Original research

Clinical profile and management outcomes of traumatic submacular hemorrhage

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Abstract

Purpose: To evaluate the anatomical and functional outcome of patients with traumatic submacular hemorrhage (SMH).
Methods: A retrospective, interventional case series of patients presenting between January 2016 and April 2018 was carried out at 4 tertiary eye care centers of India. Medical records of the patients with a history of blunt trauma and SMH were retrospectively reviewed. The intervention done was any one of the following: pneumatic displacement with 0.3 ml of intravitreal gas [100% perfluoropropane (C3F8) gas], pneumatic displacement with intravitreal 0.3 ml of 100% C3F8 gas combined with 100 µg/0.1 ml of recombinant tissue plasminogen activator (r-tpa), pars plana vitrectomy (PPV) with subretinal r-tpa and gas tamponade. The primary outcome measures included change in visual and anatomical status.
Results: Twenty eyes of 20 patients with blunt trauma were analyzed. Thirteen patients had small size SMH, 5 patients had medium size SMH, and 2 patients had massive size SMH. Sixteen patients had a favorable functional outcome, and eighteen patients had favorable anatomical outcome. The size and duration of post-traumatic SMH did not significantly affect the anatomical ($P = 0.123$) or functional ($P = 0.293$) outcome in our study. The patients who presented with initial visual acuity of 6/60 or better showed better functional outcome, which was statistically significant ($P = 0.007$).
Conclusion: Minimally non-invasive procedure including intravitreal r-tpa and gas appear to be effective in the displacement of post-traumatic SMH.

Introduction

Trauma is the major cause of severe vision loss. Ocular injuries may result in a wide range of clinical manifestations based on the mechanism and severity of injury. Submacular hemorrhage (SMH) is a common manifestation of choroidal neovascular membranes (CNVM) secondary to age-related macular degeneration (AMD) and idiopathic polypoidal choroidal vasculopathy (IPCV).[1,2] However, blunt trauma may

at times result in SMH causing loss of central vision. An early displacement of blood from the macula is advised to avoid damage to the photoreceptors and permanent loss of vision.[3,4] In order to understand the impact of blunt ocular trauma and its response to treatment, we report the anatomical and functional outcomes of our patients with SMH secondary to blunt trauma.

Methods

A retrospective, interventional case series of patients, presenting with SMH secondary to blunt trauma presenting between January 2016 and April 2018 was carried out. An approval was taken from the institutional review board, and the study was conducted in accord with the tenets of the Declaration of Helsinki. A minimal follow-up of six months was required to be included in the study. Demographic profile of the patients, nature of injury, duration between the injury and intervention, and the clinical findings on a complete ocular examination were noted.

SMH was defined as the presence of blood in between the retinal pigment epithelium (RPE) and the neurosensory retina at the macula, involving the fovea. A fundus photograph was taken at baseline and at follow-up to analyze the location, extent, and size of SMH. The size of SMH in disc diameters (DD) was determined, and grading of the size of the hemorrhage was done as follows:

a) Lesions less than 1 DD were not labeled as SMH
b) Small SMH measured 1 DD to 4 DD
c) Medium-sized SMH measured at least 4 DD, but not extending beyond the temporal vascular arcade
d) Massive SMH extended beyond the temporal vascular arcade.[5,6]

A review was done of the type of intervention which was comprised of any one of the following:

1) Pneumatic displacement with 0.3 ml of intravitreal gas [100% perfluoropropane (C3F8) gas].
2) Pneumatic displacement with intravitreal 0.3 ml of 100% C3F8 gas combined with 0.05 ml of intravitreal recombinant tissue plasminogen activator (r-tpa) (100 μg/ 0.1 ml).
3) 25 gauge microincision pars plana vitrectomy (PPV) with 41 gauge subretinal infusion needle to inject 0.1 ml of subretinal r-tpa (25 μg/0.1 ml) and gas tamponade.

The visual acuity at six-month follow-up visit was considered to be the final visual acuity. The primary outcomes measured were the final functional and anatomical outcome. A favorable functional outcome was defined as an increase in the visual acuity ≥ 2 Snellen's lines, and a favorable anatomical outcome was defined as complete displacement of the hemorrhage from the subfoveal location at the sixth-month follow-up visit.

