months after placement of the scleral flap. The flap remained in position at 2 years following surgery with sustained resolution of intra- and subretinal fluid and BCVA of 20/40. Reprinted from *Retina* 2013;33(8);1708–1714, Travassos et al., Optic pit: novel surgical management of complicated cases. Copyright 2013, with permission from Wolters Kluwer Health, Inc.

retrospective reviews. Additionally, given the simplicity of this approach, it is puzzling that anatomic outcomes have been so highly variable, with anatomic success ranging from 36% [17] to 88% in different series [14, 19, 20]. However, as this procedure is straightforward and has a low complication rate, it would be reasonable to consider vitrectomy alone as an initial therapeutic procedure. Refractory or recurrent cases could then be managed by repeat vitrectomy with slit lamp directed juxtapapillary laser and fluid-air exchange as described above. It remains unclear why vitrectomy alone is effective in some cases, although, as discussed previously, it is possible that vitreous gel plays a secondary role in the development of serous maculopathy in eyes with a cavitary disc malformation.

7.4.3 Alternative Approaches and Adjuvants

Numerous adjuvants have been used in combination with vitrectomy, including internal limiting membrane (ILM) peeling, inner retinal fenestration, and instillation of tissue plugs into the cavitary lesion. Proponents of ILM peeling postulate that the ILM exerts traction at the peripapillary retina. Larger case series do not appear to show benefit to ILM peeling, and this maneuver has resulted in macular hole formation in some eyes [21]. Vitrectomy with inner retinal fenestration yielded promising outcomes in one large series [22]. However, the inner retinal defect has been shown to close in the early postoperative period [23], and the treatment response seen in this uncontrolled study is likely the result of vitrectomy alone. A wide variety of tissue plugs, with adjuvants such as platelet-rich plasma, fibrin glue, autologous sclera, and inverted ILM flap, have been implemented with variable success. Of these adjuvants, autologous sclera appears to be the most promising (Fig. 7.7) [24], since it is unclear if the other substances result in a permanent occlusion of anomalous fluid channels. We believe that such adjuvants are unnecessary if a permanent laser-induced intraretinal barrier to fluid migration can be achieved. In refractory cases, an autologous scleral plug appears to be a reasonable next step, assuming the optic pit is of an appropriate size.

An alternative surgical approach to vitrectomy is macular buckling. This technically challenging procedure is not widely performed but has yielded promising outcomes when performed by experienced surgeons [25]. Those who advocate this approach have proposed that the buckle indentation may physically close the fluid tract extending from the optic disc to the macula.

7.5 Summary

Cavitary disc maculopathy continues to confound clinicians in the current era of advanced retinal imaging capabilities and vitreoretinal surgical techniques. The unifying anatomic theme of these lesions is a defect in the eye wall at the optic disc that permits the translaminar pressure gradient to drive fluid into the juxtapapillary retina. The natural history of this condition is variable but in many cases involves chronic macular fluid that may lead to significant visual disability. Permanent cure of the condition can be achieved by formation of a laser-induced intraretinal barrier to fluid migration in the juxtapapillary retina. Given the technical demands of this procedure, vitrectomy alone is an acceptable and conservative initial approach to achieving resolution of macular fluid, with the caveat that this may not provide a permanent cure. Ongoing studies of optic disc structure may provide further insight into this enigmatic condition.

References

1. Gass JD. Serous detachment of the macula. Secondary to congenital pit of the optic nervehead. Am J Ophthalmol. 1969;67(6):821–41.
2. Johnson TM, Johnson MW. Pathogenic implications of subretinal gas migration through pits and atypical colobomas of the optic nerve. Arch Ophthalmol. 2004;122(12):1793–800.
3. Jain N, Johnson MW. Pathogenesis and treatment of maculopathy associated with cavitary optic disc anomalies. Am J Ophthalmol. 2014;158(3):423–35.
4. Irvine AR, Crawford JB, Sullivan JH. The pathogenesis of retinal detachment with morning glory disc and optic pit. Retina. 1986;6(3):146–50.
5. Apple DJ. New aspects of colobomas and optic nerve anomalies. Int Ophthalmol Clin. 1984;24(1):109–21.
6. Slusher MM, Weaver RG Jr, Greven CM, Mundorf TK, Cashwell LF. The spectrum of cavitary optic disc anomalies in a family. Ophthalmology. 1989;96(3):342–7.
7. Brown GC, Shields JA, Goldberg RE. Congenital pits of the optic nerve head. II. Clinical studies in humans. Ophthalmology. 1980;87(1):51–65.
8. Zumbro DS, Jampol LM, Folk JC, Olivier MM, Anderson-Nelson S. Macular schisis and detachment associated with presumed acquired enlarged optic nerve head cups. Am J Ophthalmol. 2007;144(1):70–4.
9. Lincoff H, Lopez R, Kreissig I, Yannuzzi L, Cox M, Burton T. Retinoschisis associated with optic nerve pits. Arch Ophthalmol. 1988;106(1):61–7.
10. Turkcuoglu P, Taskapan C. The origin of subretinal fluid in optic disc pit maculopathy. Ophthalmic Surg Lasers Imaging Retina. 2016;47(3):294–8.
11. Patel S, Ling J, Kim SJ, Schey KL, Rose K, Kuchtey RW. Proteomic analysis of macular fluid associated with advanced glaucomatous excavation. JAMA Ophthalmol. 2016;134(1):108–10.
12. Bonnet M. Serous macular detachment associated with optic nerve pits. Graefes Arch Clin Exp Ophthalmol. 1991;229(6):526–32.
13. Gupta RR, Choudhry N. Spontaneous resolution of optic disc pit maculopathy after posterior vitreous detachment. Can J Ophthalmol. 2016;51(1):e24–7.
14. Hirakata A, Inoue M, Hiraoka T, McCuen BW II. Vitrectomy without laser treatment or gas tamponade for macular detachment associated with an optic disc pit. Ophthalmology. 2012;119(4):810–8.
15. Coca MN, Tofigh S, Elkeeb A, Godley BF. Optic disc pit maculopathy recurring in the absence of vitreous gel. JAMA Ophthalmol. 2014;132(11):1375–6.
16. Sobol WM, Blodi CF, Folk JC, Weingeist TA. Long-term visual outcome in patients with optic nerve pit and serous retinal detachment of the macula. Ophthalmology. 1990;97(11):1539–42.
17. Steel DH, Williamson TH, Laidlaw DA, Sharma P, Matthews C, Rees J, et al. Extent and location of intraretinal and subretinal fluid as prognostic factors for the outcome of patients with optic disk pit maculopathy. Retina. 2016;36(1):110–8.
18. Kiang L, Johnson MW. Formation of an intraretinal fluid barrier in cavitary optic disc maculopathy. Am J Ophthalmol. 2017;173:34–44.
19. Abouammoh MA, Alsulaiman SM, Gupta VS, Mousa A, Hirakata A, Berrocal MH, et al. Pars plana vitrectomy with juxtapapillary laser photocoagulation versus vitrectomy without juxtapapillary laser photocoagulation for the treatment of optic disc pit maculopathy: the results of the KKESH International Collaborative Retina Study Group. Br J Ophthalmol. 2016;100(4):478–83.
20. Avci R, Kapran Z, Ozdek S, Teke MY, Oz O, Guven D, et al. Multicenter study of pars plana vitrectomy for optic disc pit maculopathy: MACPIT study. Eye. 2017;31(9):1266–73.
21. Shukla D, Kalliath J, Tandon M, Vijayakumar B. Vitrectomy for optic disk pit with macular schisis and outer retinal dehiscence. Retina. 2012;32(7):1337–42.
22. Ooto S, Mittra RA, Ridley ME, Spaide RF. Vitrectomy with inner retinal fenestration for optic disc pit maculopathy. Ophthalmology. 2014;121(9):1727–33.
23. Slocumb RW, Johnson MW. Premature closure of inner retinal fenestration in the treatment of optic disk pit maculopathy. Retinal Cases Brief Rep. 2010;4(1):37–9.
24. Travassos AS, Regadas I, Alfaiate M, Silva ED, Proenca R, Travassos A. Optic pit: novel surgical management of complicated cases. Retina. 2013;33(8):1708–14.
25. Theodossiadis GP, Theodossiadis PG. The macular buckling technique in the treatment of optic disk pit maculopathy. Semin Ophthalmol. 2000;15(2):108–15.

Coloboma of the Choroid

8

Andrew Carey and J. Fernando Arevalo

8.1 Introduction

Colobomas of the choroid are a subset of uveal colobomas which result from disruption of the normal process of ocular development during organogenesis. This disruption causes a thinning or absence of a portion of the choroid. Choroidal colobomas may be isolated, associated with other ocular features such as microphthalmos, or associated with systemic features such as papillorenal syndrome and CHARGE syndrome.

8.2 Etiopathogenesis

During gestational development, the optic cup closes to form the globe along the choroidal fissure which begins at midpoint in the fifth week and extends ventrally and dorsally completing at the seventh week [1]. Typical colobomas occur along this choroidal fissure when it has failed to fully close; proposed causes have been incomplete migration for the margins to oppose or incomplete fusion of the margins [1]; an alternate etiology involves incomplete choroidal development which could also explain atypical colobomas that develop outside the choroidal fissure such as macular colobomas.

The underlying cause may be genetic or environmental. Many in utero environmental exposures have been suggested; the strongest evidence is for retinoic acid, saccharine, irradiation, nickel excess, folate deficiency, vitamin A deficiency, alcohol [1], as well as mycophenolate [2].

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Inheritance patterns for genetic causes include autosomal dominant, autosomal recessive, x-linked recessive, x-linked dominant, somatic mosaicism, sporadic, triploidy, trisomy, and chromosomal segment deletion [1, 3]. Prevalence ranges across nations from 0.4 to 2.6 per 10,000 live births [1].

Unilateral colobomas may be due to somatic mutations in these genes or other local factors interrupting the process. Often in the case of a typical coloboma that appears unilateral, there is a forme fruste or mild coloboma in the contralateral eye in the same location.

8.3 Clinical Features and Complications

Histologic evaluations of choroidal colobomas demonstrate hypoplastic or absent choroid [4]. The overlying retina is typically thin, disorganized, and avascular which is often referred to as an intercalary membrane [4]. With aging of the intercalary membrane, it undergoes atrophy with development of schisis and atrophic holes [4]. There is often thinning of the sclera at the base of the coloboma leading to staphyloma [4]. The base of the coloboma has also shown glial cells and spindle cells which have been confirmed to be smooth muscle [4, 5]. Optical coherence tomography (OCT) demonstrates continuity of the inner retina with the intercalary membrane and absence of the outer retina [6].

Coloboma severity can range in size, depth, and number of tissues involved. They can be isolated to the optic nerve, retina and choroid, ciliary body and lens, and iris or involve a combination of these structures with continuous or disjointed lesions [1] (Figs. 8.1, 8.2, and 8.3). They may be mild affecting only choriocapillaris or pigment clumping, iris transillumination, or iris heterochromia [1]. More severe lesions may have a staphylomatous component with posterior bulging and white appearance due to visible scleral and variable pigmentation due to retinal pigment epithelial hyperplasia [1]. The most severe manifestations are microphthalmos and clinical anophthalmos with orbital cyst [1].

M. Ohji (ed.), *Surgical Retina*, Retina Atlas, https://doi.org/10.1007/978-981-13-6214-9_8

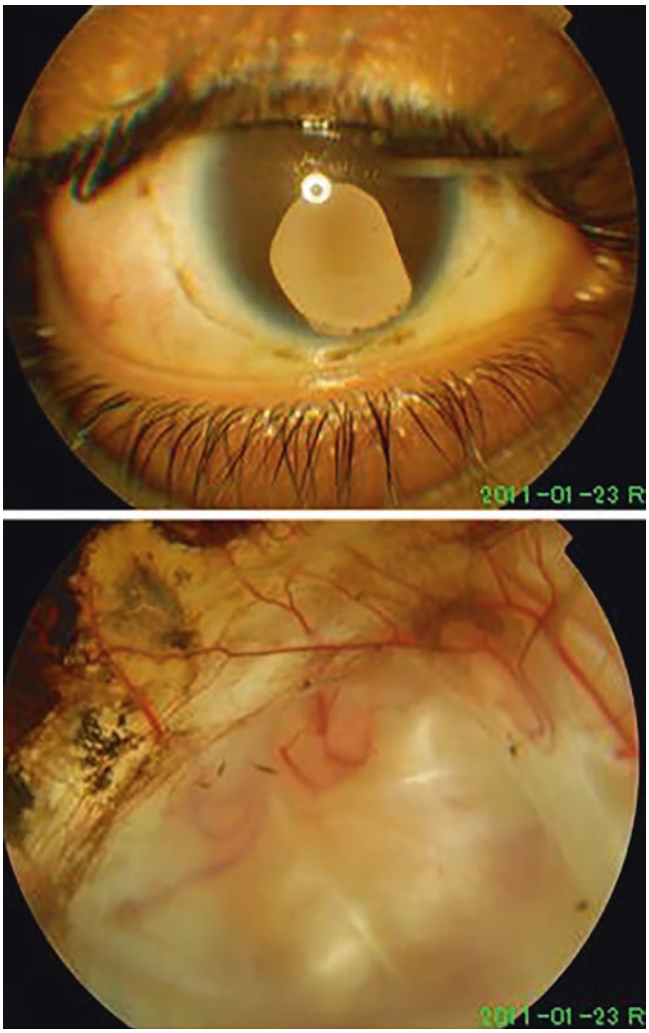

Fig. 8.1 Color photograph of the right eye with a chorioretinal coloboma. Top, iris coloboma. Bottom, chorioretinal coloboma including the optic nerve

Colobomas are often bilateral but can have marked asymmetry [1]. Visual acuity ranges from normal to no light perception, often depending on the involvement of the optic nerve and macula [1].

Some authors consider optic disc colobomas and optic disc pits to be of the same etiology; however, pits typically form inferotemporally which is not along the choroidal fissure; regardless of their etiology, they share similar complications; optic disc pit maculopathy is discussed in a separate chapter.

Colobomas may occur in isolation, with associated ocular findings or with syndromic features [1, 3]. Patients may be hyperopic in the setting of microphthalmos or myopic in the setting of staphyloma [3]. Nystagmus and strabismus occur most often in association with poor vision from birth. Orbital manifestations may include hypotelorism or hypertelorism, telecanthus, S-shaped palpebral fissures, exophthalmos, downward slanting palpebral fissures, eyelid colobomas, epibulbar dermoids, Duane anomaly, ptosis, prominent epicanthic folds, xanthelasmas, and imperforate nasolacrimal duct [3]. Anterior segment manifestations include dysgenesis; corneal abnormalities such as clouding due to limbal stem cell deficiency, sclerocornea, microcornea, posterior embryotoxon, and megalocornea in the setting of glaucoma; lens abnormalities including cataract particularly in the setting of ciliary body coloboma, small lens, lens subluxation, and ectopia lentis; glaucoma; and iris abnormalities including aniridia, posterior synechiae, lenticular iridocorneal adhesions, corectopia, and polycoria [3]. Posterior segment manifestations include persistent hyperplastic primary vitreous; panuveitis; retinal dysplasias such as congenital stationary night blindness and Leber congenital amaurosis; retinochoroidal lacunae; optic nerve anomalies including pit, hypoplasia, agenesis, morning glory anomaly, optic disc drusen, and myelinated nerve fiber layer; foveal hypoplasia; retinoblastoma; and cartilage in the eye [3].

