An endoscopic overview of the anterior vitreous base in retinal detachment and anterior proliferative vitreoretinopathy

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ABSTRACT.
Purpose: Anterior proliferative vitreoretinopathy (PVR) is an important cause of persistent or recurrent retinal detachment (RD). Endoscopy provides 360° panoramic viewing of the vitreous cavity and high-magnification viewing of the anterior vitreous base (AVB). This study describes the ‘in vivo’ anatomy and pathoanatomy of the AVB using an ocular endoscope in RD and anterior PVR.

Methods: An intraoperative analysis of over 2000 consecutive eyes undergoing vitrectomy for RD operated with endoscopy-assisted vitrectomy was performed. It was recorded in notes dictated during surgery and in standardized operative reports. Around 1500 surgical videotapes, with the exclusion of diabetic retinopathy and trauma, selected by reviewing the OR reports and notes were retrospectively reviewed.

Results: Seven endoscopic criteria associated with anterior PVR complicating RD are described: ‘en bloc’ stiff anterior vitreous retraction, ciliary detachment, seeding of the AVB by abundant pigmented and/or white granulations, anterior tissue displacement, stiff ‘wrinkling’ at the vitreoretinal juncture, persistent shallow ciliary/RD under perfluorocarbon liquids and traction-related retinal surface haemorrhages. Causes responsible for failure of conventional vitrectomy for RD are highlighted. Findings in case of hypotony and cyclitic membranes are described.

Conclusions: Endoscopy is a significant adjunct to our understanding of the development of anterior loop traction by obviating the two constitutive parts of the AVB, anterior and posterior, their interconnections and their respective connections to the anterior segment and to the retina. It provides a unique evaluation and thorough eradication of the anterior vitreous cortex as a scaffold for anterior PVR. It might be an adjunct to the prevention of anterior PVR.

Key words: anterior proliferative vitreoretinopathy – anterior vitreous base – endoscopy – ocular viewing system – vitrectomy

Introduction

Despite remarkable advances during the last three decades, including a better understanding of its pathophysiology and improvements in its treatment, anterior proliferative vitreoretinopathy (PVR) remains an important cause of surgical failure.

The importance of the vitreous base (VB) in PVR has been recognized over time. The VB has been shown to provide a scaffold for cellular proliferation; contraction of the anterior vitreous base (AVB), called ‘anterior loop traction’ by Charles (1987), has been shown to lead to anterior proliferation; and the initial classification of PVR (The Retina Society Terminology Committee 1983) has been modified according to the location of the process, reflecting the significance of the AVB.

Nevertheless, different authors have different interpretations of the AVB: it is described as anterior to the posterior insertion of the VB by some (Lewis & Aaberg 1988), while anterior to the equator by others (Machemer et al. 1991). More recently, it has been hypothesized that the pathological process in anterior PVR may be significantly different from the one in ‘postbasal’ PVR (posterior to the equator) where an intraretinal glial response appears to be involved (Charteris et al. 2007).
Endoscopy provides 360° visualization of structures such as the capsulozonular complex, ciliary body and of the AVB. As there is no need for scleral depression, and because of tangential approach and high magnification, extremely unaltered and detailed viewing of the entire AVB becomes possible: its anterior part, between the Wieger’s ligament and the medium white line, even in the phakic eye, and its posterior part, between the medium white line and the vitreoretinal juncture (C. Boscher, F. Kuhn, Endoscopic Evaluation of the Anterior Vitreous Base, submitted).

Endoscopy was first used in ophthalmology in the 1930s (Thorpe 1934). Only sporadic reports on its use followed, including a noticeable work accomplished by Norris & Cleasby (1978), until fibre-optic miniaturization and other technical developments have stimulated more pioneers’ interest, including our own clinical series since 1998 in dislocated lenses, trauma, endophthalmitis, proliferative diabetic retinopathy, expulsive haemorrhage and retinal detachment (RD) without reoperation after conventional vitrectomy. No additional endoscopic criterion was identified. Most of the time, criteria 1, 3 and 5 were associated.

