

Management strategies in malignant glaucoma secondary to antiglaucoma surgery

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Abstract

• **AIM:** To assess the outcomes of various interventions for malignant glaucoma (MG).

• **METHODS:** A retrospective, comparative analysis of case series were performed on 38 eyes of 35 MG patients treated in Aier Eye Hospital of Wuhan between Jan. 2009 and Dec. 2012. Numerous treatments were administered including medical therapy, neodymium: yttrium – aluminium–garnet (Nd:YAG) laser posterior capsulotomy and hyaloidotomy as well as 3 surgical options. The characteristic, treatment option and outcome of MG in every individual patient were reviewed and analyzed among all patients who were followed up for an average of 27.1±9.1mo.

• **RESULTS:** Four eyes of 3 patients achieved complete resolution with medical therapy. Nd:YAG laser posterior capsulotomy and hyaloidotomy were performed on 2 eyes, both of which achieved resolution after initial intervention. Thirty –two eyes were given surgical treatments with anterior vitrectomy – reformation of anterior chamber in 13 eyes, phacoemulsification – intraocular lens implantation in 10 eyes and phacoemulsification – intraocular lens implantation – anterior vitrectomy in 9 eyes. Resolution of MG was seen in almost all patients. The mean intraocular pressure decreased from 41.87 ±9.44 mm Hg at presentation to 15.84 ±3.73 mm Hg at the last visit. The mean anterior chamber depth improved from 0.28±0.27 mm to 2.28±0.19 mm. Twenty eyes with preoperative visual acuity better than counting figure/ 50 cm had various visual improvements. Complications occurred in 3 eyes of 3 patients including bleeding at the entry site of vitrectomy into vitreous cavity, corneal endothelial decompensation and allergic to atropine respectively.

• **CONCLUSION:** MG occurs as a result of multiple mechanisms involved simultaneously or sequentially. Medical therapy is advocated as the initial treatment, laser therapy is beneficial in pseudophakic eyes, and different surgical regimen is recommended based on different pathogenesis of MG when non–response occurs to nonsurgical management. MG can be managed successfully by appropriate and timely interventions with good visual outcome.

• **KEYWORDS:** malignant glaucoma; pathogenesis; medical therapy; laser therapy; surgical interventions

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INTRODUCTION

The term malignant glaucoma (MG) was first introduced by von Graefe as a rare complication of certain ocular procedures in 1869. With a history of more than 100y, the concept of MG has been expanded to include various clinical situations, which have these common features: shallowing or flattening of the central and peripheral anterior chambers in the presence of a patent iridotomy, elevation of the intraocular pressure (IOP), and unresponsiveness to or aggravation by use of miotics but frequent relief with cycloplegic-mydriatic therapy.

There is still a lack of general agreement regarding the sequence of events responsible for the development of MG, and the pathophysiology of this condition is not completely understood. MG continues to be among the most challenging problems faced by ophthalmologists. Medical treatment, such as topical cycloplegics/mydriatics, antiglaucoma medications, aqueous suppressants and hyperosmotic agents, is advocated as the initial treatment for MG. If the condition persists, various other treatment strategies have been recommended. Laser options include iridotomy, argon laser iridoplasty, diode laser cyclophotocoagulation and neodymium: yttrium-aluminium-garnet (Nd:YAG) laser capsulotomy with or without hyaloidotomy [1-7]. Surgical intervention is often required in many cases. Several surgical techniques have been reported such as pars plana vitrectomy with or without

lensectomy, vitreous puncture with aspiration, zonulohalido-vitreotomy, vitrectomy-phacoemulsification-vitreotomy and pars plana tube insertion with vitrectomy and so on^[1-2,6-13]. However, there remains no consensus about the optimal therapeutic strategy in the literature. And most publications on MG are case reports and small case series targeting some particular treatment method. We therefore performed a retrospective analysis of all patients who were treated for MG in the Department of Glaucoma at Aier Eye Hospital over the past 4y. The purpose of this study was to report the treatment outcomes of MG in the hope that it provides guidance for management strategy of MG.

SUBJECTS AND METHODS

Subjects This retrospective study reviewed 1158 patients (1432 eyes) with primary angle-closure glaucoma (PACG) undergoing anti-glaucoma surgical treatment in the Aier Eye Hospital between Jan. 2009 and Dec. 2012. Among them, 27 patients (29 eyes, 2.0%) developed MG. During this period, another 9 eyes of 8 patients (initially diagnosed as PACG) were remitted to Aier Eye Hospital for treatment of MG following anti-glaucoma surgery. Hence, 38 eyes of 35 patients with MG were included in the final analysis. Study procedures were in accordance with the tenets of the Declaration of Helsinki, and the Ethics Committee of Aier Eye Hospital approved the protocol in its entirety. All patients provided written informed consent.

