Intra-Bleb Pigmentation after Trabeculectomy†

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Abstract

Purpose : To report the presence of intra-bleb pigmentation (IBP), appearing after trabeculectomy and combined clear cornea phacoemulsification, intraocular lens (IOL) implantation and trabeculectomy (combined surgery).

Method : Ten eyes of 8 Asian patients with IBP were studied. Four eyes underwent trabeculectomy for uncontrolled glaucoma, and 6 eyes underwent combined surgery for cataract coexisting with glaucoma. Seven of the 10 eyes had adjunctive mitomycin C for the procedures.

Results : Mean follow-up time was 11.6 months (range 3-15 months). Five of the 10 eyes had intra-operative and post-operative complications requiring intraocular manipulation (ruptured posterior capsule and in-the-sulcus IOL, flat anterior chamber, malignant glaucoma, iris prolapse). Blebs were thin (8 eyes), or with moderate thickening of conjunctiva (2 eyes) with IBP either overlying the scleral flap or spread beneath the conjunctiva. IBP initially appeared at 2 to 44 weeks after the procedures. Nine of the 10 eyes (90%) had IOPs $\leq$ 22 mmHg without medication.

Conclusion : IBP is associated with iris trauma at surgery and dispersal of pigment into the bleb, where it spreads or proliferates. A thin bleb provides a clear view of IBP as well as functional filtration. IBP appears to be a favorable sign of the filtration.

Key word : Trabeculectomy, Combined Surgery, Complications, Filtering Bleb, Pigmentation

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J Med Assoc Thai 2003; 86: 183-190

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† Presented in part at the 6th Congress of the European Glaucoma Society, London, June 2000.

Filtering surgery is the most common procedure to relieve the intraocular pressure (IOP) by draining the aqueous humor through the sclerectomy to the subconjunctival area, a producing filtering bleb[1,2]. Combined phacoemulsification with intraocular lens (IOL) implantation and trabeculectomy (combined surgery) is, nowadays, favored for the treatment of coexisting cataract with uncontrolled glaucoma[3-6]. An adjunctive antimetabolite such as mitomycin C (MMC) enhances bleb function by preventing Tenon's encapsulation[7,8]. Thin appearance of the bleb has been described in full-thickness filtering procedure and in guarded filtering with adjunctive MMC and provides long-term functional filtration[7,9].

Histological investigation of filtering blebs in glaucomatous eyes revealed various cells and tissues such as fibrocytes, epithelium, collagen, inflammatory cells, blood vessels and microcystic spaces of subepithelial connective tissue[10-12]. Microcysts represented clear channels for aqueous passage and were probably a good sign of functional filtration[10]. Interestingly, the clinicopathology of an excised bleb from markedly extensive full thickness filtration demonstrated numerous melanin granules[13]. The melanin granules were likely derived from uveal tissue and flew with aqueous into the bleb. However, there is no report of melanin granule finding at the slit-lamp examination.

Pigments precipitating on the IOL after cataract extraction and combined surgery have been reported[14-16]. Iris chafing with the IOL, particularly the thicker-designed silicone one, dispersed the pigment to the IOL[14]. The most common cells deposited on the IOL are iris pigmented epithelial cells (IPE). The others were derived from iris stroma, uveal melanocytes and inflammatory cells[15]. The pigmented cellular membranes on the IOL cause visual deterioration[16]. Treatment with corticosteroid reduces the pigmented membrane. Recurrence of the membrane, occurring after discontinuation of the corticosteroid, supports the notion that the pigmented membrane is due to inflammatory reaction[16].

The authors herein describe IBP appearing after trabeculectomy and combined surgery and also correlate the IBP to its causes and effects on the filtering bleb and IOP.

PATIENTS AND METHOD

This is a retrospective chart review of 8 Asian patients (10 eyes) with brown irides, without a history of previous intraocular surgery except for laser iridectomy. Trabeculectomy was performed in 4 eyes for uncontrolled glaucoma. Combined clear cornea phacoemulsification, IOL implantation and trabeculectomy were performed in 6 eyes for a cataract coexisting with uncontrolled glaucoma. Seven of 10 eyes had adjunctive MMC during the procedures. All of the patients were treated at Rajavithi Hospital, Bangkok, Thailand. The procedures were performed between January 1998 and November 1998. Seven patients were male and 1 patient was female. Their ages ranged from 54 to 87 years. The diagnosis included primary open-angle glaucoma (POAG) (1 eye), chronic angle-closure glaucoma (CACG) (5 eyes), acute angle-closure glaucoma (1 eye), exfoliation glaucoma (XFG) (2 eyes), and uveitic glaucoma (1 eye) (Table 1). All patients provided informed consent before treatment.