In a consecutive series of 67 eyes with anterior PVR complicating RD, we identified seven endoscopic factors associated with anterior PVR, at least two of them were associated (Boscher 2001b). The first four criteria relate to the anterior part of the AVB, the remaining three to the posterior part of the AVB and the adjacent retina.

With time, the findings remained fairly consistent both in primary cases of established anterior PVR and in reoperations after conventional vitrectomy. No additional endoscopic criterion was identified. Most of the time, criteria 1, 3 and 5 were associated.

Materials and Methods

The endoscopes used (systems E1 and E2; Endooptiks, Little Silver, NJ, USA) and various prototypes are described elsewhere (Uram 1993; Boscher 1999; C. Boscher, F. Kuhn, Endoscopic Evaluation of the Anterior Vitreous Base, submitted).

The present study describes the pathoanatomy of the AVB in RD and anterior PVR.

Results

In a consecutive series of 67 eyes with anterior PVR complicating RD, we identified seven endoscopic factors associated with anterior PVR, at least two of them were associated (Boscher 2001b). The first four criteria relate to the anterior part of the AVB, the remaining three to the posterior part of the AVB and the adjacent retina.

With time, the findings remained fairly consistent both in primary cases of established anterior PVR and in reoperations after conventional vitrectomy. No additional endoscopic criterion was identified. Most of the time, criteria 1, 3 and 5 were associated.

1. ‘En bloc’ stiff anterior vitreous retraction (63% of eyes). The smooth, almost invisible normal anterior gel is replaced by a ‘curtain’ of dense and rigid agglomeration of whitish refringent fibres that illustrates the gel contraction and includes both the anterior and the posterior parts of the AVB (Video S1). The contraction of their anteroposterior and circumferential interconnections explains the powerful tractional forces exerted over the retina even in the presence of large and tight buckles (Video S1).

2. Ciliary detachment (29% of eyes). Detachment of the ciliary epithelium is instantly obliterated after introduction of the probe without the need for scleral depression, which would actually mask it. In most cases, the detachment is limited to the area of the RD and is bordered anteriorly by the medium white line. In rare cases with extremely severe vitreous contraction, it can involve the entire pars plana anterioposteriorly, even though remaining limited circumferentially (Video S2).

3. Abundant pigmented and/or white granulations in the AVB (27% of eyes). They are present especially in the anterior part of the AVB, clustered along the anterior vitreous surface mentioned above, pars plana and ciliary processes, the Salzman ligament, the zonular system and the Wieger’s ligament (Figs 1 and 2) (Video S1). They are less common along the posterior part of the AVB inside the vitreous cortex attached to the retinal surface; in that case, they can be so adherent to the ciliary and retinal epithelia that they can be revealed only during high-magnification dissection with active aspiration flow (Fig. 3) (Video S3), or scraping the tissue surfaces (Video S3). They can be located in the superior as well as in the inferior AVB; therefore, they do not seem linked to gravity.

4. Anterior displacement (12% of eyes). Increased tendency of vitreous/ciliary epithelium/retinal incarceration into the sclerotomy following instrument removal (Video S3). Obviously, it is significant only if vitrectomy is properly controlled (infusion turned ‘off’ when instruments are removed).

5. Stiff ‘wrinkling’ of the posterior attachment of the vitreous base at the

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Fig. 1. Clivage planes between anatomical structures in a phakic eye with retinal detachment; pigmented clumps are deposited along the anterior hyaloid, a ciliary detachment is associated.
vitreoretinal juncture (25% of eyes). It is considered significant only when it persists during low (1 ml/m) aspiration flow. When observed in the vicinity of fixed retinal tears (PVR B) or fixed posterior star folds (PVR C), high magnification discloses pigmented deposits and/or white clumps over the retinal surface and/or trapped behind the vitreoretinal junction (Video S1). The wrinkling does persist even when the posterior retina is stabilized under perfluorocarbon liquid (PFCL) and/or air.