The diagnosis of MG was made on the basis of the following criteria^[2]: 1) a shallow or flat central and peripheral anterior chamber and a high IOP (>21 mm Hg) during or after any intraocular surgery; 2) presence of a patent iridotomy or iridectomy; 3) absence of suprachoroidal effusion/hemorrhage or posterior segment mass lesion by indirect ophthalmoscopy and/or echography.

The following relevant demographic and clinical information were collected: age, sex, eye affected, primary ophthalmic diagnosis before MG, precipitating ocular surgery, duration between surgery and development of MG, best-corrected visual acuity (BCVA), IOP, anterior chamber depth (ACD), axial length (AL), lens status, patency of iridotomy and surgical complications. The IOPs were measured using the Goldmann applanation tonometer. AL was measured with A-scan ultrasonography; ACD was obtained by IOL-Master.

The primary outcome measure was resolution of MG based on central anterior chamber deepening with an IOP of 21 mm Hg or less with or without topical antiglaucoma medications in the absence of systemic antiglaucoma medications. All patients were initially given medical treatment. If medical treatment failed, pseudophakic eyes were treated with laser posterior capsulotomy with hyaloidotomy, and phakic eyes underwent surgical treatments. In refractory relapsed eyes with low visual potential, transscleral cyclophotocoagulation (TSCPC) was performed.

Methods

Medical management Medical treatment included the use of topical atropine 3 times daily, oral carbonic anhydrase inhibitor, intravenous mannitol, topical β blocker or α 2 agonist (or both) as well as topical or oral steroid therapy.

Laser therapy Laser posterior capsulotomy with hyaloidotomy was performed using a Nd:YAG laser (Visulass III, Carl Zeiss Meditec, Inc., Dublin, CA, USA) in pseudophakic eyes through intraocular lens (IOL) and an existing peripheral iridotomy. The power was set at 1 to 3 mJ. The number of laser shots varied depending on whether a direct communication between the AC and anterior vitreous was well formed.

Surgical treatments Surgical options: 1) anterior vitrectomy-reformation of anterior chamber was chosen if IOP increased non-progressively, the lens is transparent and the ACD is on grade II or shallower (Spaeth grading scale); 2) phacoemulsification-IOL implantation-goniosynechialysis - reformation of anterior chamber was indicated if progressive IOP increase is associated with the development or worsening of cataract. Anterior vitrectomy procedure was performed if anterior chamber failed to form during the surgery; 3) vitreous aspiration or anterior vitrectomy was performed if patients developed MG during surgery. Surgical procedures: 1) anterior vitrectomy- reformation of anterior chamber: two 23 gauge pars plana instrument cannulae were placed 4 mm posterior to limbus in the superior quadrants with one for infusion and the other for anterior vitrectomy. Balanced saline solution or viscoelastics or air bubble was injected to reform the anterior chamber through the temporal clear corneal incision; 2) vitreous aspiration-phacomemulsification- intraocular lens implantation-goniosynechialysis-reformation of anterior chamber: a tuberculosis syringe with needle was used to insert into the vitreous cavity perpendicularly at 4 mm from superior limbus, and liquid or liquefied vitreous was aspirated. If aspiration failed, anterior vitrectomy was carried out as described above. Once the eyeball was softened, temporal and lateral clear corneal incisions were made respectively, then the anterior chamber was deepened with viscoelastics, goniosynechialysis and posterior synechialysis were performed in all quadrants. A 5.0 mm continuous curvilinear capsulorhexis, phacoemulsification and cortex removal were then performed, a foldable IOL was implanted. Posterior capsulotomy was performed as necessary. A patent iridotomy was entailed during the surgery so as to perform YAG laser treatment whenever necessary; 3) anterior vitrectomy combined with the surgical procedures in 2) of surgical procedure: anterior vitreous was excised as described in 1) of surgical procedure if it was unlikely to aspirate liquid or liquefied vitreous during vitreous puncture with aspiration, and phacomemulsification- IOL implantation-

goniosynechialysis was followed. If the anterior chamber was not well formed after vitreous aspiration and phacoemulsification, posterior curvilinear capsulorhexis was performed with the bent tip of a 25 gauge needle to make a hole 3 mm in diameter through which the anterior hyaloids in the middle was partially excised with a 23 gauge vitrectome, followed by implantation of foldable IOL in the posterior chamber.