The Online Mendelian Inheritance in Man [3] database was searched for colobomas. One hundred fifty-five distinct genes were identified as causative agents for choroidal colobomas. One series suggests the rate of syndromic manifestations to be 60% [7]. CHARGE syndrome is the most common syndromic manifestation with estimated prevalence of 1 in 12,000 live births, likely followed by papillorenal (renal coloboma) syndrome whose incidence is unknown [3]. The most common syndromic manifestations shared across causative genes include skull and facial deformities at 66%, cognitive deficits at 58%, and central nervous system defects at 53% [3]. The next most common syndromic manifestations ranging 20–40% frequency include musculoskeletal defects, renal defects, growth delay, cleft lip and/or cleft palate or other oral or tooth defects, cardiac defects, skin defects, seizures, and digital or hand/foot malformations including polydactyly or syndactyly. Manifestations ranging 10–20% frequency include motor developmental defects, gastrointestinal defects, ear and throat malformations, hearing loss, endocrine defects including pituitary abnormalities, and hypogonadism. Rare manifestations include pulmonary defects or congenital diaphragmatic defects at 3% and cardiac arrhythmias at 1% [3].

Atypical colobomas occur outside the choroidal fissure; these may occur anywhere, but of greatest clinical interest are macular colobomas. Macular colobomas may be isolated or occur as part of a syndrome. Isolated presentations include North Carolina macular dystrophy and

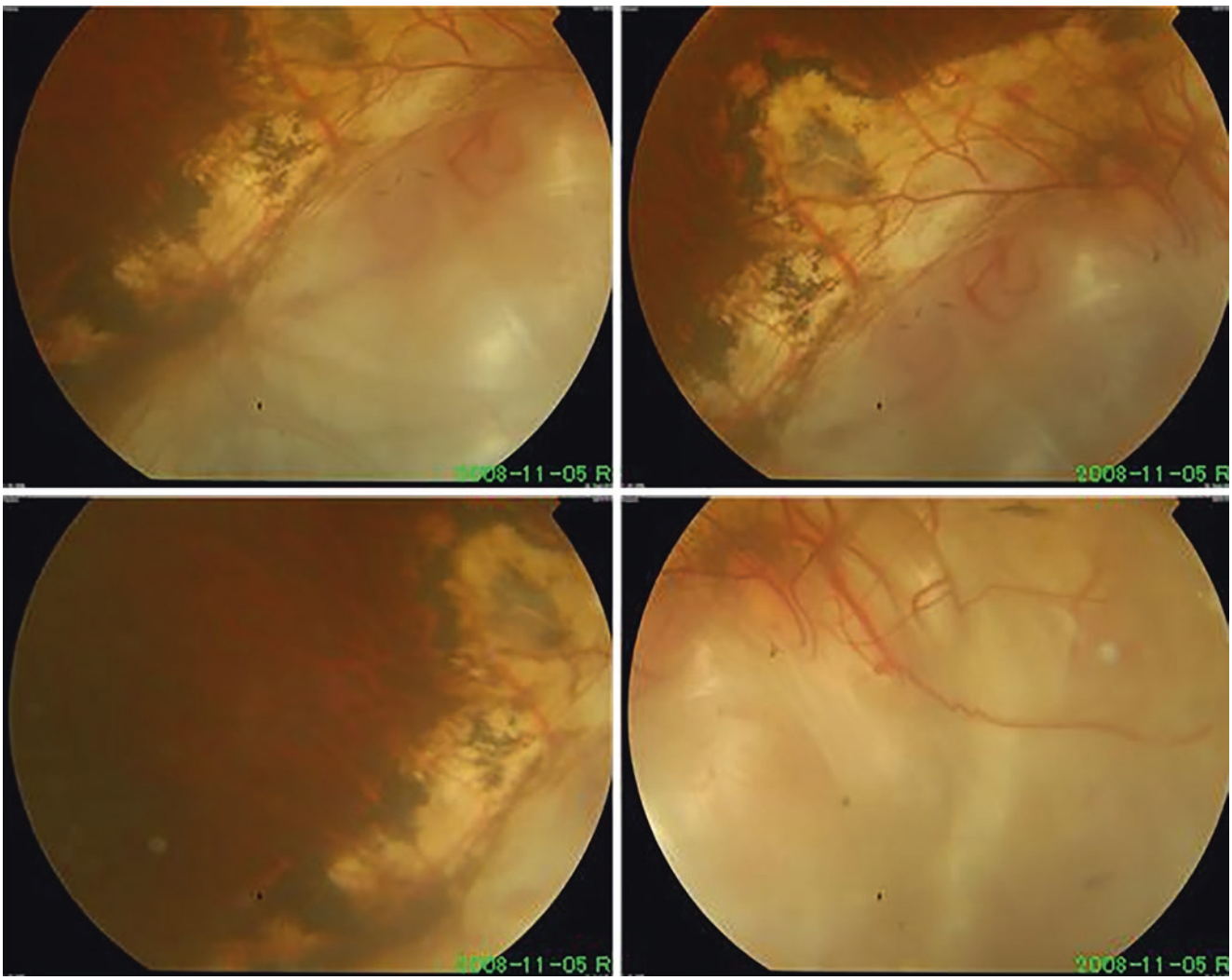

Fig. 8.2 Color photograph of the right eye with a chorioretinal coloboma

Leber congenital amaurosis syndrome 9 [3]. Syndromic manifestations include holoprosencephaly, schizencephaly, Goldenhar syndrome, coloboma-cleft lip/palate-mental retardation syndrome, and brachydactyly syndrome 1 [3].

8.4 Management

There is no primary treatment for colobomas. Rather treatment has three main goals: maximizing visual function and prevention of amblyopia; prevention of vision loss due to complications; and restoration of vision due to complications.

Nonsurgical treatment includes evaluation for and treatment of amblyopia, correction of refractive error, and low-vision rehabilitation if vision is poor to prevent socioeconomic complications associated with blindness in childhood [8]. A detailed history and comprehensive physical exam as well as abdominal ultrasound for renal defects should be undertaken to evaluate for syndromic manifestations [8]. Referral to a geneticist is also recommended to address risk of involvement in family members including unborn siblings or children [8].

8.4.1 Choroidal Neovascularization

Treatment of choroidal neovascularization may include off-label intravitreal anti-vascular endothelial growth factor injection and *LASER* photocoagulation to non-foveal involving lesions.

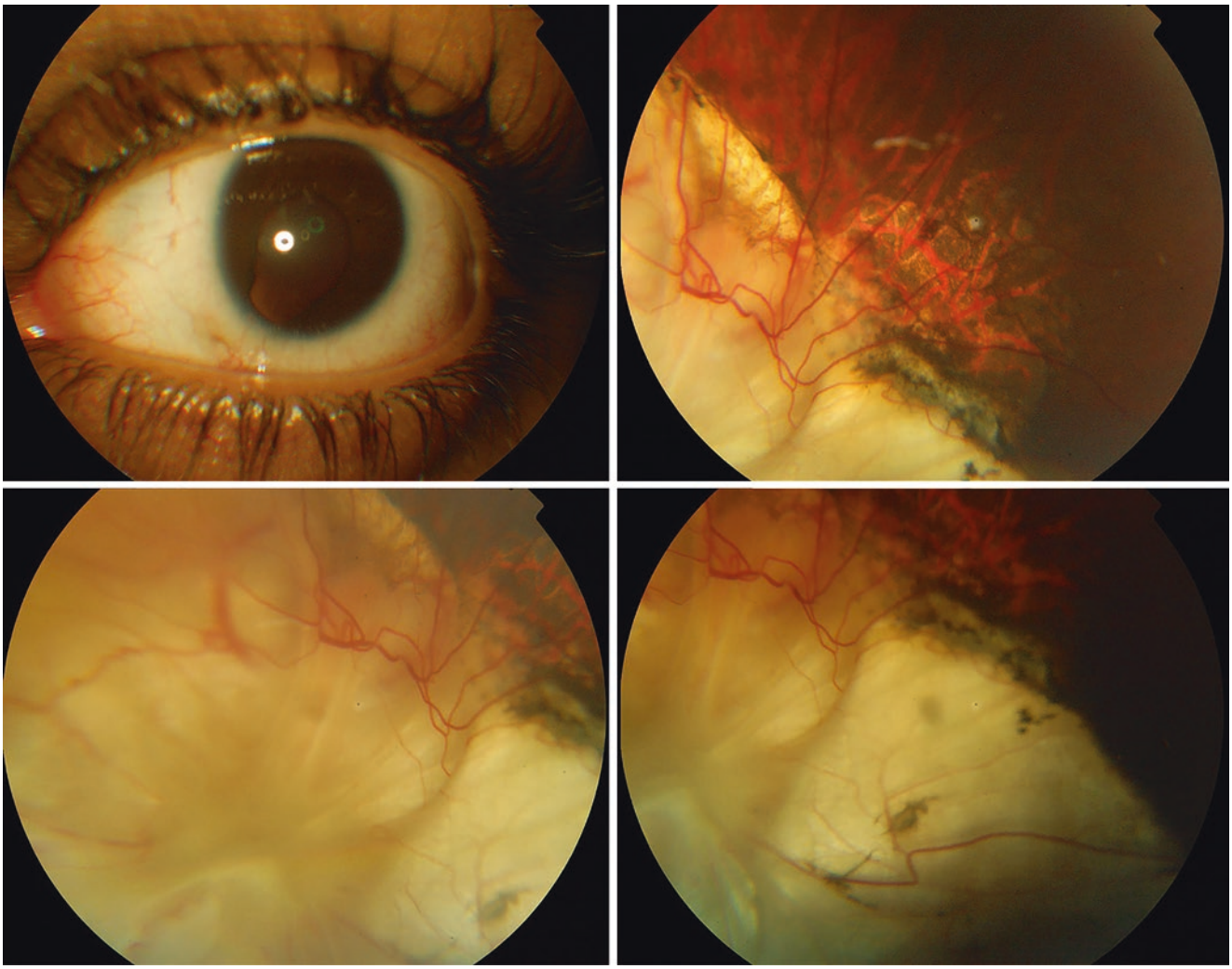

Fig. 8.3 Same patient as in Fig. 8.2. Color photograph of the left eye (top left) with iris and chorioretinal coloboma

8.4.2 Retinal Detachment

Some authors suggest prophylactic *LASER* photocoagulation to the margin of the coloboma to prevent retinal detachment; one retrospective series suggests this may reduce the risk to 1–3% [9, 10].

Treatment of retinal detachments can be complicated with early case series reporting 87% complications and low rate of success at 46% [10]. The low success rate is likely due to a combination of difficulty in the detection of the retinal break which may be as low as 44% [11] as well as associated ophthalmic manifestations. The repair of retinal detachments is most complex when the coloboma involves the optic nerve. Reported treatments include scleral buckle, cryotherapy, vitrectomy with endolaser and gas exchange tamponade, and vitrectomy with endolaser and silicone oil tamponade. There has been recent retrospective evidence toward the use of vitrectomy with endolaser and long-term tamponade (silicone oil tamponade or C_3F_8) in the literature [12] (Figs. 8.4 and 8.5).

Please see Chap. 7 dedicated on optic disc anomaly-associated macular detachments for discussion of their treatment.

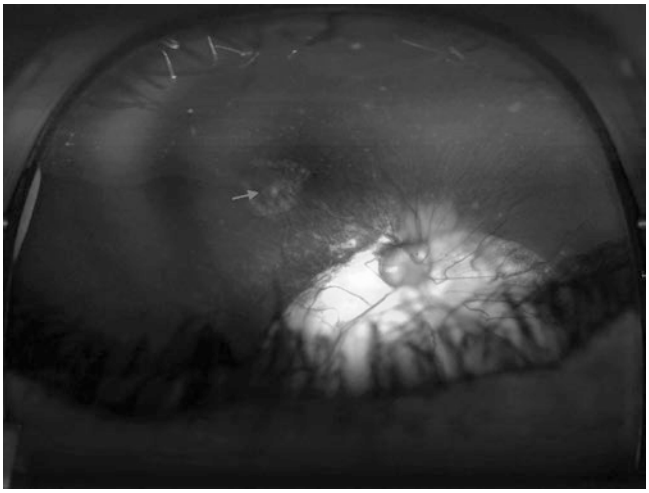

Fig. 8.4 Right eye of a 12-year-old monocular boy with a chorioretinal coloboma involving the optic nerve and macula. He had a retinal detachment and visual acuity at presentation was hand motions. Macular hole was identified intraoperatively. Pars plana vitrectomy, triamcinolone-assisted posterior hyaloid peeling, retinotomy, endolaser around the retinotomy and the coloboma, and 5000 centistokes silicone oil tamponade were performed. Postoperative wide-field fundus photograph (shown) depicting flat retina with laser scar around the retinotomy (arrow). Visual acuity 6 months after surgery was 20/400

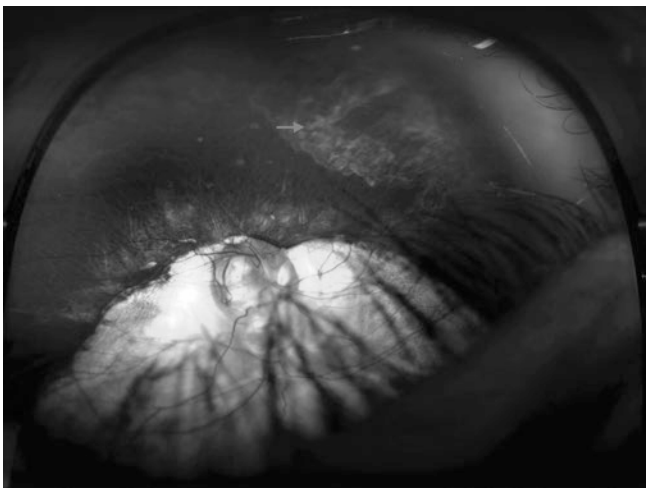

Fig. 8.5 Postoperative wide-field fundus photograph of the right eye of a 30-year-old male with chorioretinal coloboma-related retinal detachment. Presenting visual acuity was light perception. The patient underwent pars plana lensectomy, vitrectomy, triamcinolone-assisted posterior hyaloid peeling, endolaser around the primary break outside the coloboma (arrow) as well as the coloboma, and 5000 centistokes silicone oil tamponade. Visual acuity at last follow-up 6 months postoperatively was 2/200

References

1. Chang L, Blain D, Bertuzzi S, Brooks BP. Uveal coloboma: clinical and basic science update. Curr Opin Ophthalmol. 2006;17(5):447–70.
2. Merlob P, Stahl B, Klinger G. Tetrada of the possible mycophenolate mofetil embryopathy: a review. Reprod Toxicol. 2009;28(1):105–8. https://doi.org/10.1016/j.reprotox.2009.02.007. Epub 2009 Feb 25.
3. The Online Mendelian Inheritance in Man Database. Omim.org. Accessed May 2017.
4. Schubert HD. Structural organization of choroidal colobomas of young and adult patients and mechanism of retinal detachment. Trans Am Ophthalmol Soc. 2005;103:457–72.
5. Font RL, Zimmerman LE. Intrascleral smooth muscle in coloboma of the optic disk. Electron microscopic verification. Am J Ophthalmol. 1971;72(2):452–7.
6. Gopal L, Khan B, Jain S, Prakash VS. A clinical and optical coherence tomography study of the margins of choroidal colobomas. Ophthalmology. 2007;114(3):571–80.
7. Shah SP, Taylor AE, Sowden JC, et al. Anophthalmos, microphthalmos, and coloboma in the United kingdom: clinical features, results of investigations, and early management. Ophthalmology. 2012;119(2):362–8. https://doi.org/10.1016/j.ophtha.2011.07.039. Epub 2011 Nov 4.
8. Varghese M, Kavalakatt JA, Pandey S, Kolath JJ. Macular coloboma. Oman J Ophthalmol. 2016;9(1):67–8. https://doi.org/10.4103/0974-620X.176126.
9. Tripathy K, Chawla R, Sharma YR, et al. Prophylactic laser photocoagulation of fundal coloboma: does it really help? Acta Ophthalmol. 2016;94(8):e809–10. https://doi.org/10.1111/aos.12975. Epub 2016 Jan 29.
10. Uhumwangho OM, Jalali S. Chorioretinal coloboma in a paediatric population. Eye (Lond). 2014;28(6):728–33. https://doi.org/10.1038/eye.2014.61. Epub 2014 Mar 28.
11. Fu SJ, Weng NQ. Retinal detachment associated with coloboma of choroid. Zhonghua Yan Ke Za Zhi. 1989;25(1):15–7.
12. Abouammoh MA, Alsulaiman SM, Gupta VS, Younis A, Chhablani J, Hussein A, Casella AM, Banker AS, Arevalo JF; King Khaled Eye Specialist Hospital (KKESH) International Collaborative Retina Study Group. Surgical outcomes and complications of rhegmatogenous retinal detachment in eyes with chorioretinal coloboma: the results of the KKESH International Collaborative Retina Study Group. Retina. 2017. doi: https://doi.org/10.1097/IAE.0000000000001444. [Epub ahead of print].