(6) Persistent shallow ciliary/retinal detachment under PFCL at the pars plana/ora serrata (12% of eyes). Such a detachment is recognizable under high endoscopic magnification and tangential viewing, even when successful retinal flattening seems accomplished via panoramic viewing. It is indicative of residual tractional forces at the ciliary/retinal surface (Video S4). (7) Traction-related retinal surface haemorrhages in the posterior part of AVB (8% of eyes). They can be either spontaneous (Video S1) or ‘provoked’ during VB dissection.

Reoperation after failure of conventional vitrectomy

Eighteen of the 67 eyes had been reoperated after failure of conventional vitrectomy. Endoscopy identified the following pathologies, unrecognized prior to reoperation, variably associated (Boscher 2001b):

(1) Persistent radial and/or circumferential vitreous adherences of the anterior part of the AVB to the ciliary body, zonules, posterior lens capsule, iris (67%);
(2) persistent circumferential adherences inside the posterior part of the AVB (Video S5); and
(3) both (Video S6).

White and pigmented granulations inside the residual gel are usually associated. Proliferation over persistent vitreous cortex can be sufficiently powerful to oppose the counteracting effect of scleral buckles (Video S6). Stiffness of the contracted residual gel can be considerable, with generating shrinking and then tractional slits in the retinal tissue. Once all the cortical gel remnants have been dissected at high magnification, retinectomy is the last resort if retinal shortening is obviated: retinectomy is therefore limited to the strict minimum necessary; its edges observed under high magnification are unrolled, free from significant adherent gel, which is crucial to prevent further reproliferation.

(4) Re/proliferation at the sclerotomy site (11%), connected to the remaining rigid vitreous cortex (Video S7); (5) ciliary detachment (11%). It is associated with persistent radial adherences, which can generate a true avulsion of the CE (Video S8); (6) retinal break (new or reopened) (6%) induced by chronic traction with shortening of the retina, even in the presence of a scleral buckle; (7) anterior neovascularization (3%) (Video S9); this criterion is associated with long-standing anterior loop traction and loss of blood supply into the anterior retinal vessels. (8) Subretinal proliferation (6%); it can be mild, in which case it can be left in place, or severe, leading to retinal contraction, in which case it must be removed. In some cases, it is so stiff that it constitutes a sort of ‘subretinal anterior loop’; most of the time it was induced by subretinal haemorrhage (Video S10).

With time, we found that all the above criteria can be observed with minor and/or localized expression in

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**Fig. 2.** The endoscope is located approximately 3–4 mm behind the lens equator, inside the anterior vitreous cortex. Pigmented granulations are embedded into the Wieger ligament.

**Fig. 3.** Endoscopic high magnification and tangential viewing brings to light pigmented clumps along the pars plana ciliary epithelium, trapped in the anterior vitreous cortex at the level of the medium white line, in a case of retinal detachment with anterior Proliferative Vitreoretinopathy reoperated after conventional vitrectomy and circumferential 7 mm buckle. Vitreous fibers are so rigidified that aspiration flow has to be raised up to 6 cc/ mn (red circle in the vitrectomy parameters on the left hand side of the Figure) in order them to be effectively aspirated into the cutter’s tip (with the flow control vitrectomy machine used, the usual aspiration flow in the anterior part of anterior vitreous base ranges between 1 and 3 cc/mn).
some RD without established 360° anterior loop. Proliferative vitreoretinopathy grade B at least is associated. The degree of gel contraction (criterion 1) can be evaluated on a case-by-case basis observing the spontaneous variations in the depression (vacuum), which correlate with the variations in the vitreous viscosity when using a flow-control pump vitrectomy machine (C. Boscher, F. Kuhn, Endoscopic Evaluation of the Anterior Vitreous Base, submitted). Most of the time the granulations (criterion 3) are much less abundant than in established anterior PVR. They do not seem to be related exclusively, neither to the size and number of retinal tears nor to the duration of the RD: they can be found in eyes with RD as recent as 1 day old and with one single small tear; in rare cases of recent RD, they may constitute a real seeding of the AVB, comparable with what is observed in established long-standing anterior PVR (Video S11); they are less commonly found than in established anterior PVR below the posterior attachment of the posterior hyaloid, as well as in the vicinity of retinal tears (Fig. 4), and they can even be absent in case of recent giant tears. Criterion 4 indicates starting contraction of the gel and carries the risk of postoperative sclerotomy-related complications. It must be differentiated from the ‘normal’ vitreous incarceration, which does not involve attraction of other tissues, retina and/or ciliary epithelium. Occasionally, early epiretinal membrane formation (Fig. 4) with or without early shortening of the retina (tortuosity of retinal vessels and white deposits along the vessel walls) is associated with criterion 5 in the vicinity of retinal tears (Video S12).