Transscleral cyclophotocoagulation The OcuLight SLx 810-nm diode laser photocoagulator with the Iris G-probe (Iris Medical Instruments, Iridex Corporation, Mountain View, CA, USA) was used to perform the TSCPC. The settings for the power varied from 1500 to 2000 mW, with a duration of 2000ms. The number of shots ranged from 20 to 30, and the treatment area was confined to 2 to 3 quadrants.

Statistical Analysis SPSS software version 10.0 was used for statistical analysis. Paired *t*-test was employed to compare the IOP and ACD before and after treatment. Independent sample *t*-test was used to compare age, AL, pre-operative IOP between the 2 groups with or without visual improvement. Mann-Whitney *U* test was used to compare visual acuity, pre-operative duration of shallow or flat anterior chamber and cup/disk ratio between the two groups. Chi-square test was utilized to compare categorical variables. A *P* value of <0.05 was considered statistically significant.

RESULTS

A total of 35 patients (38 eyes) received treatments for MG in our case series. Thirty-one patients were female and 4 were male, and the mean age was 46.4 ±10.0y (range: 18-72y). Thirty-one patients (34 eyes) had a pre-existing diagnosis of primary chronic angle-closure glaucoma, 4 patients (4 eyes) had a diagnosis of acute angle-closure glaucoma. MG developed in 32 eyes (84.2%) after trabeculectomy, in 4 eyes (10.5%) during trabeculectomy, and in 2 eyes (5.3%) after glaucoma and cataract combined surgery. Thirty-six eyes were phakic and 2 eyes were pseudophakic. The mean AL was 21.18 ±0.65 mm (range: 19.00-22.41 mm). The mean follow-up time is 27.1 ±9.1mo.

Four eyes of 3 patients achieved resolution with medical therapy alone, but were maintained on intermittent atropine therapy. Two eyes in which MG developed after combined glaucoma and cataract surgeries resolved with YAG laser posterior capsulotomy and hyaloidotomy.

Surgical management were administered on 32 eyes which were categorized into 3 groups: anterior vitrectomy-restoration of anterior chamber in 13 eyes (vitrectomy group); vitreous aspiration-phacoemulsification-IOL implantation-goniosynechialysis-reformation of anterior chamber in 10 eyes (phaco group); phacoemulsification-IOL implantation combined with anterior vitrectomy in 7 eyes or with posterior capsulotomy and hyaloidotomy in 2 eyes, a total of 9 eyes were included in this group (combination group).

In vitrectomy group, recurrence took place in 2 eyes, which achieved complete resolution following phacoemulsification and IOL implantation; another 1 eye had decreased vision resulting from the development of significant cataract 2mo after the initial intervention and then underwent phacoemulsification and IOL implantation. One month later, this eye demonstrated recurrence and achieved resolution with anterior vitrectomy and reformation of anterior chamber.

Comparison of Best Corrected Visual Acuity Before and After Treatments Table 1 showed the visual changes in all groups. All 4 eyes with medical therapy alone and 2 eyes undergoing YAG have gained vision at the last follow up. Among 32 eyes receiving surgical intervention, 12 eyes had visual acuity not better than counting figure (CF)/near at the time of diagnosis of MG, none of these eyes had improved vision at the final follow-up. Of the 20 eyes that had visual acuity better than CF/ 50 cm, 1 eye had decreased vision due to corneal opacity, 2 eyes maintaining the initial vision, while the other 17 eyes had gains of 2 lines or more of visual acuity. In vitrectomy group, 8 eyes (8/13, 61.54%) had visual improvement, 5 eyes (5/10, 50%) in phaco group and 4 eyes (4/9, 44.44%) in combination group had improvement. No significant difference was noted in the rate of visual improvement among vitrectomy, phaco and combination groups ($\chi^2=0.681$, *P*=0.711).

In total, 23 eyes gained better vision and 15 eyes had no improvement or decreased vision after MG management in our study. Between these two groups, there was no significant difference in age, pretreatment mean IOP, and AL, while statistical difference was observed in duration of shallow anterior chamber and cup/disk ratio. Details were shown in Table 2.