Intraocular Cysticercosis

9

Gopal Lingam and Tarun Sharma

9.1 Parasitology

9.1.1 Natural Life Cycle [1]

Taenia solium belongs to phylum Platyhelminthes; class Cestoda; order Cyclophyllidea; and family Taeniidae. It is a variety of tapeworms infesting the humans.

In its natural life cycle, the man is the definitive host and pig the intermediary host. Hence, the man was intended to host the adult worm, while the pig harbors the larval form (*Cysticercus cellulosae*). Humans harboring the adult worm in their intestines shed the mature and fertilized proglottids (containing the ova) in their fecal matter. The pig consumes the fertilized ova whence the ova penetrate the intestinal wall and enter the bloodstream. The ova lodged in various parts of body develop into cysticerci. Man ingests the measly pork (containing the larvae). Once in the intestine, the cysticercus latches on to the intestinal wall and grows into the adult worm thus completing the life cycle.

9.1.2 Origin of Cysticercosis in Man

Under some circumstances, man can act as the intermediate host and thus suffer from cysticercosis. Ingestion of food contaminated with the fertilized ova can result in cysticercosis (just as in the pig). Massive cysticercosis can also occur due to regurgitation of a fertilized proglottid into the stomach in a person harboring the adult worm or due to feco-oral autoinfection.

Once the ova penetrate the intestinal wall, the cysts can lodge in various organs including the brain, skeletal muscle, eye, subcutaneous tissue, etc. Death of cyst can release toxins that incite profound inflammatory reaction.

9.1.3 Route of Infestation in the Eye

The ova can access the interior of the eye through either the ciliary/choroidal or the retinal circulation. If the ova access the vitreous cavity directly through retinal or ciliary circulation, the cyst can grow to large size in vitreous cavity with very little structural damage to underlying retina and choroid. However in most cases, the initial location is at choroidal level (since choroidal circulation is ten times more than retinal circulation) [2]. The cyst can migrate through the retina into vitreous cavity after a variable period of growth in subretinal space, which explains the often-present variable chorioretinal scar while the cyst is located in the vitreous cavity (Figs. 9.1 and 9.2).

9.2 Geographical Distribution

In general, human ocular parasitosis is common in developing and underdeveloped countries with poor sanitary conditions and environmental factors that favor easy transmission. However, developed countries are not immune from this condition in view of the migrant population [3].

9.3 Clinical Presentation

9.3.1 Introduction

Related to the eye, the cyst can be present in subconjunctival space; extraocular muscles, orbit, the anterior chamber, vitreous cavity, and subretinal space. In addition, intracranial cysticercosis can present with ocular signs and symptoms

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Fig. 9.1 Preoperative fundus photograph showing intravitreal cysticercus. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

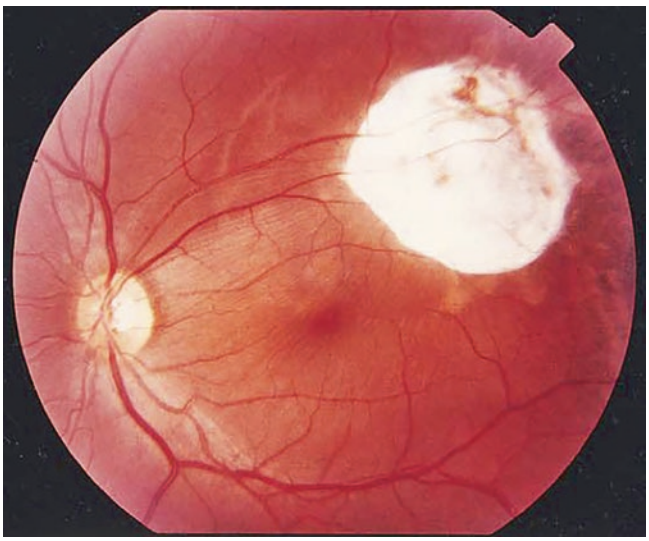

Fig. 9.2 Postoperative photograph showing the site of chorioretinal scar where the cysticercus originally stayed in subretinal space before migrating into the vitreous cavity. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

such as diplopia (sixth nerve palsy) or papilledema. Atypical optic neuritis can occur due to optic nerve cysticercosis [4]. In this chapter, we discuss manifestations and management of intraocular cysticercosis.

9.3.2 Symptomatology

9.3.2.1 Loss of Vision

While loss of vision is an important symptom, it is not uncommon to have cysts in anterior chamber and vitreous with well-retained vision if the inflammatory reaction is still limited. Visual acuity is affected due to the inflammatory reaction and its sequelae such as vitritis, vitreous membranes, traction retinal detachment, and chorioretinal scarring. The lesions may involve the posterior pole including macular area. While a dead cyst is expected to incite inflammation, a live cyst can also leak toxins and produce significant inflammation.

9.3.2.2 Subjective Appreciation of Motile Obstruction to Vision

A sensitive patient with reasonable visual acuity can actually appreciate the motile obstruction to his/her vision. On occasion, they can even appreciate when the invaginated cyst has become evaginated with scolex protruding outside the cyst (Fig. 9.3).

9.3.2.3 Pain and Redness

Patients can also present with non-specific signs such as pain and redness due to inflammation or glaucoma or both. Complicated cataract can occur and be the presenting feature—especially in the milieu of underdeveloped countries where access to medical care is limited.

9.3.2.4 Others

Coexisting intracranial cysticercosis can result in seizures, as well as localizing signs based on the location of the cyst. Cutaneous nodules can also be a presenting feature.

9.3.3 Examination

9.3.3.1 Anterior Segment

In addition to inflammatory signs, anterior chamber could also be the seat of the cysticercus itself. While the cyst is alive, the inflammatory reaction can be surprisingly not severe even with relatively large cysts [5]. As alluded to, cataract can occur secondary to the chronic inflammation in the posterior segment.

9.3.3.2 Posterior Segment

If the media is clear enough, the cyst and its location (intravitreal vs. subretinal) can be appreciated with the ophthalmoscope (Fig. 9.4). The motility of the cyst is seen as undulating folds in the cyst wall. The cyst wall has a glistening golden sheen that is rather characteristic. In addition, on occasion, the scolex may be evaginated and well appreciated. A subretinal cyst may be less obvious in its identity on clinical evaluation, especially when it is small.

There is variable reaction to the cyst seen as vitritis and vitreous membranes. The retina could be variably detached due to

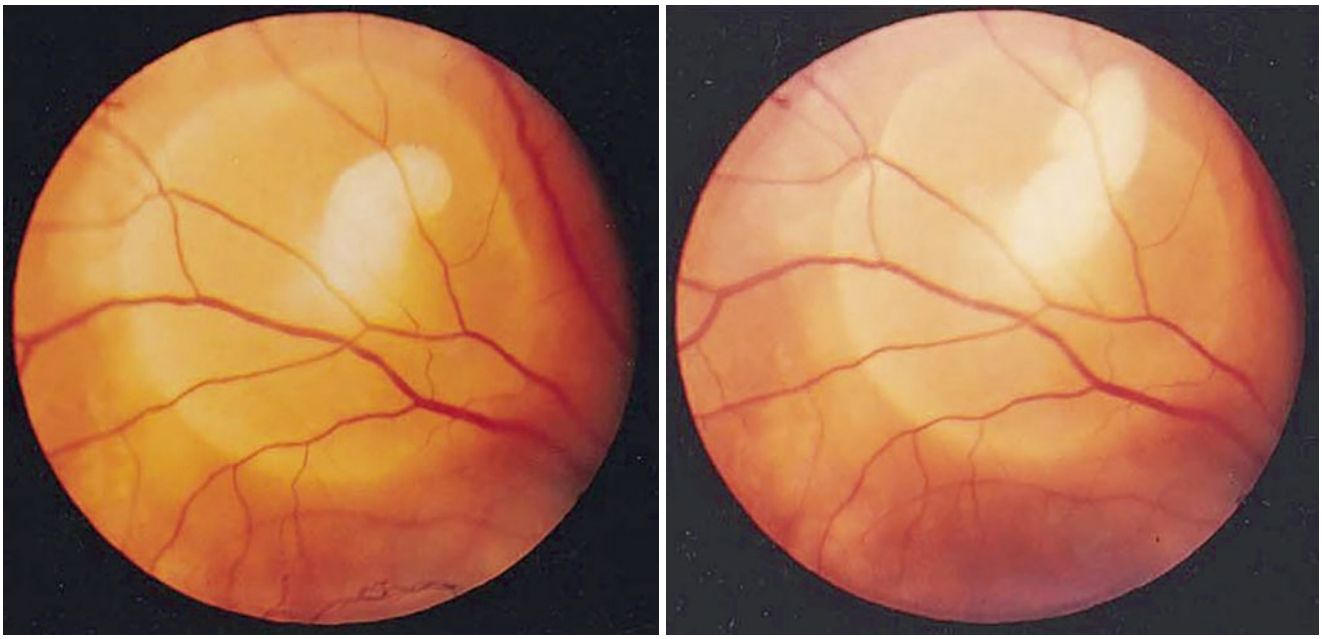

Fig. 9.3 Two photographs clicked few minutes apart showing the attempt at evagination of the scolex in a case of subretinal cysticercosis. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

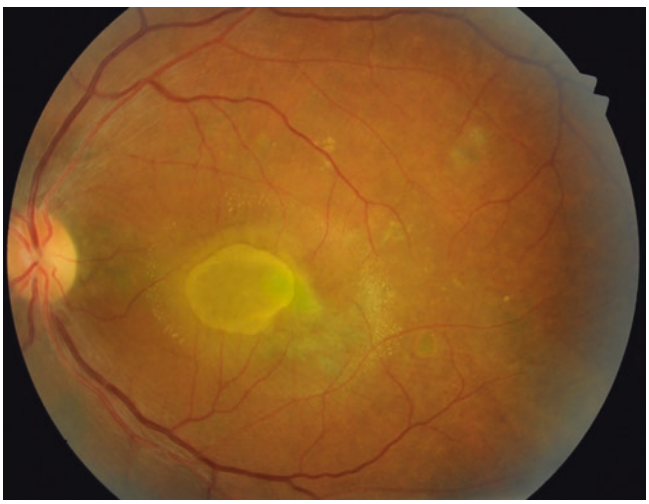

Fig. 9.4 Fundus photograph showing submacular *Cysticercus cellulosae*

the traction caused by the inflammatory membranes. The extent of chorioretinal scarring is also variable and could be so extensive as to make the eye functionless. In eyes with severe reaction, very often it is not possible to assess the true extent of damage to the retina and the consequent visual potential. The preretinal membranes are distinct from the membranes seen in proliferative vitreo-retinopathy that one sees in rhegmatogenous retinal detachments. They are more easily removed from the retina. Vitreous hemorrhage as a rare presenting feature of intraocular cysticercosis has been described [6].

9.4 Investigations

9.4.1 Ultrasonography [7]

In eyes with opaque media, ultrasonography helps in the diagnosis of the underlying pathology. The cyst is seen as a well-circumscribed hyperechoic lesion with central hypoechoic space. The scolex is often decipherable as a hyperechoic spot (Fig. 9.5).

9.4.2 Optical Coherence Tomography (OCT)

Takkar et al. [8] have described OCT features of the cyst in anterior chamber. However, OCT does not add value in terms of diagnosis since the cyst is fairly obvious on slit lamp evaluation.

9.4.3 Neuroimaging

Neuroimaging must be done in all cases of intraocular cysticercosis in view of the close association with cerebral cysticercosis. In a report by Sharma et al., 24.4% of patients with intraocular cysticercosis had evidence of cerebral cysticercosis [9]. The cysts can be located in the subarachnoid space or within the cerebral parenchyma—typically at junction of white and gray matter [10]. The cyst fluid has

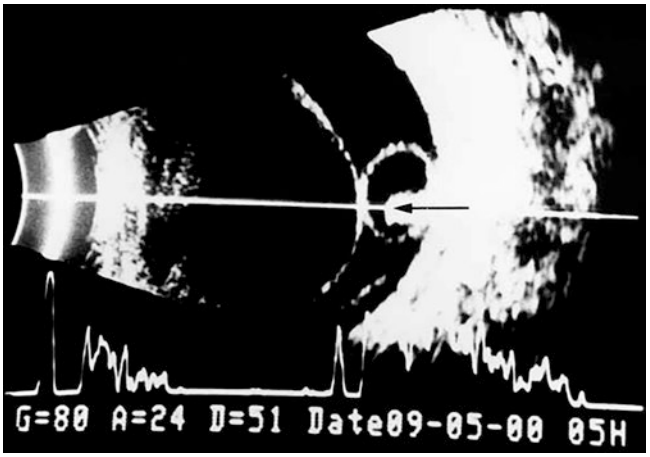

Fig. 9.5 Ultrasonogram demonstrating the well-delineated subretinal cysticercus with intra-cyst scolex (Black arrow). Retinal detachment is also demonstrable as a high reflective membrane in front of the cyst. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

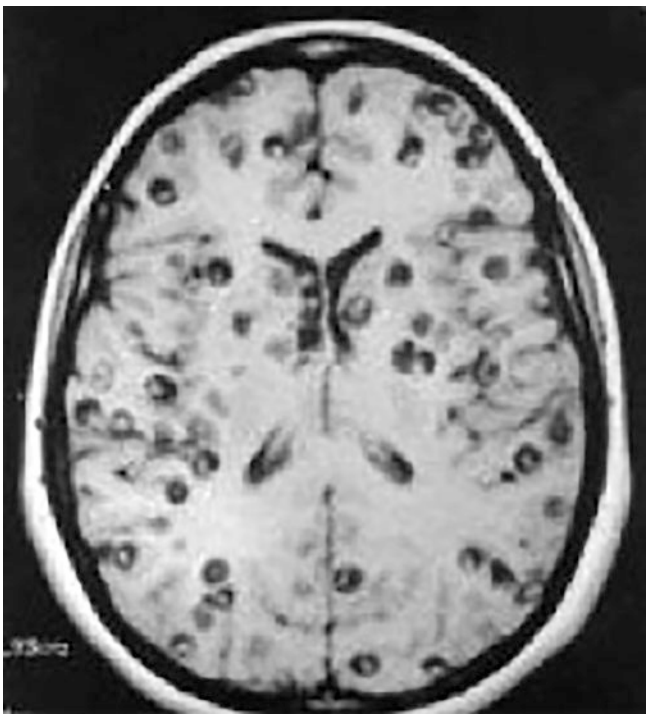

Fig. 9.6 MRI of the brain showing multiple cysticercus lesions—predominantly at junction of gray and white matter

same imaging features as the cerebrospinal fluid (CSF) both on magnetic resonance imaging (MRI) and computerized tomography (CT) scan. The scolex is identified as hyperdense lesion on CT scan and is iso- to hyperintense on T1- and T2-weighted MRI images (Figs. 9.6 and 9.7). Specialized techniques such as FLAIR (fluid-attenuated inversion

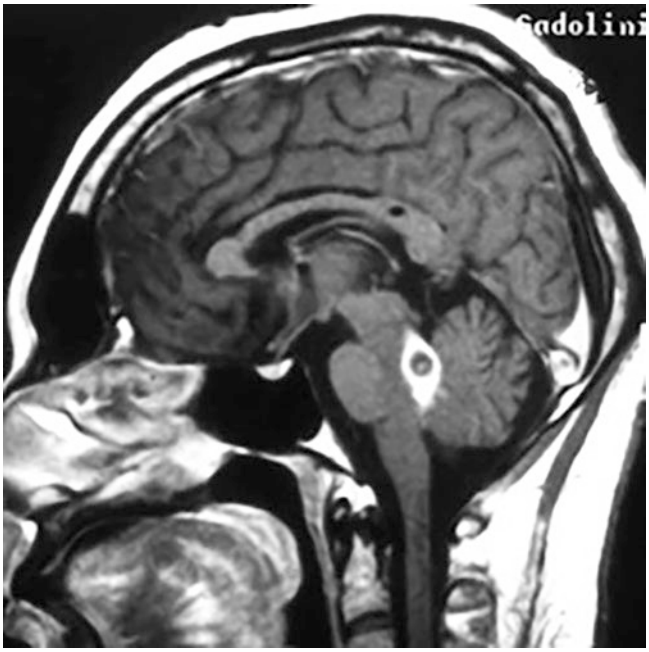

Fig. 9.7 MRI of the brain showing cysticercus lesion in midbrain

recovery sequence) and DWI (diffusion-weighted imaging) help identify the scolex better [10]. As the cyst degenerates, perilesional edema is made out due to enhanced inflammatory reaction. The dead parasite gets calcified, at which stage it loses inflammatogenic potential, but the perilesional fibrosis can be significant in causation of seizures. These calcified lesions are best made out on CT scan.