Cyclic membranes and hypotony

The cause of hypotony is often impossible to discern by traditional diagnostic methods, including surgical exploration. Conversely, endoscopy-assisted vitrectomy (EAV) allows identifying pathologies such as persisting anterior retinal and/or ciliary detachment; anterior subretinal silicone oil; and subretinal proliferation.

Endoscopy-assisted vitrectomy permits differentiating the three layers of cyclic membranes: (i) residual anterior vitreous cortex fibres; (ii) zonular fibres and capsular bag or posterior capsule remnants; and (iii) ciliary body, pars plana and ciliary processes/iris’s epithelia. The membranes may extend over the pars plana and the anterior retina, including the anterior remnants of previous retinectomies. The thickness and appearance of the membranes, ranging from diaphanous to bright white, is determined by the amount of residual vitreous fibres, fibrin and blood as well as the amount of scar tissue.

In less advanced cases, the ciliary processes maintain their round shape and normal colour, and eventually the ciliary vessels are still visible. In more advanced cases, the ciliary processes show elongation, discoloration and atrophy with the endoscopic appearance described previously as ‘white caps’ (Hammer & Grizzard 2003) (Video S13). The three layers may adhere so tightly to each other and to the iris that identification and separation of different membrane layers may prove hazardous and difficult; ultimately, the ciliary processes become smaller and eventually disappear in some areas, and tissues are shrunked and hardly recognizable. Performing proper membrane dissection is impossible without creating ciliary epithelium tear, supraciliary detachment or iris injury, requiring further manipulations to be abandoned.

In certain cases, the membranes are vascularized. The new vessels are fairly large and rigid, originating from the proximal areas of the detached retina/ciliary epithelium or from retinectomies, and may communicate with the iris vasculature, even with rubecitic vessels.

Discussion

The potential development of anterior PVR after incomplete vitrectomy has been recognized as early as in the 1970s (Buettner & Machemer 1977; Pulhorn et al. 1977); additional human and animal studies followed in the 1980s and early 1990s (Ho et al. 1984; Lewis et al. 1987; Kreiger 1991, 1993; Lewis et al. 1991; Elner et al. 1988; Koch et al. 1994, 1995). And as early as the beginning of the 1990s, anterior PVR was found to be significantly more frequent in eyes with previous vitrectomy than in eyes without prior surgery (Lewis & Aaberg 1991; Lewis et al. 1991). It was therefore suggested that cleansing of the VB should be as complete as possible during the first operation. However, the rate of retinal redetachment after silicone oil removal remains relatively high, between 20 and 25% in the 2000s (Jonas et al. 2001; Jiang et al. 2002; Lam et al. 2008). As noted in cases of reoperations, what is commonly referred to as ‘vitreous base peeling/shaving’ is often effective for the posterior part of the AVB only and even then – especially in the phakic eye – mostly inferiorly. This is true despite unquestionable advances in technology (panoramic viewing with external scleral depression, improved endoillumination, dusting of the gel) or changes in surgical philosophy (removal of a clear crystalline lens for the purpose of viewing and/or access). Additional
scleral buckle may not improve the success of primary vitrectomy that remains around 70% only (Heimann et al. 2007; Kinori et al. 2011). And despite ongoing efforts since the late 1980s, adjunctive antiproliferative pharmacology has been and still remains (Kaiser et al., The Retina Society 2013 meeting) non-conclusively.