Pre-operative and post-operative examinations included visual acuity, slit-lamp biomicroscopy, applanation tonometry, gonioscopy, dilated ophthalmoscopy. Automated visual field tests were performed in all patients with program 30-2 of Humphrey instrument. Serial photographs were taken.

Surgical procedures were performed under topical anesthesia using tetracaine eyedrops 0.5 per cent, or retrobulbar anesthesia with a combination of lignocaine 1 per cent and bupivacaine 0.25 per cent. In brief, the surgical technique for trabeculectomy was performed superonasally by limbul-based conjunctival incision, with or without local application of MMC (0.5 mg/ml for 5 minutes) intra-operative adjunction and irrigation with Balanced Salt Solution (BSS Plus; Alcon, Fort Worth, TX) 60 ml. A triangular scleral flap was made and a superior paracenthesis was performed. Sclerectomy was performed by a Descemet's punch, followed by iridectomy. The scleral flap and conjunctival incision were sutured. The anterior chamber (A/C) was reformed with BSS and the eye was patched. The surgical technique for combined surgery included temporal clear cornea phacoemulsification with IOL implantation, leaving the viscoelastic substance inside the eye. Then a separate-site trabeculectomy was performed superonasally. Irrigation/aspiration (I/A) of the remaining viscoelastic substance and reforming the A/C with BSS was done. The eye was patched post-operatively.

Post-operative medications were prednisolone acetate 1 per cent and tobramycin eyedrop four times a day for 4 to 6 weeks. Follow-up examination was, at least, on post-operative day 1, week 1, week 2,

Table 1. Pre-operative patient summary.

Case	Age (yrs)	Sex	Diagnosis	Eye	Laser/Surgery	Pre-op IOP (mmHg)
1	72	M	POAG	OD	-	32
2	69	M	CACG	OD	SI	55
3	54	M	Uveitic glaucoma	OD	-	52
4	61	M	AACG	OS	LI	42
5	71	M	CACG	OS	LI	30
6	74	M	CACG	OS	LI	27
7	87	M	XFG	OD	-	26
			XFG	OS	-	10
8	73	F	CACG	OD	LI	22
			CACG	OS	LI	20

M = male, F = female, OD = right eye, OS = left eye,
AACG = acute angle-closure glaucoma, CACG = chronic angle-closure glaucoma,
POAG = primary open-angle glaucoma, XFG = exfoliation glaucoma, LI = laser iridectomy, SI = surgical iridectomy

week 3, month 1, and then every 2-3 months. Patients who developed complications were followed more frequently.

All of the enrolled subjects (8 cases) had IBP. IBP was defined as the bleb with pigment precipitated inside the wall, either overlying the scleral flap or beneath the conjunctiva. Two patterns of the IBP were observed including clumps of pigment and discrete pigment. Grading of IBP was light (+), moderate (++, brown) which was easily observed by a slit-lamp and dense pigmentation (+++, dark brown or black). Oculodermal melanocytosis was excluded from the study. An eye with iris incarceration at the sclerectomy site or one with iron line outside the bleb wall also excluded.

RESULTS

Duration of the follow-up period ranged from 3-15 months (mean, 11.6) and age ranged from 54-87 years (mean, 70.1). Pre-operative IOPs ranged from 10-55 mmHg (mean 31.6).

Five eyes had complications. One eye had a ruptured posterior capsule during phacoemulsification which required anterior vitrectomy and in-the-sulcus IOL implantation (case 7 left eye). Other complications were flat anterior chamber which was reformed with BSS or viscoelastic substance or air bubble (cases 3, 4), malignant glaucoma requiring vitreous tapping (case 5) and reformation of the A/C, iris prolapsed with sutureless corneal incision which required repositioning of the iris and reformation of the A/C (case 8 right eye) (Table 2).

Bleb appearances were avascular to minimal vascular with thin (8 eyes) to moderate thickening (2 eyes) of Tenon's capsule. Light to dense IBP was noted during follow-up and the pigmentation did not disappear over time. The pigments were noted 2-44 weeks after the initial or later procedures for complications. Patterns of IBP were described as either pigment spreading over the scleral flap (cases 2, 5, 6, 8 both eyes) or spreading beneath the conjunctiva (cases 1, 3, 4, 7 both eyes) (Table 3). All but one had IOPs $\leq$ 22 mmHg without antiglaucoma medication.