9.4.4 Laboratory Investigations

Serological investigations such as ELISA and indirect hemagglutination test are of benefit in neurocysticercosis, but in pure intraocular cysticercosis, the serological tests may fail to guide the diagnosis.

9.5 Management

9.5.1 Introduction

The primary management of intraocular cysticercosis is surgical. Surgery permits removal of the entire parasite and thus the antigens and toxins that incite the inflammatory reaction. Surgery also permits the management of the associated damage to the intraocular structures. Medical management with antihelminthic drugs such as albendazole is not recommended for intraocular cysticercosis. Killing the parasite with albendazole can trigger more severe reaction in the eye with destructive damage to the sensitive retina. Systemic

Fig. 9.8 Intact cysticercus that was delivered from the eye. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

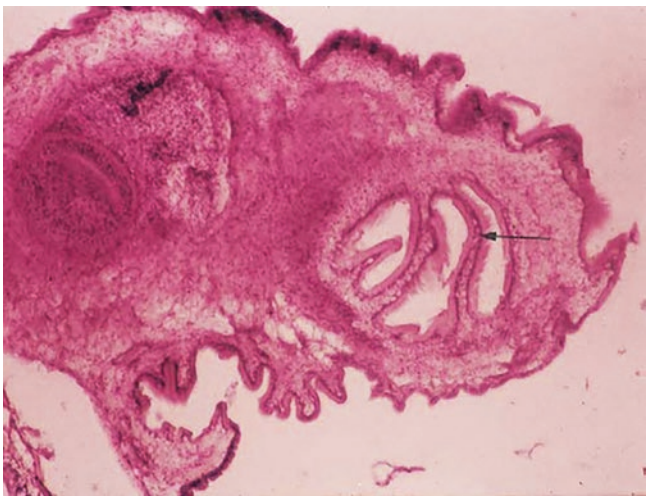

Fig. 9.9 Histopathology of the *Cysticercus cellulosae*. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

steroids are useful addendum to control the coexisting inflammation—both preoperatively and postoperatively.

Despite some reports indicating that delay in removal of the cyst does not alter the prognosis [11], the recommendation would be to remove the cyst as soon as possible. Procrastination brings in the impossibility to gauge the future course of inflammation or migration of the cyst. With the current status of the excellent techniques of vitreoretinal surgery, there is no reason to postpone the surgical removal of the causative agent.

9.5.2 Removal of Anterior Chamber *Cysticercus cellulosae*

Cysticercus in the anterior chamber is easily removed through a limbal wound. Viscoelastic fluids are injected through a stab incision in the opposite quadrant to aid the delivery of the cyst. The incision for delivery of the cyst needs not be the same diameter as the cyst, since the cyst molds itself in the process of being delivered and can be removed through an incision smaller than the actual diameter of the cyst.

However, it is the scolex that is the non-compressible part of the cysticercus, and the wound must be large enough to admit the scolex freely for atraumatic delivery. Removal of the intact cyst is not only elegant but also desirable (Figs. 9.8 and 9.9). Rupture of the cyst in the anterior chamber leads to liberation of the antigens and theoretical risk of inciting inflammatory reaction. It is of course possible to irrigate the anterior chamber and reduce the risk of inflammation.

9.5.3 Removal of Intravitreal *Cysticercus cellulosae*

Pars plana vitrectomy and removal of the cyst is a relatively easy procedure. The cyst can either be delivered through the sclerotomy or can be cut and aspirated by the vitreous cutter. If removal of intact cyst is aimed at, the vitreous membranes are first removed with the cutter, and once the cyst is freely mobile in the vitreous cavity, one sclerotomy may have to be enlarged depending on the size of the cyst. A good vitrectomy near the sclerotomy aids the free exit of the cyst. The cyst needs to be brought close to the sclerotomy site by either suction of the flute needle or endo-cryoprobe (Fig. 9.10). Once the cyst is engaged into the sclerotomy site, the fluid thrust progressively pushes it out. However, if the sclerotomy site is not enlarged to the required degree, the scolex can get stuck. Enlarging the sclerotomy at this stage is not possible since the sharp instruments can rupture the cyst.

A partly prolapsing cyst can be gently nudged out by applying pressure on either side of the sclerotomy and at the same time using external cryoprobe to pull on the cyst. A rupture of the cyst can occur at this stage but does not compromise on the final result. Once the contents are evacuated outside the eye, the rest of the cyst can be more easily pulled out.

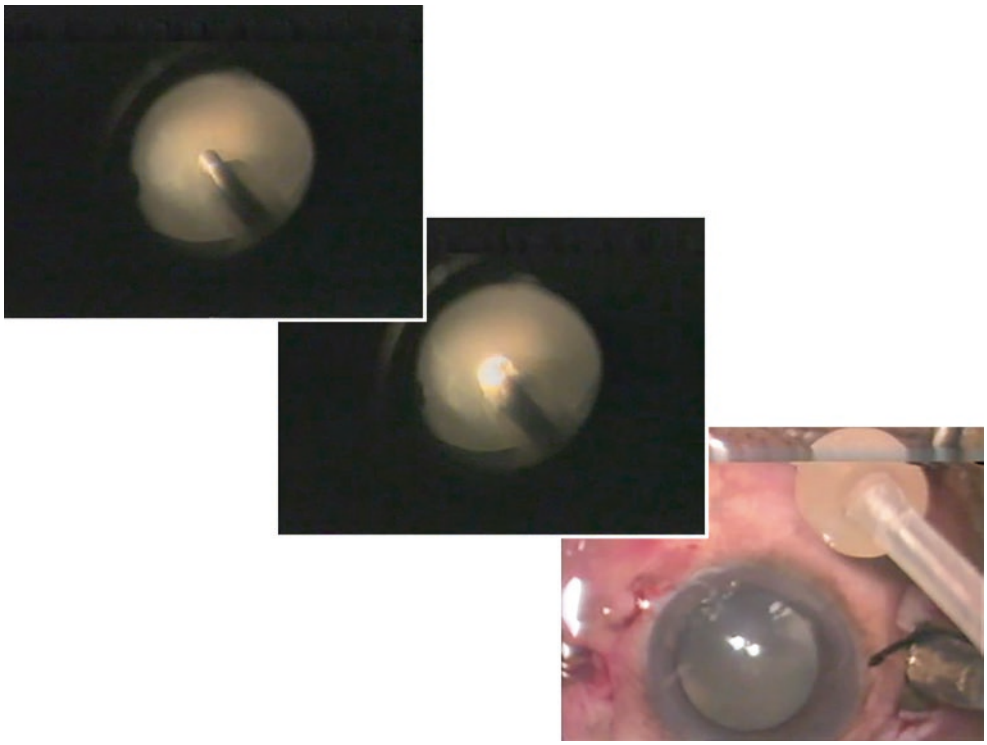

Fig. 9.10 Serial frames from video of intravitreal cyst delivered out of the eye with help of endo-cryoprobe

9.5.4 Removal of Subretinal *Cysticercus cellulosae*

Cysticercus under the retina can be approached by either external route or transvitreally. In general, an anteriorly located subretinal cyst is best approached by scleral route, while a posteriorly located subretinal cyst is approached transvitreally.

9.5.4.1 External Route

A well-defined cyst under the retina with clear vitreous cavity and located anterior to equator can be managed by transscleral route of delivery. The muscles are tagged as for a retinal detachment surgery, and the site of cyst is localized on the sclera. A scleral cut and exposure of choroid is made as for drainage of subretinal fluid. The choroid is then diathermized and incised. Very often, there is considerable fibrosis around the subretinal cyst, and unless this is also incised, the cyst does not exit the subretinal space (Fig. 9.11). A good indirect ophthalmoscopic assessment just before incising the choroid can acquaint the surgeon of the anatomy as well as whether the cyst has shifted position in the interim. The white fibrous tissue that presents itself at the choroidal incision can be confused with cyst or retinal prolapse.

Once the cyst is delivered, the sclerotomy is closed and the fundus inspected. There is usually no need to perform any additional procedures. If in doubt of retinal hole formation at that site, one can treat it with cryo and buckle.

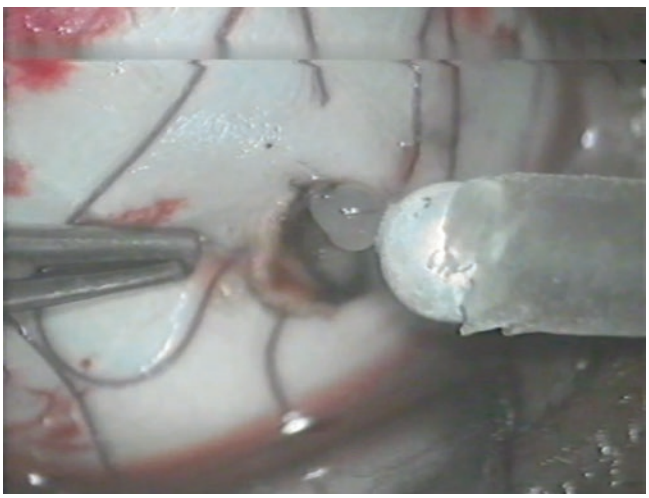

Fig. 9.11 External delivery of cysticercus: intraoperative photograph showing the sclerotomy with preplaced sutures; choroidotomy; and the partially prolapsing cysticercus that is being guided out by external cryo application

9.5.4.2 Transvitreal Approach

After the vitrectomy, the location of the subretinal cyst is evaluated. If the cyst is extramacular, the retinotomy can be placed directly over the cyst. If, however, the cyst is located under macula, one can place a retinotomy temporal to the macula and displace the cyst temporally with the help of perfluorocarbon liquids and suction applied using subretinal

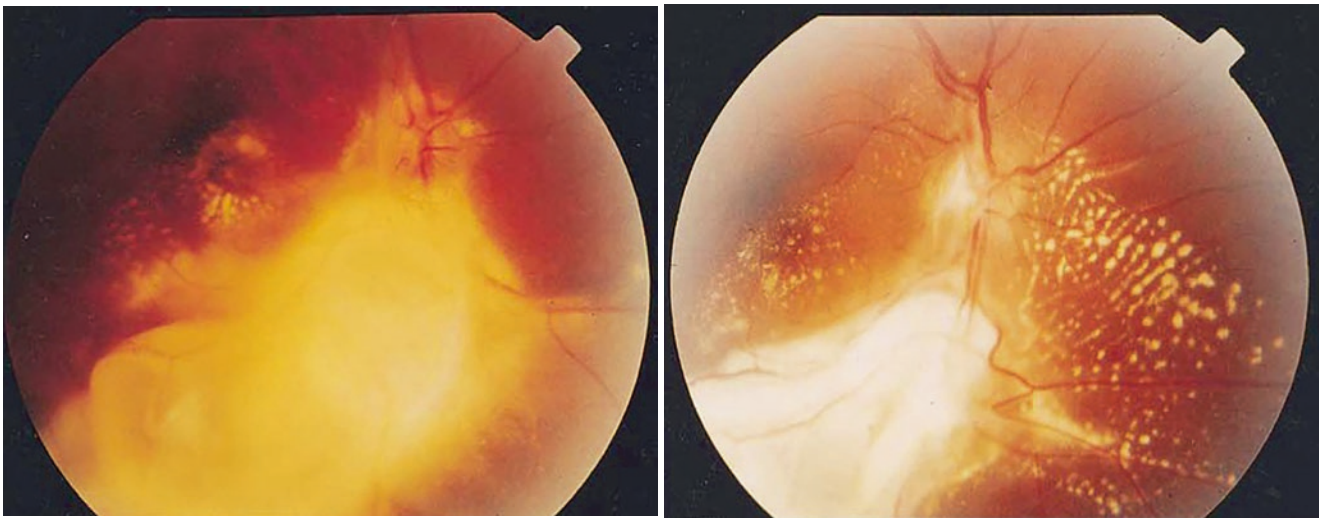

Fig. 9.12 Pre- and postoperative photographs of an eye with subretinal cysticercus and extensive chorioretinal scarring. Despite the scarring the vision improved substantially. Figure printed with permission from Elsevier publishers from our article "Intraocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery." Ophthalmology May 2003 Vol 110 Issue 5 Pages 996–1004

soft-tipped cannula via the retinotomy. The retinotomy need not match the size of the cyst. The cyst can mold itself out of relatively smaller retinotomy or at the worst the retinotomy enlarges to admit the cyst. Once delivered into the vitreous cavity, the rest of the procedure is similar to the intravitreal cysticercosis.

9.5.4.3 Additional Procedures

Once the cyst is removed, the preretinal membranes are removed and the retinal damage assessed. Combined traction and rhegmatogenous retinal detachments need usual procedures of fluid air exchange, endolaser and internal tamponade with gas, or silicone oil. In a majority of cases, the area of chorioretinal scarring (which represents the original subretinal location of the cyst before it migrated into the vitreous cavity) does not harbor any retinal break contributing to retinal detachment. Even large retinal holes in the area of scarring have enough fibrosis around them as to not cause rhegmatogenous retinal detachment. It is more often the retinal breaks caused elsewhere by the traction that need attention.

9.6 Results

In general, the results of management will depend on the existing damage to the retina at the time of intervention. Once the cyst is removed, the tendency for ongoing inflammation is limited. Despite extensive scarring, one finds that the eyes quieten down and recover some useful vision (Fig. 9.12). Cysts only in the anterior chamber or in vitreous cavity without coexisting chorioretinal damage will obviously have better visual results. Most published reports were individual case reports with the occasional case series. The largest published case series is by Sharma et al. of 45 eyes [9]. There were 27 eyes with intravitreal cysticercosis and 18 with subretinal cysticercosis. Retinal detachment was noted in 48.8% with significant proliferative vitreo-retinopathy seen in roughly half of these eyes with retinal detachment. In 4 eyes, the cyst was delivered transsclerally, and in the rest a transvitreal route was preferred. Rupture of cyst during delivery occurred in 13.3% of the eyes. But this did not affect the visual or anatomical outcome. In 4 eyes, the retinal detachment was found inoperable due to extensive destruction of the retina. At last follow-up, they had attached retina in 86.6% of the eyes and navigational visual recovery in 67.5%.