Intraocular Pressure and Anterior Chamber Depth Changes Before and After Treatments At the final follow-up, 8 eyes of 8 patients still required topical antiglaucoma medications, and 4 of them then obtained an IOP of below 21 mm Hg, the other 4 had an IOP between 23 and 26 mm Hg with 2 eyes from vitrectomy group and the other 2 from combination group. Seventy-seven percent of patients (30 out of 38 eyes) had IOP under 21 mm Hg with no medication. The mean IOP at the final follow-up was 15.84 ±3.73 mm Hg (9-26 mm Hg), significantly lower compared with the IOP of 41.87 ±9.44 mm Hg (25- 82 mm Hg) at the diagnosis of MG (*P* <0.001). The AC in all eyes deepened after treatment from a pretreatment mean ACD of 0.28 ±0.27 mm (0-1.60 mm) to 2.28 ±0.19 mm (1.9-2.8 mm) (*P* <0.001) at the final follow-up. Table 3 showed the IOP and ACD changes obtained through different treatment modalities. For all treatment options, there were significant differences in IOP and ACD between pre-treatment and post-treatment. And the mean IOPs and ACDs at final follow-up in all groups were below 21 mm Hg and above 2 mm respectively.

Table 1 Visual outcome before and after treatment for MG

Parameters	LP	HM/near	CF/near	0.02-<0.1	0.1-<0.3	0.3-<0.5
Baseline						
Medical therapy		1	2	1		
YAG					2	
Vitrectomy group	1	2	1	3	6	0
Phaco group	1	1	2	2	3	1
Combination group	1	1	2	4	1	0
Sub total	3	4	6	11	13	1
End point						
Medical therapy				1	1	2
YAG						2
Vitrectomy group	1	2	1	3	3	3
Phaco group	1	1	2	1	2	3
Combination group	1	1	3	1	3	0
Sub total	3	4	6	6	9	10

Baseline refers to the time of diagnosis of MG; End point refers to the final follow up. LP: Light perception; HM: Hand motion; CF: Counting figure.

Table 2 Comparisons between groups with visual improvement and with no improvement

Groups	Age (a)	AL (mm)	Baseline IOP (mm Hg)	Mean cup/disk ratio	Mean days of shallow AC
Non-improvement	43.87±11.53	21.18±0.79	45.00±10.76	0.93	107.45
Improvement	48.04±13.27	21.17±0.85	39.83±13.28	0.78	6.33
<i>P</i>	0.325	0.982	0.2156	<0.001	<0.01

Table 3 IOP and ACD changes before and after MG treatment

Groups	IOP (mm Hg)			ACD (mm)		
	Baseline	End point	<i>P</i>	Baseline	End point	<i>P</i>
Medical therapy	29.75±2.87	14.50±3.32	0.01	0.80±0.62	2.33±0.21	0.005
YAG	45.50±3.54	16.50±2.12	0.02	0.25±0.07	2.3±0.14	<0.001
Vitrectomy group	42.92±11.32	15.38±5.14	<0.001	0.09±0.08	2.32±0.25	<0.001
Phaco group	38.90±9.77	16.30±3.06	<0.001	0.41±0.39	2.26±0.23	<0.001
Combination group	48.22±16.7	16.44±6.00	<0.001	0.09±0.15	2.26±0.27	<0.001

Complications One eye exhibited bleeding at the entry site of vitrectomy into vitreous cavity. Corneal endothelial decompensation occurred to 1 eye, and another eye showed positive response to medical therapy but allergy to atropine.

DISCUSSION

Our data showed MG occurred to 2.0% of all eyes with PACG undergoing glaucoma surgery, 2.9% of all trabeculectomy surgeries between Jan. 2009 and Dec. 2012 in Aier Eye Hospital of Wuhan. The incidence was within the range of 2% to 4% as reported by other researchers in their case series [14-16]. The demographic data of our MG patients was also similar to previous Chinese reports [16-18]. Comparing the eyes with visual improvement to those without visual improvement, we found that under the same high IOP, the determinant factors of visual prognosis were the duration of shallow anterior chamber and the progress of primary conditions. For management of phakic MG, various treatments have been reported[1-12]. In our case series, different treatment modalities were used according to the individual condition of each patient. Nearly all patients obtained

resolution of MG and a majority gained more of visual acuity. Medical treatment was beneficial in mild cases. Laser posterior capsulotomy with hyaloidotomy was beneficial in pseudophakic eyes. Different surgical interventions were chosen for appropriate patients, most were successful in this series.

The precise pathophysiology of MG is not completely understood. The more popular theories include: 1) posterior pooling of aqueous and decreased permeability of anterior hyaloids; 2) slackness of lens zonules theory; 3) Quigley [19] proposed new explanation for the mechanism of MG in his choroidal expansion theory in 2009. He thought past suggestions that MG results from "misdirected" aqueous are not consistent with physiological principles. The mechanism of MG seems likely to result from poor conductivity of fluid through the vitreous. This could lead to a disequilibrium situation, since the increased demand for posterior to anterior fluid flow would not be relieved by sufficient fluid movement. The vitreous gel would compress and move forward, leading to poorer vitreous conductivity and then

"chandler's vicious cycle". Quigley^[19] believed that the inciting event for MG is more likely to be the inability to generate fluid flow across the vitreous sufficient to compensate for aqueous outflow anteriorly under the higher pressure conditions that are generated by choroidal expansion.