CASE REPORTS

Case 3

A 54 year-old man, with uveitic glaucoma right eye, underwent trabeculectomy with MMC for uncontrolled glaucoma. Three days post-operatively, he had flat A/C with irido-lenticular touch, and IOP of 0 mmHg. Filtering bleb revealed a thin bleb without pigmentation. The A/C was reformed with air bubble. Two weeks later, IBP was noted and the IOP was 10 mmHg (Fig 1). Pigment precipitation was also present on the crystalline lens.

Case 4

A 61 year-old man developed hypotony and flat anterior chamber after trabeculectomy with MMC of the left eye. Uncorrected visual acuity was light projection IOP was 0 mmHg. Examination revealed a thin, avascular bleb, Descemet's folds of the cornea, and flat A/C with irido-corneal touch. B-scan ultra-

Table 2. Operations and complications.

Case	Procedure	IOL	MMC	Complications	Remarks
1	Trabeculectomy	-	-	-	
2	Trabeculectomy	-	Yes	-	
3	Trabeculectomy	-	Yes	Flat A/C	Reformed A/C
4	Trabeculectomy	-	Yes	Flat A/C	Reformed A/C, Timolol, ECCE + IOL
5	Combined	Acrylic	-	Malignant glaucoma, flat A/C	Tap vitreous, reformed A/C
6	Combined	Acrylic	Yes	-	
7 OD	Combined	Silicone	Yes	-	LSL
7 OS	Combined	PMMA	-	Ruptured P/C, vitreous loss	A. vit, IOL in-the-sulcus
8 OD	Combined	Acrylic	Yes	Iris prolapsed, flat A/C	Reposition iris, reformed A/C
8 OS	Combined	Acrylic	Yes	-	

Combined = combined surgery, LSL = laser suture lysis, MMC = mitomycin C,
P/C = posterior capsule, A. vit = anterior vitrectomy, Acrylic IOL = (AcrySof®, MA30BA, Alcon, Dallas TX),
Silicone IOL = (CHIRON, C10UB), PMMA IOL = (CILCO®, LX10BD, Alcon, Dallas TX)

Table 3. Summary of post-operative results.

Case	Bleb appearance	IBP	Pigment noted (wks post-operatively)	Patterns	F/U (mos)	IOP range (mmHg)
1	MT	Trace	28	U, D	12	4-8
2	Thin	+++	12	O, C	15	5-12
3	Thin	+++	2	U, D	7	0-10
4	Thin	+, +++	3,10	U, D	12	0-30
5	Thin	+++	2	O, C	3	6-14
6	MT	++	44	O, D	15	4-22
7 OD	Thin	++	5	U, D	11	7-10
7 OS	Thin	+	11	U, D	11	9-17
8 OD	Thin	+++	11	O, C	15	2-20
8 OS	Thin	++	10	O, C	15	6-16

IBP = intra-bleb pigmentation, MT = moderate thickening of Tenon's capsule,
+, ++, +++ indicate light, moderate, and dense intra-bleb pigmentation respectively,
U = underneath inner side of filtering blebs, O = overlying scleral flap, C = clump of pigments, D = discrete pigments

sonography revealed choroidal effusion. A/C was reformed with viscoelastic agent, air bubble and an inserted symblepharon ring to treat overfiltration. Three weeks later, IBP was noted underneath the lower part of the bleb (Fig. 2). IOPs ranged from 2-30 mmHg, A/C was deep, and a white mature cataract was seen. With timolol maleate O.5 per cent treatment, the IOP decreased to 10 mmHg. Four months later, temporal clear cornea extracapsular cataract extraction (ECCE) with polymethylmethacrylate (PMMA) IOL insertion was performed. Ten weeks after the procedure, IBP was newly demonstrated beneath the upper part of the bleb (Fig. 3), with IOP of 30 mmHg. With timolol maleate 0.5 per cent treatment, IOPs ranged from 10-12 mmHg.