References

1. Del Brutto OH, Roman GC, Sotelo J, editors. Neurocysticercosis: a clinical handbook. Chapter 3. Tokyo: Swets & Zeitlinger Publishers; 1959. p. 29–35.
2. Alm A. Ocular circulation. In: Hart WM, editor. Adler's physiology of the eye. St Louis: Mosby–Year Book; 1992. p. 198–227.
3. Padhi TR, Das S, Sharma S, Rath S, et al. Ocular parasitoses: a comprehensive review. Surv Ophthalmol. 2017;62:161–89.
4. Menon V, Tandon R, Khanna S, Shanna P, Khokkar S, Vashisht S, Garg I. Cysticercosis of the optic nerve. J Neurophthalmol. 2000;21:59–60.
5. Singh SP, Rana J, Duker J, Singh PA. Extracting a large live freely floating cysticercosis cyst from the anterior chamber of the eye using visco expression technique: a case report. Saudi J Ophthalmol. 2016;30:56–9.
6. Jain RS, Kumar S, Bhana I, Agarwal R. Ocular cysticercosis with vitreous hemorrhage: a rare complication of a common disease. Springerplus. 2015;4:217.
7. Bhende M, Kamat H, Krishna T, Shanta B, Khetan V, Sen P, Pradeep S. Atlas of ophthalmic ultra sound and ultra sound biomicroscopy. Chapter 15. New Delhi: JP Medical Ltd; 2013. p. 119–25.

8. Takkar B, Mehdi MU, Ahmed NR, Chandra P, Vanathi M. Anterior segment optical coherence tomography of live ocular cysticercosis. Clin Exp Ophthalmol. 2014;42:896–8.
9. Sharma T, Sinha S, Shah N, Gopal L, Shanmugam MP, Bhende P, Bhende M, Shetty NS, Agarwal R, et al. Intra ocular cysticercosis: clinical characteristics and visual outcome after vitreo retinal surgery. Ophthalmology. 2003;110:996–1004.
10. Venkat B, Aggarwal N, Makhaik S, Sood R. A comprehensive review of imaging findings in human cysticercosis. Jpn J Radiol. 2016;34:241–57.
11. Messner KH, Kammerer WS. Intraocular cysticercosis. Arch Ophthalmol. 1979;97:1103–5.

Basic Principles in 23-, 25-, and 27-Gauge Pars Plana Vitrectomy

10

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Abbreviations

cSt	Centistokes
mmHg	mm of mercury
ppV	Pars plana vitrectomy
PVD	Posterior vitreous detachment

10.1 Brief History of Small-Gauge Vitrectomy

Although sutureless techniques for 20-gauge vitrectomy had previously been described by several groups, it was not until the advent of 25-gauge vitrectomy that transconjunctival sutureless vitrectomy became popular. Contrary to the expectations incited by the order of increasing gauge numbers, the era of small-gauge vitrectomy started with the advent of 25-gauge instruments, first presented in 2002 [1]. The development of a less invasive approach to vitrectomy had been prompted by typical complications that can occur with 20-gauge pars plana vitrectomy (ppV) like iatrogenic entry site breaks, the attempt to shorten suturing and operating time, and the desire to spare the conjunctiva from scarring, which would be particularly advantageous in eyes with concomitant glaucoma, potentially requiring filtering surgery in the future. Despite some encouraging reports for conditions like vitreo-macular interface pathologies, it was felt that the initial outcomes of 25-gauge ppV were inferior to 20-gauge surgery for retinal detachment repair and other more complex procedures necessitating significant manipulation of the globe and thorough removal of peripheral vitreous. The reduced stiffness of instruments and initially longer surgery times were unfamiliar to many surgeons and provoked skepticism among retina specialists. Hence, the initial uptake of 25-gauge vitrectomy was slow. Apart from lower stiffness of 25-gauge cutters and light pipes, the limited array of instruments was another major issue. It was for these reasons that Claus Eckardt engineered 23-gauge vitrectomy instruments first published in 2005 [2]. The adoption of the 23-gauge ppV was then quick, and the technique spread rapidly. The next step in the evolution was 27-gauge vitrectomy, introduced by Oshima in 2010 [3]. Progress and innovation in materials and design have made instruments stiffer and improved maneuverability of the globe during surgery. However, the significance of 27-gauge technique remains marginal to date, being regularly used by only few surgeons according to the most recent Preferences and Trends (PAT) survey among international vitreoretinal surgeons by the American Society of Retinal Specialists [4]. Nevertheless, some surgeons use 27-gauge systems almost exclusively for nearly the entire spectrum of vitreoretinal pathology, and a paradigm shift toward smaller incisions seems just a matter of time. Even injection of viscous silicon oil (5000 cSt) is feasible with 27-gauge cannulas [5], and the range of instruments available for small-gauge surgery is being constantly expanded. Hybrid techniques have also been described, allowing the use of tools that require larger sclerotomies [6].

10.2 Common Platforms and Performance Characteristics

There are four major vitrectomy platforms available: Constellation® from Alcon (Fig. 10.1), Stellaris® PC from Bausch + Lomb (Fig. 10.2), EVA from the Dutch Ophthalmic Research Center (DORC, Fig. 10.3), and the OS4 system from Oertli Instruments. Cutting speed varies from 5000 to 8000 cpm. However, with the newly designed double-cutting open-port vitrectomy probes, the effective cut rate goes up to 16,000 cpm [7, 8], and flow rates are increased with this new

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Fig. 10.1 Instruments of the Constellation® 27-gauge platform by Alcon

design. Performance characteristics of cutters are important to vitreoretinal surgeons because vitreous removal should be as efficient as possible with minimal retinal traction to avoid complications such as iatrogenic retinal breaks. High cut rates result in less pulsatile flow and minimal retinal traction. However, flow is affected by many factors other than cut rate like viscosity of aspirated material, the size of fragmented vitreous, or resistance inside the tubing system. With conventional cutters, the aspiration rate at constant vacuum is somewhat dependent on the cutting rate, although to a lesser extent in smaller-gauge surgery. The decrease of the aspiration flow with increasing cut rates can be explained by a less efficient duty cycle. However, in an experimental setting investigating double-cutting open-port probes at maximum fixed vacuum (650 mmHg), the flow rates measured were almost independent of the cut rate [7, 8]. In the same setting with fixed maximal cut rate, the flow increased approximately threefold to 10 ml/min with 23-gauge cutters when the vacuum was augmented from 100 to 650 mmHg. With 27-gauge cutters the flow remained constant, however, at a much lower rate of only about 2.5 ml/min. Hence, with modern 27-gauge instrumentation, the flow is almost independent of the vacuum applied.

10.3 Advantages and Limitations of Small-Gauge Vitrectomy

The use of small-gauge microcannulas has advantages both during and after surgery. During the procedure, such systems ascertain alignment between conjunctiva and sclerotomy. As a result, tissue trauma and traction on the vitreous base are minimized, and the microcannulas facilitate smooth insertion and removal of instruments from the globe. Furthermore, the infusion line can be connected to any of the microcannulas intraoperatively if needed. In the postoperative course, small-gauge surgery causes less inflammation and reduces morbidity including pain and irritation. Recovery and healing are faster, and surgically induced corneal astigmatism is almost inexistent. Shorter operating times and minimal wound size paved the way for the widespread use of local anesthesia.

Another advantage of small-gauge surgery is decreased and less pulsatile intraocular flow, which, combined with high cutting rates, makes retinal detachment repair safer, reducing the incidence of iatrogenic breaks. In general, the sphere of influence is smaller for small-gauge cutters, but the efficiency is greater. This results in reduced traction and safer work in close proximity of the retina [9]. Additionally, in the modern small-gauge vitrectors, the distance between the mouth and the tip of the cutters is minimal. This allows more precise dissection for segmentation and delamination of fibrovascular preretinal tissue. For complex cases, a bimanual approach with the use of a chandelier endoillumination system allows even more sophisticated surgical manipulations.

Furthermore, valved microcannula systems increase the stability of the vitreous cavity during surgery and reduce reflux of fluids and the risk of retinal incarceration when no instrument is inserted, thus making the use of plugs superfluous. This is particularly relevant for retinal detachment repair [10]. Many surgeons use valved microcannulas for the majority of cases [4].

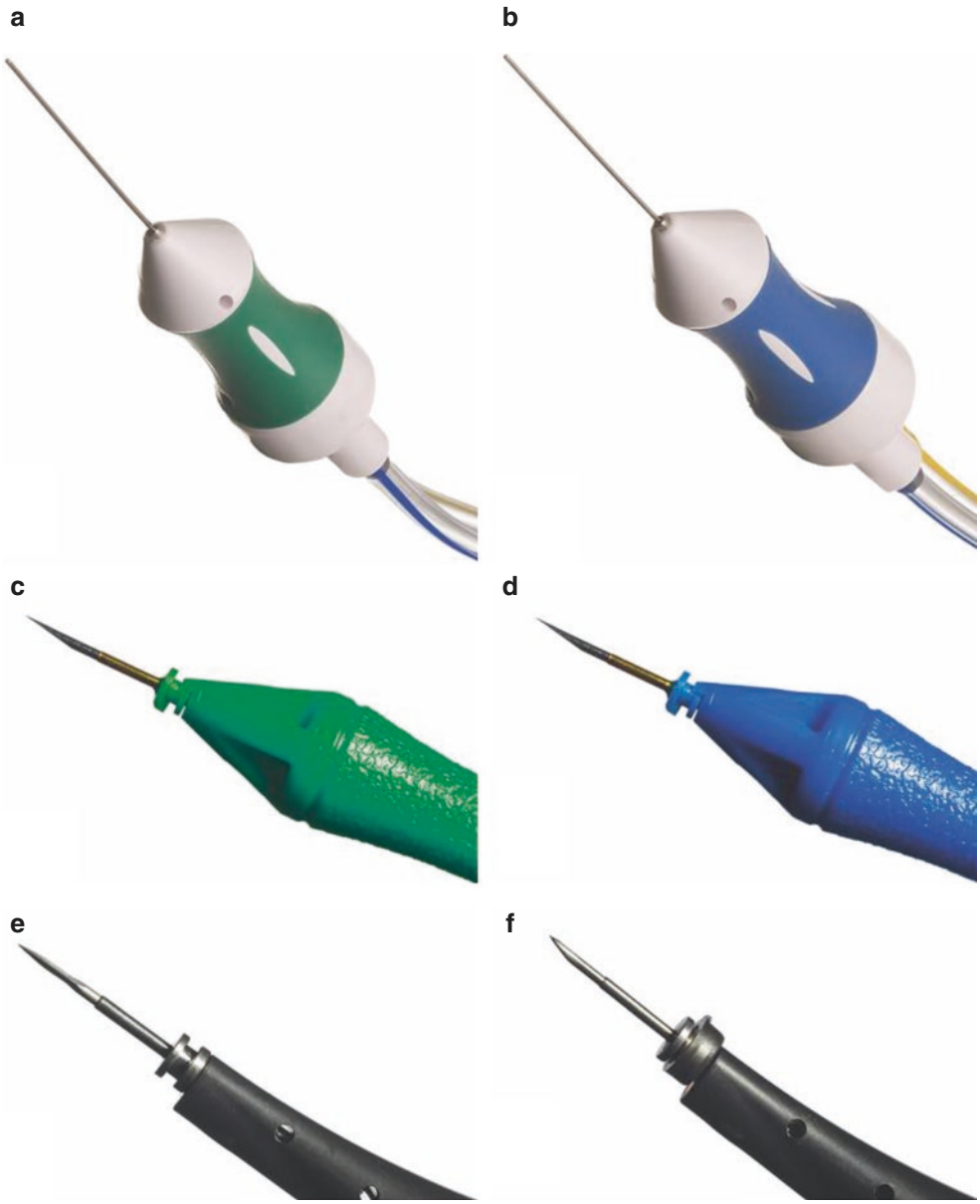

Fig. 10.2 Stellaris® PC platform from Bausch + Lomb with color coding. Cutter (**a**) with non-valved trocar/microcannula system (**c**) in 23-gauge (green) and 25-gauge (**b**, **d**, blue), respectively. 27-gauge trocar/microcannulas with non-valved (**e**) and valved (**f**) microcannulas

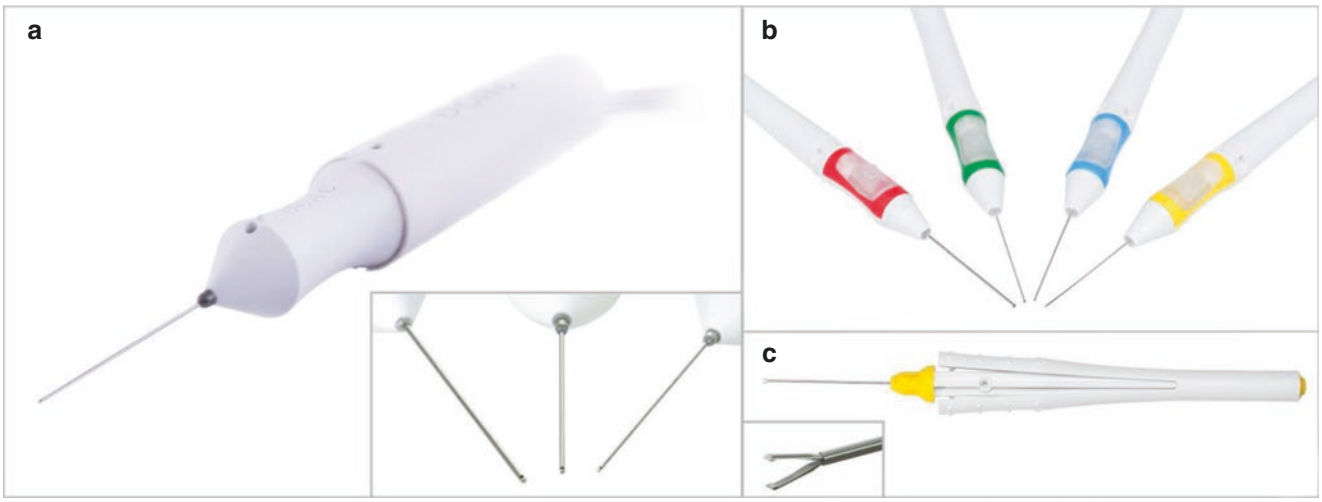

Fig. 10.3 Instruments from the EVA platform by DORC. (**a**) Uniform design of double-cutting open-port vitrectors with tips available in 23-, 25-, and 27-gauge shown in inset. (**b**) Backflush cannulas of different sizes (20-, 23-, 25-, and 27-gauge) with color coding. (**c**) Disposable 27-gauge microforceps with extended reach and wide grip (tip shown at higher magnification in inset)

10.4 Limitations of Small-Gauge Vitrectomy

10.4.1 Instrument Stiffness and Learning Curve

One of the main limitations of smaller-gauge vitrectomy is the instruments are prone to deforming and flexes during manipulation (Fig. 10.4). Practically, this makes maneuvering the globe for anterior retinal pathology difficult, especially in phakic patients. Globe movement and rotation from incomplete eye block or light general anesthesia can also contribute to this problem. Poor access can add to the problem, e.g., patients with prominent brow, high nose bridge, and deep-set eyes. This can be partially circumvented by proper patient positioning. Superior-inferior access can be improved by aligning the cheek bone to the brow line, while horizontal access can be improved by aligning the lateral canthus to the level of the top of the nose bridge. While this positioning can help improve access, it can be rather uncomfortable for the patient.

To overcome this inherent disadvantage of flimsy instruments, some manufacturers have reinforced the base of the instruments to increase overall stiffness of the instrument while maintaining the size. Surgeons who are new to smaller-gauge vitrectomy often find that their instruments are completely deformed after the case. Dealing with the instrument's lack of stiffness represents most of the learning curve associated with transitioning to smaller-gauge vitrectomy.