High-magnification EAV clearly shows that the AVB is not a single entity. No technique is able to provide what EAV offers for visualization and management of AVB pathologies: 360-degree undistorted access to AVB structures, irrespective of media transparency, whenever the eye is phakic or pseudophakic, and independently of pupillary dilation, corneal and lens transparency, whenever the eye is phakic or pseudophakic, and independently of media transparency, irrespective of media transparency.

Identifying clinical criteria for the PVR risk has been long attempted (Bonnet 1984; Yoshino et al. 1989; Hiroshi et al. 1991; Girard et al. 1994; Bonnet & Guenoun 1995; Bartz-Schmidt et al. 1996; Nagasaki et al. 1998; Kon et al. 2000). Designing a clinical model predictive of postvitrectomy PVR development has been more recently attempted (Asaria et al. 2001; Wickham et al. 2011). The lack of a conclusive finding has stimulated research in genetics, and variants at risk have been recently identified (Pastor-Idoate et al. 2013).

Based on the teachings of the findings in anterior PVR cases and in reoperations after conventional vitrectomy, the contribution of endoscopy in primary cases is a case-by-case identification of criteria associated with anterior PVR (ciliary detachment, granulations, anterior displacement, persistent anterior detachment and anterior retinal haemorrhages). Combined with the use of a flow-control vitrectomy machine, an increase in anterior gel viscosity can be detected and the severity of its contraction can be quantified. Residual gel cortex in the AVB is then actively searched for and dissected, and traction relief between the AVB and the anterior segment can be achieved. The combination of tangential approach and high magnification affords the surgeon the closest elimination of the scaffold for (re)proliferation constituted by the vitreous cortex, at the AVB, at the vitreoretinal interface (Fig. 4), and around retinal breaks, without the need for dusting the gel (Video S12).

In rare cases, however, the contraction of residual cortex considered minor via endoscopic viewing, at the vitreoretinal juncture and/or between the anterior and the posterior parts of the AVB, proves able to redetach the retina. Some specific genetic variants might stimulate PVR inside the little gel canvas left (Pastor-Idoate et al. 2013). Whatever the cause, vitreous liquefaction and vitreoretinal separation are enhanced by enzymatic agents that might be helpful in those rare cases (Chen et al. 2009).

Certain endoscopic findings (stiff anterior contraction, anterior granulations and posterior wrinkling) are on line with long-established data that abnormal contact between the retinal pigment epithelium (RPE) and the vitreous induces mitogenic and chemotactic activity, with RPE cells proliferating and then migrating into the gel with subsequent contraction especially in the presence of growth factors and serum proteins (Fastenberg et al. 1982; Campochiaro et al. 1984; Vidaurri-Leal et al. 1984; Wiedemann et al. 1985; Forrester et al. 1986; Glaser et al. 1987; Jerdan et al. 1989; Kirchhof et al. 1989; Bishara & Buzzet 1991; Baudouin et al. 1991; Bresgen et al. 1993).

Indeed it is likely that pigmented granulations in the posterior part of AVB, in the vicinity of retinal tears, along the detached retina at the vitreoretinal juncture (Fig. 4), and subretinally, originate from such dedifferentiation and migration of RPE cells. It remains to be explained the significance of granulations located in the anterior part of the AVB, far from retinal tears – especially when they seem to adhere to the ciliary processes and to thepars plana/plicata, and when they are non-pigmented. In addition, the granulations may be abundant in fresh RDs and/or caused by a small, single retinal tear and conversely be relatively absent in some cases of fresh RDs with large tears. Different reactions among cases initially submitted to comparable stress, posterior vitreous detachment and retinal tear(s) might be explained by genetic predisposition (Pastor-Idoate et al. 2013).