Case 8 (right eye)

A 73 year-old woman with chronic angle-closure glaucoma, post laser iridectomy, and cataract of the right eye, underwent combined surgery (combined sutureless temporal clear cornea phacoemulsification with IOL and superonasal trabeculectomy). On the following day, prolapsed iris at the sutureless corneal incision was noted. The iris was repositioned by a cyclodialysis instrument. A/C was reformed and the incision was sutured. Eleven weeks after the pro-

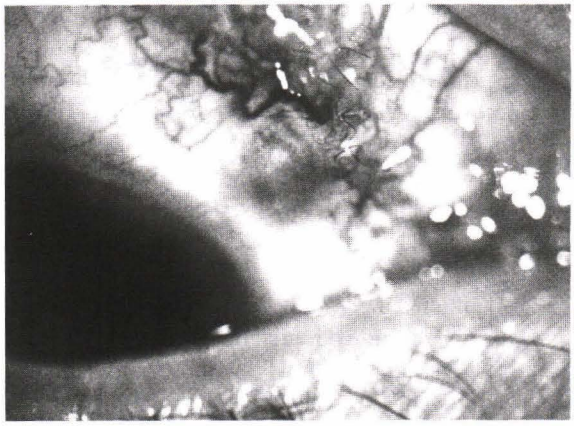

Fig. 1. Thin bleb with pigmentation is noted, underneath the inner side of the filtering wall.

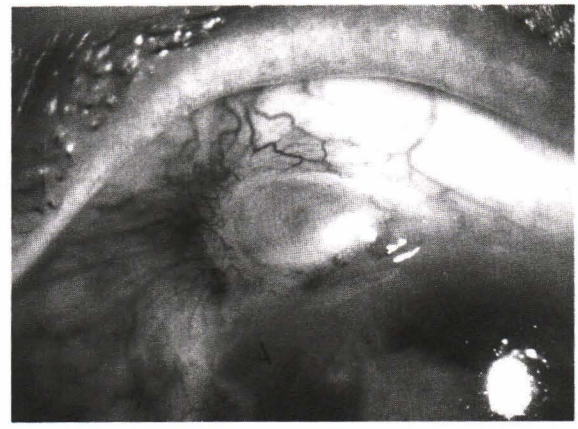

Fig. 2. Intra-bleb pigment underlies the lower part of the thin conjunctiva. A white mature cataract is noted at the inferior part of the figure.

Fig. 3. After temporal corneal incision ECCE with PMMA IOL, IBP is particularly increased in the upper part of the filtering bleb, as well as in the lower part. (Artifact of light reflection is shown on the right side of the bleb)

Fig. 4. Thin bleb with pigmentation overlies the scleral flap.

cedure, IBP was noted. The pigment spread over the scleral flap (Fig. 4). Post-operative follow-up at 15 months, the bleb was thin and avascular, and IOP was 6 mmHg.

Comment

In IBP, the pigment is most likely to be dispersed from the IPE and uveal tissue which contains melanin[13,15,17-19]. It flows with aqueous through the sclerectomy site to the subconjunctival space following iridectomy, I/A of the phacoemulsification, reformation of the A/C, or repositioning of the prolapsed iris post-operatively.

IBP occurred more commonly in combined surgery than in trabeculectomy alone (6 of 10 eyes). Iris manipulations are greater in combined surgery than in trabeculectomy alone. Angle-closure glaucoma is more prone to surgical iris trauma (4 of 6

combined surgery eyes). Since angle-closure glaucoma has a shallower A/C than normal, when the surgeon inserts the phacoemulsification tip through the clear corneal incision, the instrument can ruff against the iris. In XFG, eye No.8, which had a ruptured posterior capsule, we inserted in-the-sulcus IOL. Iris-IOL chafing provoked dispersion of the IPE. Furthermore, in combined surgery, after the authors performed trabeculectomy including iridectomy, the pigment would be flushed from the iridectomized cutting edge through the I/A step (with removal of the remaining viscoelastic substance) through the sclerectomy. The irrigation flow was continuous and longer than that required for A/C reformation in trabeculectomy alone.

IBP was more likely to be associated with the complicated procedure (cases 3, 4, 5, 7 left eye and 8 right eye). Flat A/C was the most common complication (cases 3, 4, 5 and 8 right eye). Intraocular manipulation of flat A/C induced iris trauma and dispersed the pigment. Proliferation of IPE in the bleb is likely to produce late appearance of the IBP.

To the authors' knowledge, IBP has never been investigated previously. Though various cells [11,12] and numerous melanin granules[13] were found in histopathological studies of filtering blebs, slit-lamp biomicroscopy of the bleb has never been correlated to the histopathologic findings. IBP appeared to be unrelated to inflammation since it persisted even with topical corticosteroids.