10.4.2 Range of Instrumentation and Endoillumination

During its infancy, smaller-gauge vitrectomy suffered from paucity of range of instruments and poorer level of illumination. However, as popularity of small-gauge surgery increased and improved stiffness of the instruments was achieved, the range of instrumentation in both disposable and reusable is now comparable to the larger-gauge platforms. Due to the smaller bore size of the fiber-optic cable, smaller-gauge vitrectomy also has poorer illumination. Various methods of circumventing this have been described, the simplest of which is to maximize the illumination intensity or supplementing the main light source with a chandelier illumination. While Xenon is the main source of endoillumination, advances in laser and high output LED light source are evolving and promising to deliver brighter light source while minimizing the risk of phototoxicity. However, increasingly brighter illumination may not be necessary with the advent of digitization of the viewing system. Digitization allows the level of brightness to be digitally "gained" while keeping the actual light input the same. Having too much light can "flood" the range of the camera and may lead to degradation of contrast.

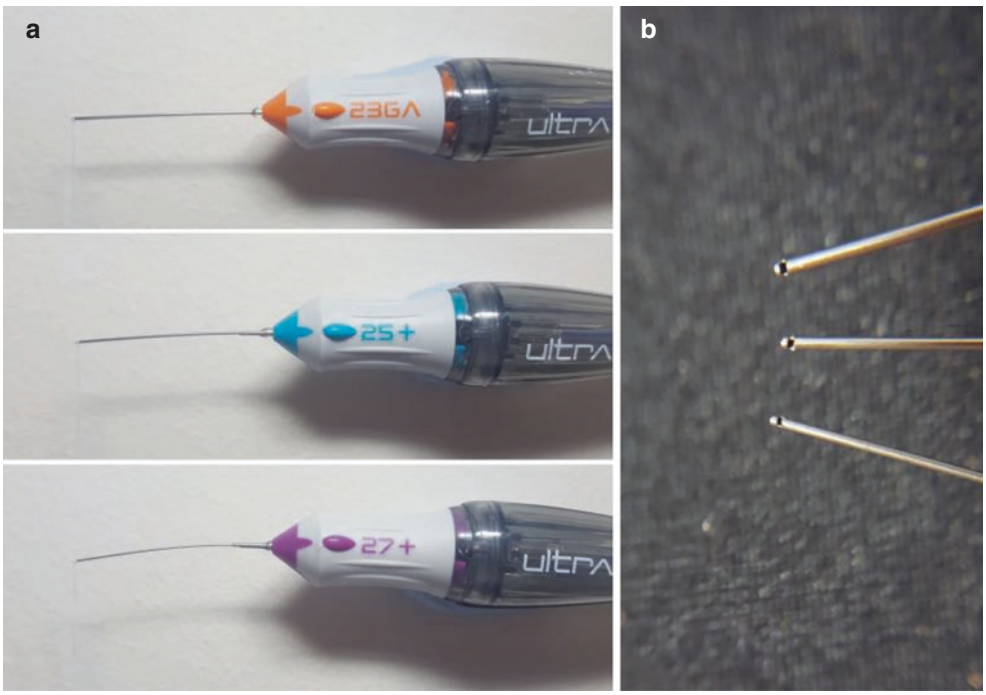

Fig. 10.4 Cutter characteristics of different gauge sizes. (**a**) Comparison of instrument stiffness with identical weight hanged to end of vitrectors. (**b**) Comparison of diameter size and cutting opening to tip distance for 23-, 25-, and 27-gauge. "+" sign on instruments indicates reinforced base of the instruments and special materials for enhanced stiffness

10.5 Complications Specific to Small-Gauge Vitrectomy

10.5.1 Hypotony

Although sclerotomies in small-gauge vitrectomy are primarily self-sealing, hypotony is not an uncommon finding after transconjunctival sutureless vitrectomy. Risk factors predisposing to wound leakage include previous vitreoretinal surgery (in particular 20-gauge ppV with opening of the conjunctiva), multiple exchanges of instrument, larger instrument diameter, young patient age, high myopia, connective tissue disorders such as Marfan's disease, and extensive vitreous base dissection. Rates as high as 25% have been reported 2 h after surgery [11], but postoperative hypotony is generally transient and resolves within hours to a few days. Nevertheless, hypotony increases the risk for serious postoperative complications like expulsive hemorrhages or decompression retinopathy and is associated with higher endophthalmitis rates. Several techniques have been described to lower the incidence of hypotony. Surgeons have advocated gentle massaging of wounds after removal of microcannulas, partial air tamponade and supine positioning, counter stab incisions, use of fibrin glue, or suturing of scleral incisions. If sutures are required after small-gauge vitrectomy, dissolvable transconjunctival sutures are most commonly used (e.g., Vicryl 7-0). Importantly, in children, all sclerotomies are routinely closed with sutures because of the high elasticity of the sclera. We also tend to use sutures when silicone oil tamponade is used to consistently avoid subconjunctival leakage.

10.5.2 Endophthalmitis

Initial papers reported elevated endophthalmitis rates after 25-gauge vitrectomy, attributed to the lack of mechanical closure, lower rate of sterile fluid flow during the procedure, and less thorough removal of vitreous from the vitreous base. However, more recent reports have not confirmed this difference in postoperative endophthalmitis incidence [12]. Several technical modifications such as angled wound construction, misalignment of conjunctival and scleral incisions, or use of sutures for leaking incisions in any doubt about sealing might have contributed to improvement. Interestingly, despite identical spectrum of microorganisms, visual outcomes of endophthalmitis after small-gauge vitrectomy have been reported to be better than in 20-gauge cases [13].

10.5.3 Jamming

Jamming was first described in 25-gauge vitrectomy [14]. It means mechanical blockage of an instrument in the microcannula, which can result in inadvertent dislocation of the microcannula upon removal of the instrument from the eye. Jamming is caused by organized vitreous membranes accumulating in the microcannula and occurs frequently during surgery for dense vitreous hemorrhages. It is more likely to happen with small-gauge instrumentation with reduced lumen diameter. To avoid this complication, 23-gauge vitrectomy seems more appropriate than 25- or 27-gauge surgery for dense vitreous hemorrhages.

10.5.4 Difficult Induction of Posterior Vitreous Detachment (PVD)

The presence of a complete vitreous detachment is key for successful outcomes in many vitreoretinal procedures, in particular retinal detachment repairs. For better visualization of the posterior vitreous face, triamcinolone acetate is commonly used. A major drawback of smaller-gauge instrumentation is reduced purchase of vitreous fibers at the optic nerve head because of the smaller cutter opening. The small inner diameters of 25- and 27-gauge cutters result in a lower aspiration rate by about a factor of 6 compared to 20-gauge ppV [1]. Despite higher vacuum settings, it is harder to engage and hold vitreous with small-gauge instrumentation, which can result in substantial difficulty in inducing a PVD, particularly in younger patients with more adherent vitreous.

10.5.5 Iatrogenic "Jet Stream" Injury

The small lumen of cannulas produces a high velocity of fluids injected, to the extent that the impact of the fluid on the retina can cause tissue damage. The jet of fluid can disrupt the retina, which can result in subretinal penetration, typically when vital dyes are injected manually. Iatrogenic breaks and localized retinal detachments have also been reported to be caused by the infusion fluid flow [15]. Obviously, the smaller the diameter of instruments, the higher the risk of such complications. Hence, surgeons need to be aware of this hazard and take precautions injecting slowly.

10.6 Technique

10.6.1 Wound Construction

In modern small-gauge vitrectomy, the incisions are most commonly created in single-step angled or two-step technique (Fig. 10.5) using microcannulas that are preloaded on needle trocars with a handle (representative images in Fig. 10.2c–f). For 27-gauge systems, some surgeons even use one-step vertical insertion [3, 16].

The blade design determines wound architecture and to some extent postoperative sealing of sclerotomies [17]. It is important to bear in mind that during insertion of trocars and microcannulas, relatively high intraocular pressures are generated, and special caution should be taken in eyes with structural weakness. Therefore, recent corneal or scleral wounds sometimes need to be secured with sutures. A 30° angle of entry is commonly used for trocar insertion to create self-sealing scleral tunnels tangential to the limbus. Once past the trocar sleeve, the angle is changed to be perpendicular to the ocular surface, and the microcannula is fully inserted into the eye. Most surgeons aim to place the three microcannulas 3–4 mm from the limbus in the conventional locations inferotemporal, supero-temporal, and supero-nasal. The microcannula for the infusion inferotemporally should be inserted first and the infusion line then connected immediately. Before placement of the microcannulas in the superior quadrants, the infusion is preferably turned on after verification that the tip of the microcannula reaches into the vitreous cavity, visualizing the tip by pushing the microcannula centrally or shining light on its tip using the light pipe while observing through the pupil. Visualization of the tip is crucial to avoid suprachoroidal infusion. Inserting the microcannulas in the superior quadrants is easier and safer if the infusion is running and the globe pressurized, especially in previously vitrectomized eyes, which otherwise provide no resistance for insertion of the trocars. A chandelier illuminator can be placed inferonasal (Fig. 10.6) if needed, preferably before insertion of any of the trocars. To improve sealing, the conjunctiva/Tenon's capsule is displaced anteriorly when inserting the trocars. This results in misalignment of the conjunctival and scleral incision after withdrawal at the end of surgery, decreasing the likelihood of microorganisms gaining access to the scleral incision and intraocular contents. Carefully constructed wounds generally seal well. However, if there is any doubt about leakage, the sclerotomy should be sutured with a single Vicryl 7-0 transconjunctival suture to avoid postoperative hypotony and endophthalmitis.

10.6.2 Vitrectomy

After insertion of the light pipe and the cutter, the viewing system is adjusted to get an overview over the intraocular situation. A core vitrectomy is then performed, followed by injection of a small amount of triamcinolone acetonide to visualize the vitreous. If a PVD is not present, this is achieved by lifting the posterior vitreous hyaloid membrane at the optic nerve head. As soon as vitreous is engaged, maximum suction is applied, and the vitreous is pulled in a sweeping centrifugal movement anteriorly. This process needs to be executed repetitively in case of adherent posterior hyaloid. The area of the papillo-macular bundle should best be avoided. Once the Weiss ring is fully mobilized, it is pulled anteriorly to extend the posterior hyaloid detachment toward the periphery. If needed, more triamcinolone acetonide can be injected to visualize remaining cortical vitreous, particularly in eyes with suspected vitreoschisis. With very few exceptions (e.g., endophthalmitis), it is of paramount importance for the success of the surgery to achieve a complete PVD. Once the PVD is complete, the vitreous can be quickly removed up to the vitreous base. If needed, the vitreous base can be shaved using indentation, for which different techniques exist that are not further discussed here. In phakic eyes, the surgeon needs to be bear in mind that the space to maneuver with instruments in the eye is restricted by the crystalline lens. When crossing the midline in phakic eyes, the tip of the cutter should not move anterior to the equator to avoid a lens touch.

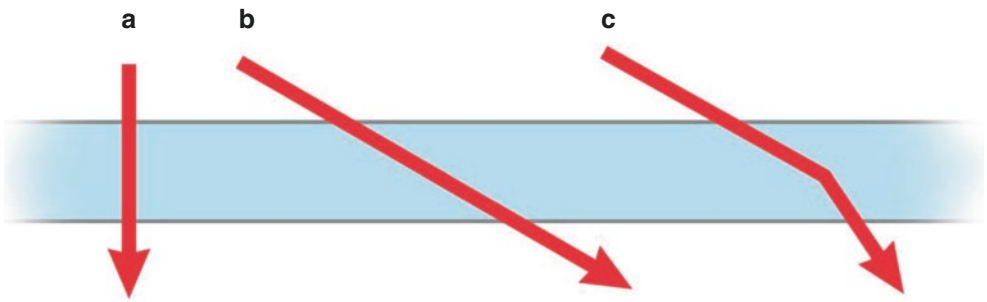

Fig. 10.5 Different types of wound construction. (**a**) One-step straight perpendicular to sclera, possible for 27-gauge instrumentation only. (**b**) One-step angled (30°). (**c**) Two-step angled (30°)

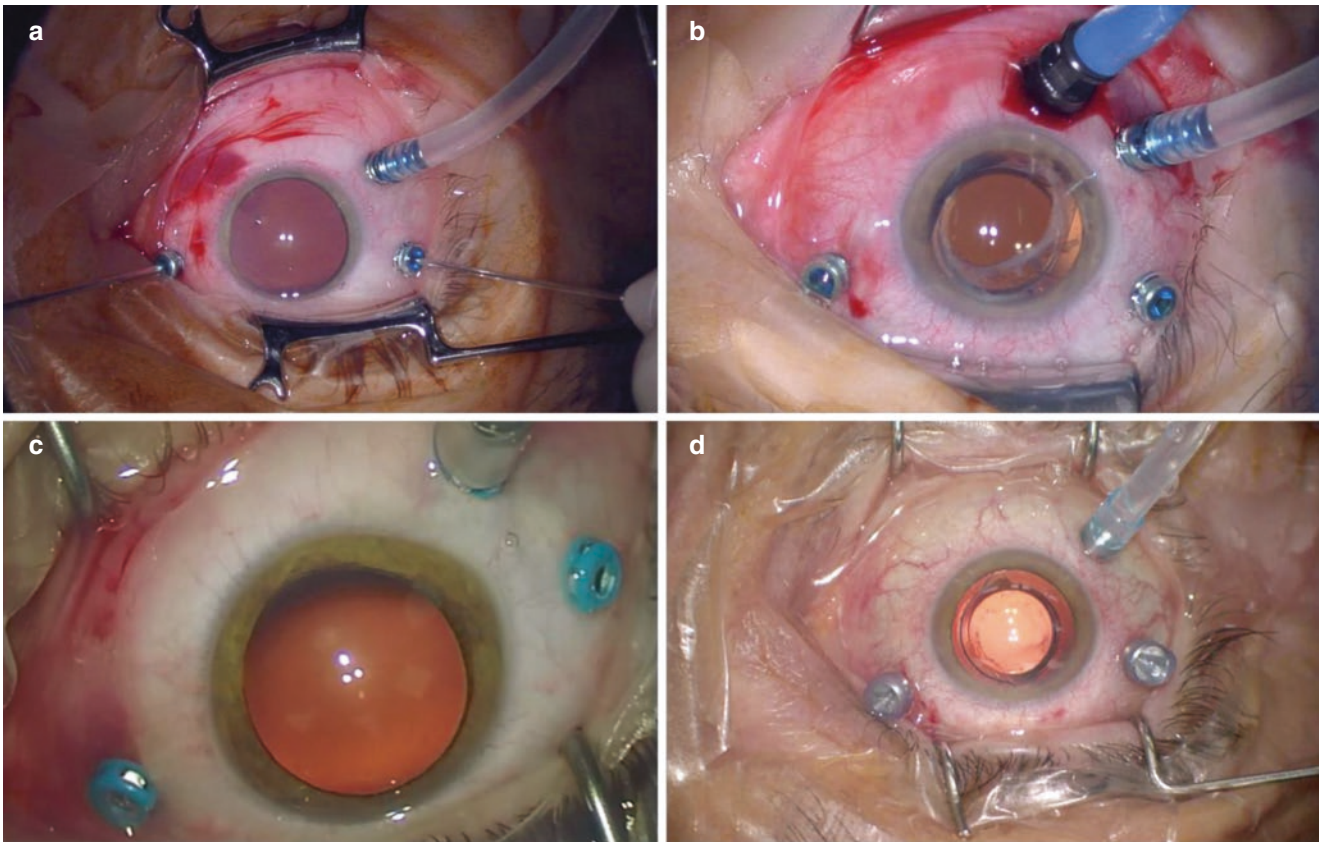

Fig. 10.6 Setup for 23-gauge pars plana vitrectomy without (**a**) and with chandelier illumination (**b**), 25- (**c**) and 27-gauge (**d**) surgery

10.6.3 Removal of Ports

It is very important to lower the infusion pressure to about 20–25 mmHg before removal of the ports, in particular with small-gauge surgery because the infusion pressures are typically high. The infusion microcannula is removed last to keep the posterior chamber pressurized and enhance sealing of the other sclerotomies. The infusion line is removed together with its microcannula. Occlusion is further promoted by gentle massaging of the conjunctiva and Tenon's capsule. Subconjunctival antibiotics are routinely given at the end of surgery to prevent postoperative endophthalmitis.