By analyzing the pretreatment examinations, findings during surgeries and those relapsed cases in our case series, we speculated the possible pathophysiology of MG as follows:

1) Ciliolenticular block or anterior hyaloid obstruction: the removal of liquid or liquefied vitreous by aspiration in 16 eyes of both phaco and combination groups indicates ciliary block may be the pathogenesis of this condition and lens plays an important role. Anterior hyaloid face may contribute to ciliolenticular block because in 2 eyes of the combination group, the anterior chamber failed to form after vitreous aspiration and cataract surgery but re-formed when extra steps such as posterior capsulotomy and anterior hyaloidotomy were performed. Another 6 eyes in combination group required anterior vitrectomy for anterior chamber deepening, which was believed to be associated with anterior vitreous obstruction.

2) Slackness of lens zonules: among our patients, 6 eyes were identified with slackness of lens zonules during the surgery. This change might be primary, or might be the result of severe and prolonged angle closure, or ciliary muscle spasm induced by surgery, miotics, inflammation or other unknown reasons. Two eyes of 2 patients demonstrated a recurrence after vitrectomy. These two patients had shallow anterior chamber lasting more than half a year, we postulated the relapse was mainly due to the thickened lens moving forward and exerting persistent forward pull over zonules, thus causing slackness of the lens zonules.

3) Severe postoperative inflammation: two eyes undergoing combined glaucoma and cataract surgery and 1 eye undergoing vitrectomy and cataract extraction had recurrence of MG. Among these 3 patients, 1 patient suffered from diabetes mellitus, the other 2 patients had a history of multiple intraocular surgeries. Upon examination, exudative membrane was seen in pupil area with posterior synechia and posterior capsular opacity in all these 3 patients. It is believed that the exudative membrane impedes the normal communication between the vitreous cavity and the anterior and posterior chambers.

4) Non ciliary block: a) ten out of 13 eyes in vitrectomy group presented with no relapse at final follow-up visit. The MG in these patients was postulated to involve other mechanisms than ciliary block because they were given cycloplegics and hyperosmotics before surgical intervention, their IOPs took non progressive increase and no liquid could be aspirated during surgery; b) it was observed that those

patients who developed MG during surgery all showed a high stress level and poor operative cooperation. We speculated that such status caused constriction of extraocular muscles pressing forward, bringing about the increase of ocular venous pressure. Vortex venous pressure and choroidal vascular pressure were also elevated with it. MG in these patients occurred as a result of choroidal expansion caused by the increase in choroidal volume which is adjusted by vascular pressure. Sehuman *et al*^[20] found the Valsalva effect of trumpet playing increases IOP to 40 mm Hg with a 20% increase in choroidal thickness by ultrasound biomicroscopy (UBM). Though our study lacked the real time accurate measurement of the thickness of the ciliary body and choroid before and after MG, we still believe this physiological change contributes to the pathophysiology of MG.

In summary, MG occurs as a result of multiple mechanisms involved simultaneously or sequentially. Medical therapy is advocated as the initial treatment, laser therapy is beneficial in pseudophakic eyes, and timely surgical intervention is needed when non-response occurs to nonsurgical management. Surgical option is often based on the degree of lens opacity, the duration of shallow anterior chamber and effects of vitreous puncture with aspiration, and individualized therapeutic regimen is chosen as follows: 1) if there is non-progressive IOP increase and shallow anterior chamber between Grade II and III, but no response to medical therapy and no liquid extracted from vitreous cavity, other mechanism than ciliary block is suggested in MG. Anterior vitrectomy combined with reformation of anterior chamber is indicated, and lens removal is performed when necessary; 2) if the status of shallow anterior chamber is prolonged (>2mo), and cataract develops or worsens, then multiple mechanisms may co-exist in the pathogenesis of MG. When there is progressive IOP elevation and liquid aspirated from vitreous cavity during surgery, MG is believed to primarily occur through ciliary block, and moreover lenticular block is considered as the main factor. Phacoemulsification-IOL implantation is recommended. Posterior capsulotomy or anterior vitrectomy is performed depending on situations during or after surgery. Excessive intraocular disturbance and disruption should be avoided when optimal outcome is warranted.

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