The role of the pigment on filtering bleb is unknown. Not only does aqueous humor have an inhibitory effect on fibroblast proliferation of the filtering bleb[20-22], but iris tissue and IPE may also have effects on wound healing of the filtering surgery. Fan et al[23] incubated human IPE with cultured fibroblasts from human Tenon's capsule and reported an inhibitory effect on fibroblast proliferation. They found that the higher concentration of IPE cultured with fibroblast induced the lower amount of tritiated thymidine incorporation. In iris wound healing, IPE demonstrated apposition proliferation without fibrosis on its cutting edge[24-26]. When aqueous humor with IPE spread into the filtering bleb, they may prevent fibrous scarring of the conjunctiva and provide functional filtration. In the full-thickness filt[27, 28] Because of the thin bleb, the pigment can easily be observed in the bleb in the full-thickness procedure. In iridencleisis, iris inclusion at the sclerectomy site promotes aqueous drainage[29] and may prevent scarring in the drainage area.

Interestingly, 8 of the 10 eyes in the present series revealed thin conjunctiva and 9 of the 10 eyes achieved IOPs $\leq$ 22 mmHg without antiglaucoma medication. These results appear to support the evidence above. On the other hand, not only does an encapsulated bleb obstruct the aqueous flow, but it may also obscure the appearance of IBP, if it ever exists. This may explain why there was no failed filtering from an encapsulated bleb in IBP case series. However, most eyes had primary surgery with MMC, which really contributed to the high success rate.

The possible bias of the study is due to its retrospective review. The notion of IBP in some eyes is quite late (e.g. 28 and 44 weeks after the procedures), which means IBP might be overlooked for a period of time. The case series is small and the follow-up period is intermediate term. A case control study between the filtering blebs with and without IBP and their long-term success rate should be conducted to elucidate these questions.

In summary, the authors describe IBP, an interesting bleb sign, which has never been investigated previously. IBP is associated with complicated operations, either trabeculectomy alone or combined surgery. The pigment is likely to be dispersed from iris trauma during surgery, flows through the existing fistula of A/C, and spreads into the bleb. Late appearance of IBP may also be associated with IPE proliferation. In addition, a thin bleb provides a clear view of the pigment as well as functional filtration. In all but one, IOPs were controlled without medication. IBP, serving as a "tracer elements" of the aqueous flow[13], appears to be a favorable sign of these filtrations.

(Received for publication on September 14, 2002)

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เม็ดสีที่แผลผ่าตัดต้อหิน†

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วัตถุประสงค์ : เพื่อรายงานผลการพบเม็ดสีใน bleb (intra-bleb pigmentation, IBP) หลังการทำผ่าตัดต้อหิน (trabeculectomy) และหลังการผ่าตัดสลายต้อกระจกและใส่แก้วตาเทียมร่วมกับการผ่าตัดต้อหิน (combined clear cornea phacoemulsification with IOL and trabeculectomy, combined surgery)

วิธีการ : ศึกษาในตา 10 ตาของผู้ป่วยรวม 8 ราย โดยทำผ่าตัด trabeculectomy ใน 4 ตา และ combined surgery ใน 6 ตา และมีการใช้ mitomicin C ร่วมด้วยใน 7 ตา

ผลการศึกษา : ระยะเวลาติดตามอาการโดยเฉลี่ย 11.6 เดือน (ตั้งแต่ 3-15 เดือน) พบภาวะแทรกซ้อนทั้งในขณะผ่าตัดและหลังผ่าตัดที่ต้องได้รับการแก้ไข 5 ตา (ruptured posterior capsule and in-the-sulcus IOL, flat anterior chamber, malignant glaucoma, iris prolapse) ส่วนใหญ่ bleb มีผนังบาง (8 ตา) และที่เหลือมีผนังหนาปานกลาง (2 ตา) ซึ่งทุกรายพบมี IBP อยู่เหนือ scleral flap หรือ กระจายอยู่ใต้ผนังเยื่อบุตา ระยะเวลาที่เริ่มพบมี IBP ปรากฏครั้งแรก ได้แก่ 2-44 สัปดาห์หลังการผ่าตัด ส่วนใหญ่คือ 9 ตา (90%) มีความดันลูกตา ≤ 22 mmHg โดยไม่ได้ใช้ยาลดความดันตาใด ๆ

บทสรุป : IBP สัมพันธ์กับ iris trauma ในขณะผ่าตัดซึ่งทำให้มีการกระจายของเม็ดสีเข้าไปใน bleb ผนัง bleb ที่บางจะช่วยให้เห็นเม็ดสีได้ชัด และยังเป็นลักษณะของ bleb ที่ดี IBP น่าจะถือว่าเป็น favorable sign ของการผ่าตัดต้อหิน

คำสำคัญ : การผ่าตัดต้อหิน, ผลแทรกซ้อนการผ่าตัด, เม็ดสีที่แผลผ่าตัด

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