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References

1. Fujii GY, De Juan E Jr, Humayun MS, Pieramici DJ, Chang TS, Awh C, Ng E, Barnes A, Wu SL, Sommerville DN. A new 25-gauge instrument system for transconjunctival sutureless vitrectomy surgery. Ophthalmology. 2002;109(10):1807–12.
2. Eckardt C. Transconjunctival sutureless 23-gauge vitrectomy. Retina. 2005;25(2):208–11.
3. Oshima Y, Wakabayashi T, Sato T, Ohji M, Tano Y. A 27-gauge instrument system for transconjunctival sutureless microincision vitrectomy surgery. Ophthalmology. 2010;117(1):93–102.
4. PAT Survey. Membership survey preferences and trends. Chicago, IL: American Society of Retina Specialists; 2017.
5. Toygar O, Mi CW, Miller DM, Riemann CD. Outcomes of transconjunctival sutureless 27-gauge vitrectomy with silicone oil infusion. Graefes Arch Clin Exp Ophthalmol. 2016;254(11):2111–8.
6. Khan MA, Samara WA, Hsu J, Garg S. Short-term outcomes of hybrid 23-, 25-, and 27-gauge vitrectomy for complex diabetic tractional retinal detachment repair. Retin Cases Brief Rep. 2017. https://doi.org/10.1097/icb.0000000000000571.
7. Ribeiro RM, Teixeira AG, Diniz B, Fernandes RB, Zhong Y, Kerns R, Humayun MS. Performance analysis of ultrahigh-speed vitreous cutter system. Retina. 2013;33(5):928–32.
8. Zehetner C, Moelgg M, Bechrakis E, Linhart C, Bechrakis NE. In vitro flow analysis of novel double-cutting, open-port, ultrahigh-speed vitrectomy systems. Retina. 2018;38(12):2309–16.
9. Dugel PU, Zhou J, Abulon DJ, Buboltz DC. Tissue attraction associated with 20-gauge, 23-gauge, and enhanced 25-gauge dual-pneumatic vitrectomy probes. Retina. 2012;32(9):1761–6.
10. Oellers P, Stinnett S, Mruthyunjaya P, Hahn P. Small-gauge valved versus nonvalved cannula pars plana vitrectomy for retinal detachment repair. Retina. 2016;36(4):744–9.

11. Acar N, Kapran Z, Unver YB, Altan T, Ozdogan S. Early postoperative hypotony after 25-gauge sutureless vitrectomy with straight incisions. Retina. 2008;28(4):545–52.
12. Govetto A, Virgili G, Menchini F, Lanzetta P, Menchini U. A systematic review of endophthalmitis after microincisional versus 20-gauge vitrectomy. Ophthalmology. 2013;120(11):2286–91.
13. Oshima Y, Kadonosono K, Yamaji H, Inoue M, Yoshida M, Kimura H, Ohji M, Shiraga F, Hamasaki T. Multicenter survey with a systematic overview of acute-onset endophthalmitis after transconjunctival microincision vitrectomy surgery. Am J Ophthalmol. 2010;150(5):716–25.
14. Shinoda H, Nakajima T, Shinoda K, Suzuki K, Ishida S, Inoue M. Jamming of 25-gauge instruments in the cannula during vitrectomy for vitreous haemorrhage. Acta Ophthalmol. 2008;86(2):160–4.
15. Oshima Y, Ohji M, Tano Y. Surgical outcomes of 25-gauge transconjunctival vitrectomy combined with cataract surgery for vitreoretinal diseases. Ann Acad Med Singap. 2006;35(3):175–80.
16. Khan MA, Durrani AK, Hsu J, Regillo CD. 27-Gauge vitrectomy wound integrity: a randomized pilot study comparing angled versus straight entry in fluid-filled vitrectomized eyes. Retina. 2018;38(4):678–83.
17. Inoue M, Abulon DJ, Hirakata A. Comparison of the effects of 23-gauge and 25-gauge microincision vitrectomy blade designs on incision architecture. Clin Ophthalmol. 2014;8:2307–18.

Robot-Assisted Retinal Surgery: Overcoming Human Limitations

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11.1 Introduction to Robotic Eye Surgery

Robotics offer the potential to improve the precision and safety of retinal surgery. The starting point of advanced mechanical assistance in vitreoretinal surgery may be traced back to the invention of the motorized vitreous cutter by Machemer in the 1970s [1]. This revolutionized vitreoretinal surgical techniques and made it possible to treat complex retinal detachments, vitreous haemorrhage, epiretinal membranes and macular holes. Over the last decade, the use of vital dyes to stain retinal membranes has further improved the safety of some of the most intricate surgical steps such as peeling internal limiting membrane (ILM), stripping epiretinal membrane (ERM) and removing proliferative vitreoretinopathy (PVR), but minor retinal trauma remains inevitable even in experienced hands. Further improvements in the precision of retinal surgery are limited by human physiology, not only in terms of hand tremor and stability but also the resolving power of human vision even with the aid of the operating microscope. Modern laser-based in vivo imaging techniques such as intraoperative OCT can provide histological levels of detail, yet the limitations of human depth perception and hand-eye coordination mean that it remains a challenge for a surgeon to translate detailed imaging information into enhanced surgical performance. Various types of robotic assistance could help propel intraocular surgery beyond these human physiological limitations.

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11.2 Co-manipulation

The first stepping-stone towards true robotic intraocular surgery are the advanced 'hand stabilization devices'. These can provide co-manipulation of the instrument by sensing the forces from the surgeon's hand movements, in order to smooth out instrument motion and suppress unwanted physiological tremor in real time [2]. Co-manipulation devices have seen some limited clinical applications so far, in particular during the most delicate but relatively static surgical manoeuvers, such as the cannulation of retinal blood vessels to enable the injection of thrombolytic agents to treat occluded retinal vasculature [3, 4]. While this limited robot-assisted approach allows the surgeon to maintain intuitive and direct control over the instrument, it introduces increased dampening or motion resistance during dynamic movements. Co-manipulation devices could potentially be integrated with intraoperative imaging (e.g. intraoperative OCT) to provide live feedback about the relative position of the instrument tip to the retina but would offer limited options for robotic automation.

11.3 Telemanipulation

To fully take advantage of the potential benefits of robotic assistance, telemanipulation systems have been engineered to give the surgeon remote control of robotic instrument manipulators, usually via a motion controller ('joystick') or console (Fig. 11.1). This approach not only enables tremor filtering as does co-manipulation devices but also dynamic motion scaling and semiautomation of surgical tasks (Table 11.1).

The da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) is one of the first telemanipulation robots to receive FDA approval and see widespread application in various types of minimally invasive surgery [5]. However, the microscopic scale of ocular surgery and rotational instability of the globe within the orbit place additional

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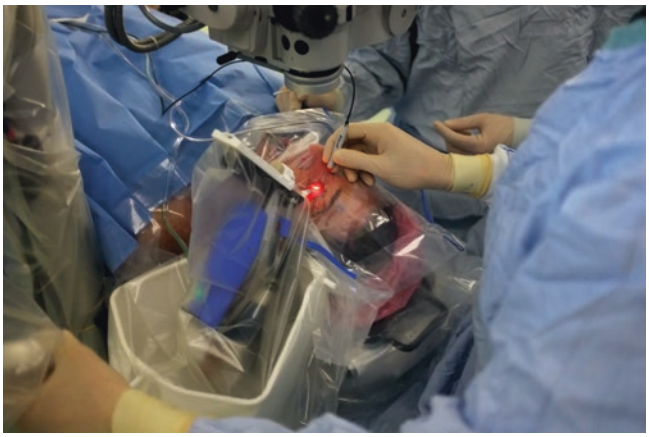

Fig. 11.1 A telemanipulated robotic vitreoretinal surgical system. The Preceyes Surgical System (Preceyes BV, Eindhoven, The Netherlands) allows the surgeon to control a robotic instrument manipulator mounted on the side of the headrest via a motion controller ('joystick', left hand), while endoillumination is provided by a light pipe held in the right hand. The system can also be mounted on the opposite side of the headrest for right eye surgery

Table 11.1 Comparison between co-manipulation and telemanipulation robotic systems

Key functionalities	Co-manipulation	Telemanipulation
Tremor filtering	✓	✓
Motion scaling	X	✓
Remote centre of motion	✓	✓
Semiautomation of tasks	O	✓
Static tasks, e.g. drug delivery	✓	✓
Dynamic tasks, e.g. peeling	X	✓
Intuitive control	O	O
Operating room workflow integration	O	O
Ergonomics	X	✓

Suitability of functions: ✓ (yes), X (no), O (potentially)

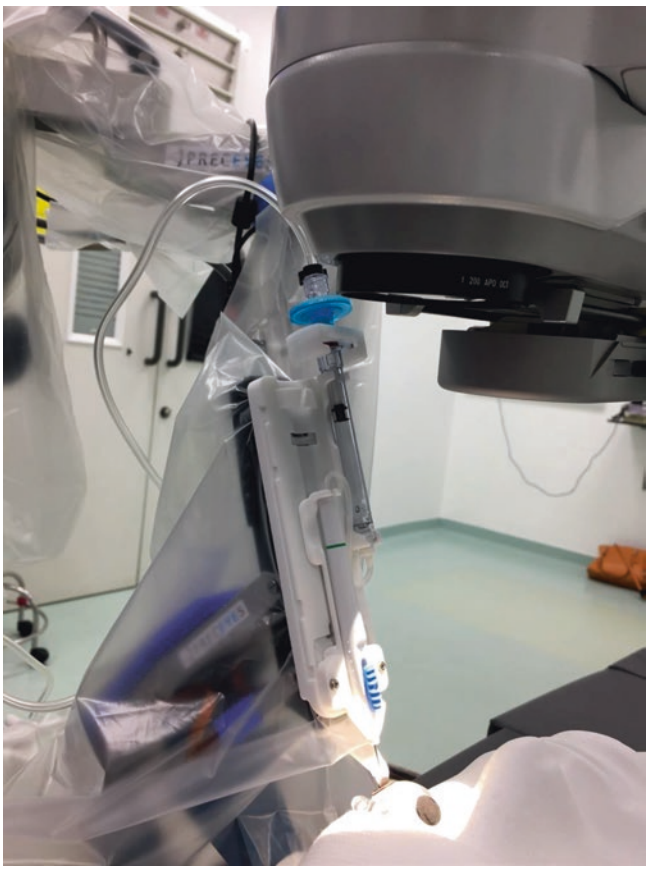

Fig. 11.2 A robotic instrument manipulator. Close-up view of a retractable robotic manipulator from the Preceyes Surgical System mounted on the side of a standard operating table headrest. Its motions in the *x*- and *y*-axes pivot around a virtual remote centre of motion (RCM) corresponding to the location of the sclerostomy. In this case, the manipulator has been fitted with a 41-gauge extendable subretinal cannula connected to a 1 ml syringe driven by the standard air pressure control port of a vitrectomy system. Other surgical instruments can be mounted to the robotic manipulator using different adaptors

demands. One of the key design features of ophthalmic robotic systems has been the introduction of a remote centre of motion (RCM), which is a virtual pivot point (usually at the site of the sclerostomy) around which all instrument *x*- and *y*-movements are centred [6] (Fig. 11.2). The first human clinical trial of a telemanipulation system for intraocular surgery (the Preceyes Surgical System) demonstrated the safety and feasibility of robot-assisted membrane peeling and subretinal injection supported by a microscope with integrated intraoperative OCT (Zeiss Rescan 7000, Carl Zeiss Meditec AG, Jena, Germany) [7].

The Preceyes Surgical System is sufficiently compact to be attached to the side of the patient's headrest when on 'stand by' and 'swung' into the surgical field when ultraprecise instrument control is required. The robotic system can assist instrument manipulation by one hand, while the other hand could maintain patient contact, e.g. by holding a light pipe. This is called 'hybrid surgery' and a major contributor to safety as the surgeon is still able to sense and anticipate patient movement. One of the key design features of the robot to enable intuitive and predictable instrument tip movements is the design of the conical docking system between the instrument manipulator and the scleral port (Fig. 11.3). The docking system aligns the instrument axis with that of the scleral port, enabling flexible angles of approach, rotational stabilization of the globe within the orbit and pivoting movement of the instrument around the RCM located at the sclerostomy. Once the instrument tip has been advanced to a point near the surface of the retina, the Preceyes robotic manipulator can be commanded to execute longitudinal movements of the instrument tip in the *z*-axis by preset increments as small as 10 μm. In addition, by setting a virtual *z*-axis boundary which limits further instrument advancement, it is possible

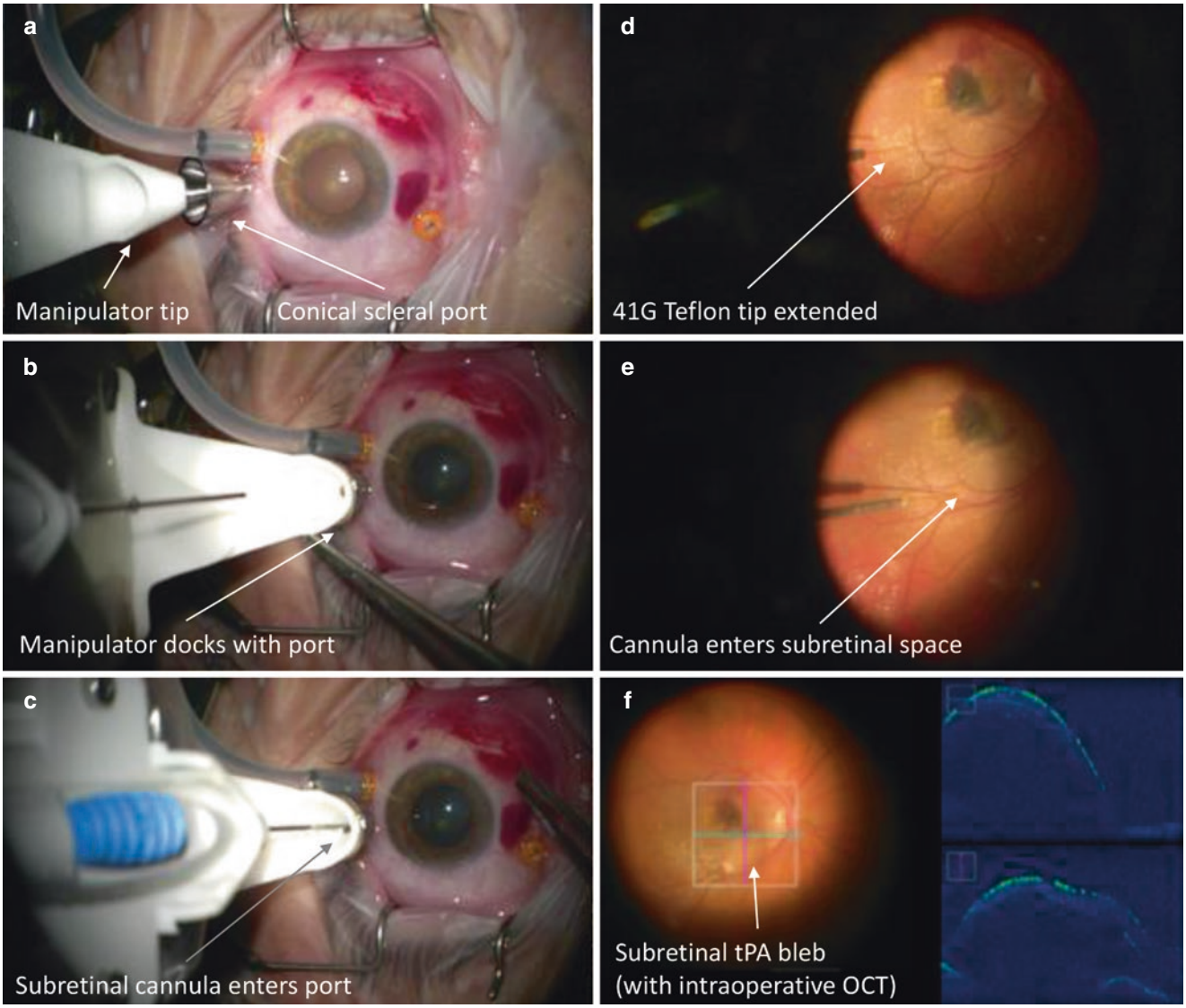

Fig. 11.3 Robot-assisted subretinal injection of tissue plasminogen activator for sub-macular haemorrhage. (**a**) The Preceyes Surgical System (Preceyes BV, Eindhoven, The Netherlands) utilizes a conical docking mechanism between the robotic instrument manipulator and the scleral port. (**b**) Once docked, the whole system exerts gentle pressure onto the globe which prevents unwanted rotation within the orbit. (**c**) A 23G/41G extendible subretinal cannula (Dutch Ophthalmic Research Center) can be passed through the scleral port into the eye. (**d**) The 41G Teflon tip is extended inside the eye and moved to a location close to the retinal surface. (**e**) The robotic system allows precise advancement of the cannula tip by increments as small as 10 μm to gently penetrate the retina. (**f**) Slow sub-macular injection of tissue plasminogen activator can be performed via Viscous Fluid Control pedal with intraoperative OCT guidance

to engage the ILM or ERM in a controlled manner without disturbing deeper retinal structures and perform controlled penetration of the retina to enter the subretinal space under intraoperative OCT feedback.