Also, endoscopic features such as the presence of stiff anterior vitreous retraction and pigmented and/or white granulations in the anterior part of AVB might relate to a role of the ciliary body in PVR development. The ciliary body plays a major role in ocular inflammation and white and pigmented granulations can be observed at the AVB in uveitis in the absence of retinal tears. It has long been shown that uveal cells and blood components can be displaced into the vitreous cavity (Kreiger 1991). Morphological ciliary stress has been found to be induced at the sclerotomy (Inoue et al. 2011), and ciliary epithelial changes at the pars plana incisions suggested the formation of new vitreous collagen (Koch et al. 1994). Hyalocytes have been suggested to stimulate cell migration, proliferation and gel contraction and to play a central role in macular pucker pathogenesis (Kohno et al. 2009). They are long known to be present along the basal lamina of the ciliary epithelium (Sebag 1989). Similar phenomena might occur at the VB. High-magnification endoscopic removal of vitreous sheets closest to basal laminae of ciliary epithelium might prove essential. In any case, EAV allows high-magnification-controlled irrigation/cleansing at the vitreociliary juncture, aspirating the released debris, either promoted under genetic control or generated by surgical manoeuvres (as cryopexy). Besides, accelerated clearance of inflammatory components from the uvea has been attributed to aphakia (McLeod 1991). Complete hyaloido-capsulonuclear dissection during EAV resembles this process by creating a state of ‘pseudo-aphakia’ that also facilitates the penetration into the vitreous cavity of the anti-inflammatory factors secreted by the trabecular meshwork. Furthermore, EAV also prevents traction over the ciliary epithelium and rupture of the ciliary blood–aqueous barrier (Lopez et al. 1992).

Hypotony and eventual phthysis remain a concern in eyes treated with traditional vitrectomy techniques, even in eyes where the retina has been successfully reattached (Zarbin et al. 1991; Lopez et al. 1992; Hammer & Grizzard 2003). One potential source is ciliary body detachment, which is rarely detected preoperatively, and which is masked intraoperatively when scleral depression is employed. Certainly endoscopic hyaloido-capsulonuclear
dissection cannot palliate the difficulties/ impossibilities of dissection of cyclitic membranes in cases with too advanced scarring, and there are still unknown factors related to hypotony that restrict its cure (role of duration of the condition, role of ischemia, duration of recovery time). But endoscopy displays on 360°, at high magnification, even mild persistent adherences between the pars plicata, capsulozonular bundles and vitreous cortex, a potential canvas for subsequent development of pathological membranes. In some rare cases, we have discovered at the time of silicone oil removal that a certain degree of cyclitic proliferation can develop despite an endoscopic preventive cleansing that proves sufficient most of the time. Specific genetic predisposition might account for these cases.

In conclusion, the unique intraoperative information provided by endoscopy correlates with experimental and pathological studies about the pathogenesis of anterior PVR. Endoscopy-assisted vitrectomy allows to perform the closest eradication possible of the vitreous basement membrane component of PVR development and may help diminishing the cellular component by removing the cell reservoir at the AVB. Endoscopic findings, when more commonly known and evaluated, might be incorporated in a future PVR classification or PVR risk calculation. Along with identification of patients with genetic risk and with various pharmaceutical agents, EAV might be a crucial element in increasing the success of the primary surgery.

References


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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Video S1. Criterion 1 ‘en bloc’ stiff anterior vitreous retraction.

Video S2. Criterion 2 ciliary detachment.

Video S3. Criterion 3 abundant pigmented and/or white granulations in the AVB.

Video S4. Criterion 6 persistent shallow ciliary/retinal detachment under PFCL at the pars plana/ora serrata.

Video S5. Persistent circumferential adherences inside the posterior part of the AVB.

Video S6. Persistent radial and/or circumferential vitreous adherences in both the anterior and posterior parts of the AVB.

Video S7. Re/Proliferation at the sclerotomy site.

Video S8. Ciliary detachment in displayed during reoperation after conventional vitrectomy.


Video S10. Subretinal proliferation.

Video S11. Criterion 3 in a case of RD with PVR B.

Video S12. Early modifications of the posterior retina displayed at endoscopic high magnification.