For prolonged static tasks such as performing a slow drug injection in a precise location, robotic assistance provides clear advantages over manual surgery. Laboratory studies have demonstrated the static stability of the robotic instrument tip to be under 2 μm, whereas the hand-held instrument tip showed micro jerks in the regions of 100 μm which worsened with time (Fig. 11.4).

In addition to increased stability and therefore precision, semiautomation of robotic motion could help with specific tasks. For instance, minute robotic spiral motion of a fine cannula tip has been used to create transscleral subretinal blebs with higher rate of success compared with manual surgery: improving the successful rate of this technically challenging procedure by an inexperienced surgeon from 10% unaided to 92% robot-assisted, compared with 84% for an experienced unaided surgeon [8] (Fig. 11.5). Therefore, robotic assistance has the potential to make complex retinal procedures more accessible to patients. Moreover, robotic

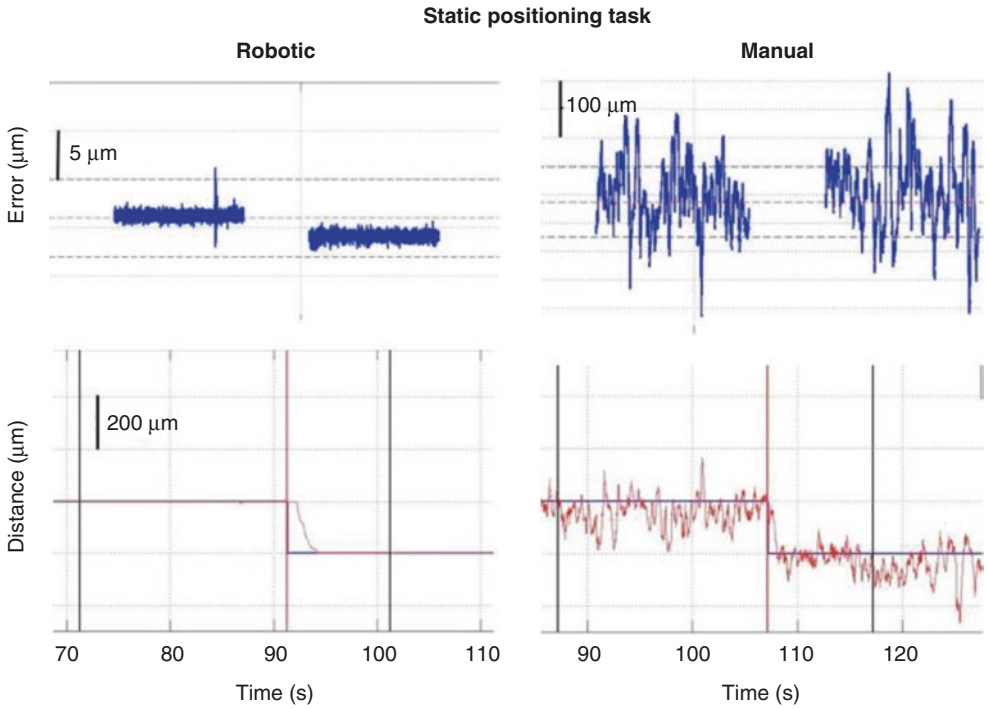

Fig. 11.4 Comparison of static stability between robotic and manual instrument tips. The robotic instrument tip position was measured to deviate around 2 µm, while the human-held instrument tip showed jerky movements in the region of 100 µm and worsened over time. Note that a spike in the robotic instrument position measurement was due to a person hitting the base of the table

assistance could also lead to the development of entirely new surgical techniques which are not possible to perform safely by hand. For example, the Preceyes Surgical System has been used to perform ultrafine cannulation of retinal blood vessels and injection of antithrombotic agents in the pig model [9] (Fig. 11.6). These applications may be extended to the slow infusion of drugs, gene therapy vector or stem cells into the subretinal space in the future.

As with the introduction of any new technology into the operating room, there is an initial learning curve associated with training of the surgeon and assistant and integration of the robotic system into existing surgical workflow. Clinical trials have shown that while surgical time is somewhat increased using the Preceyes Surgical System for routine membrane peels, it provides comparable or superior safety (e.g. in terms of the amount of retinal microtrauma caused) compared with conventional manual surgery. To facilitate surgeon training and system validation, a telemanipulation robotic system can be linked to a virtual reality surgical simulator, such as the Eyesi Surgical (VRmagic GmbH, Mannheim, Germany) (Fig. 11.7). This would enable the trainee's performance to be assessed and recorded in an objective manor using the simulator's evidence-based scoring metrics to quantify instrument handling, surgical efficiency and tissue treatment.

11.4 Future Perspective

While current robotic ophthalmic surgical systems can provide suprahuman levels of motor precision, future developments towards enhanced surgical manoeuvrability, adaptability and, ultimately, automation would require improved sensory input. For instance, the limitation of human depth perception could be overcome using an OCT-based distance sensor built into the instrument tip, which could precisely monitor the distance between the instrument and the retina [10]. This sensory input could enable computer-generated safety boundaries during tissue manipulation and potentially semiautomated vitrectomy through real-time feedback. One of the practical challenges of robotic assistance during vitreoretinal surgery is that some of the added stability can be negated by small degrees of voluntary and involuntary patient movement under local anaesthesia, e.g. head tilt or rhythmic head movements associated with breathing. While initial development of robotic intraocular surgery will involve improving the safety of challenging surgical steps, future developments will require a rethink in our approach to retinal surgery, trials of novel surgical techniques and potential introduction of artificial intelligence (AI)-based software to connect sensory input (e.g. from intraoperative OCT imaging) with robotic motor output.

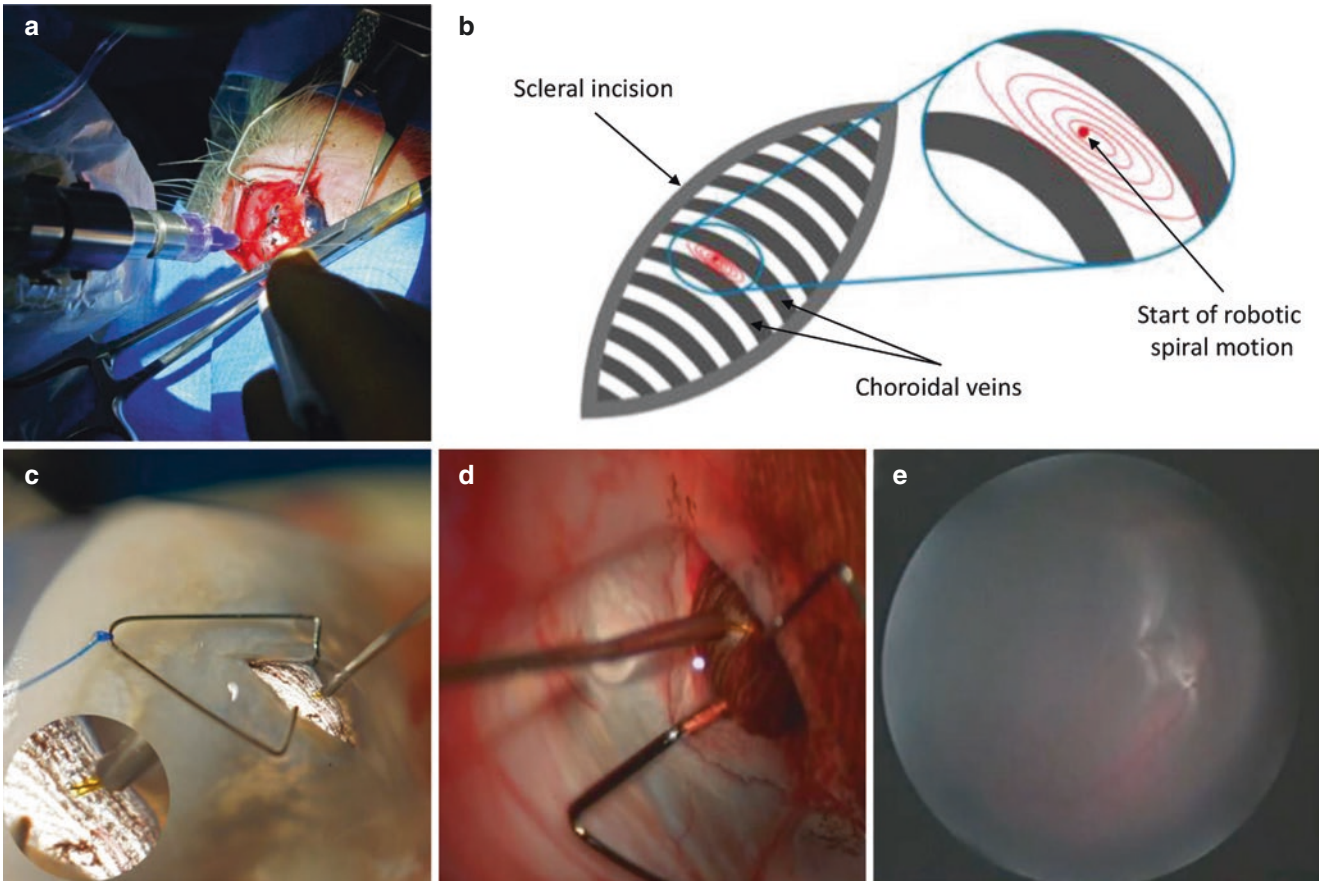

Fig. 11.5 Transscleral subretinal bleb formation involving a scleral incision and passage of a fine cannula in between choroidal vessels using a robot-assisted spiral motion of the cannula tip to reach the subretinal space without causing choroidal haemorrhage or retinal perforation

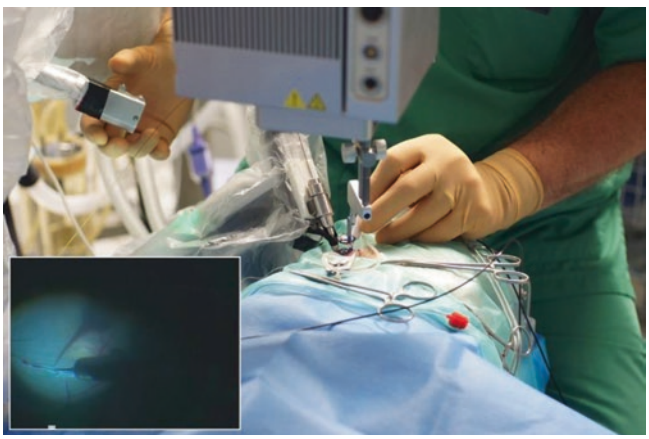

Fig. 11.6 Robot-assisted cannulation of a retinal vein in the pig eye. The surgeon can be seen holding the robotic motion controller in the right hand, which controls the robotic instrument manipulator, and an endoillumination light pipe in the left hand. Inset: cannulation of a retinal vein and injection of thrombolytic agent

Fig. 11.7 Robotic eye surgery training using the Preceyes Surgical System linked to the virtual reality simulator, Eyesi Surgical (VRmagic GmbH, Mannheim, Germany)

References

1. Machemer R, Parel J-M, Buettner H. A new concept for vitreous surgery: 1. Instrumentation. Am J Ophthalmol. 1972;73(1):1–7.
2. Taylor R, Jensen P, Whitcomb L, et al. A steady-hand robotic system for microsurgical augmentation. Int J Robot Res. 1999;18(12):1201–10.
3. Gonenc B, Handa J, Gehlbach P, Taylor RH, Iordachita I. Design of 3-DOF force sensing micro-forceps for robot assisted vitreoretinal surgery. Conf Proc IEEE Eng Med Biol Soc. 2013;2013:5686–9.
4. Gijbels A, Smits J, Schoevaerdts L, Willekens K, Vander Poorten EB, Stalmans P, Reynaerts D. In-human robot-assisted retinal vein cannulation, a world first. Ann Biomed Eng. 2018. https://doi.org/10.1007/s10439-018-2053-3.
5. Himpens J, Leman G, Cadiere GB. Telesurgical laparoscopic cholecystectomy. Surg Endosc. 1998;12(8):1091.
6. Roizenblatt M, Edwards TL, Gehlbach PL. Robot-assisted vitreoretinal surgery: current perspectives. Robot Surg (Auckland). 2018;5:1–11. https://doi.org/10.2147/RSRR.S122301.
7. Edwards TL, Xue K, Meenink TC, Beelen MJ, Naus G, Simunovic MP, Latasiewicz M, Farmery AD, de Smet MD, MacLaren RE. First-in-human study of the safety and viability of intraocular robotic surgery. Nat Biomed Eng. 2018. https://doi.org/10.1038/s41551-018-0248-4.
8. de Smet MD, Meenink HCM, Beelen M, Naus GJL, Popma SH. Comparison of robotic assisted ab externo sub-retinal bleb formation to manually performed surgery. 2014. Conference abstract at Jules Gonin Meeting, Zurich, Switzerland.
9. de Smet MD, Meenink TC, Janssens T, et al. Robotic assisted cannulation of occluded retinal veins. PLoS One. 2016;11(9):e0162037.
10. Cheon GW, Huang Y, Cha J, Gehlbach PL, Kang JU. Accurate real-time depth control for CP-SSOCT distal sensor based handheld microsurgery tools. Biomed Opt Express. 2015;6(5):1942–53.

Correction to: Surgical Retina

Masahito Ohji

Correction to:
M. Ohji (ed.), *Surgical Retina*,
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In the original publication, the series title and the names of series editors on the cover and in the front matter pages had been inadvertently omitted. The series title "Retina Atlas" and the names of series editors (Sandeep Saxena, Richard F. Spaide, Eric H. Souied and Timothy Y.Y. Lai) have been included on the cover and the series title page in the front matter in the updated version.

The updated online version of this book can be found at
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