IBM SPSS software version 22.0 (SPSS Inc, Chicago, Illinois, USA) was used for all statistical analyses. Categorical data were represented by frequency, and they were analyzed by Fisher's exact test. A P value of less than 0.05 was considered statistically significant.

Results

Twenty eyes of 20 patients with a history of blunt trauma were included in the study (Table 1). Five patients were females, and fifteen were males. The average age of the patients was 30.15 years (range, 18–55 years). The mean duration of SMH was 10.6 days (range, 1–30 days). The size of the SMH in 13 patients was small, medium in five patients, and massive in two patients.

The intervention done was as follows: four patients underwent intravitreal gas injection, 15 patients had intravitreal r-tpa and gas tamponade, and one patient had PPV with subretinal r-tpa and gas tamponade.

No intraoperative complications were noted.

Postoperatively, one patient developed secondary glaucoma, and one patient showed a full thickness macular hole. Ninety percent (18 patients) showed a favorable anatomical outcome, and eighty percent (16 patients) had a favorable functional outcome.

The four patients with unfavorable functional outcome were secondary due to the presence of a choroidal rupture passing through the macula in two patients and macular scarring in the other two patients.

Out of the 13 patients with a small SMH, 12 patients showed a favorable anatomical outcome, and one patient had an unfavorable anatomical outcome. Fig. 1 demonstrates favorable anatomical outcome (B) in a case of small SMH (A) after a duration of 6 months. All the five patients with medium size SMH showed a favorable outcome. Out of the two patients with a massive SMH, one patient showed a favorable anatomical outcome. This was, however, not found to be statistically significant ($P = 0.123$, Fischer's exact test).

Out of the 13 patients with a small SMH, ten patients showed a favorable functional outcome, and three patients had an unfavorable functional outcome. All of the five patients with medium size SMH showed a favorable functional outcome. Out of the two patients with a massive SMH, one patient showed a favorable functional outcome. This also was not found to be statistically significant ($P = 0.293$, Fischer's exact test).

Ten patients underwent an intervention for the displacement of the SMH within seven days of the trauma, three patients between 7 and 14 days, and seven patients between 14 and 30 days.

Nine patients out of the ten patients treated within seven days showed a favorable anatomical outcome, and seven patients showed a favorable functional outcome ($P = 0.30$). Three patients with an unfavorable functional outcome were secondary to macular scar in one patient and choroidal rupture in two patients.

Table 1
Visual acuity and treatment profile of patients.

S. no	Age	Gender	Eye	Duration of SMH (days)	Pre-op BCVA	Final BCVA	Grading of Size	Treatment	Anato-mical out-come	Funct-ional out-come
1.	22	M	OD	15	6/24	6/9	SMALL	GAS + I/V TPA	FAV	FAV
2.	42	M	OD	8	6/36	6/12	MEDIUM	GAS + I/V TPA	FAV	FAV
3.	41	F	OD	22	FC 1 M	6/36	SMALL	GAS + I/V TPA	FAV	FAV
4.	33	F	OS	17	6/60	6/6	SMALL	GAS + I/V TPA	FAV	FAV
5.	25	F	OD	2	6/24	6/9	SMALL	GAS + I/V TPA	FAV	FAV
6.	18	M	OD	7	6/18	6/18	SMALL	GAS + I/V TPA	FAV	**NON FAV**
7.	23	M	OS	7	FC 1 M	6/12	SMALL	GAS + I/V TPA	FAV	FAV
8.	25	M	OD	17	FC 1 M	6/36	MEDIUM	GAS + I/V TPA	FAV	FAV
9.	25	M	OD	3	6/60	6/36	SMALL	GAS + I/V TPA	FAV	**NON FAV**
10.	22	M	OS	18	FC 4 M	6/36	MEDIUM	GAS + I/V TPA	FAV	FAV
11.	18	M	OD	16	FC 0.5 M	FC 3 M	SMALL	GAS + I/V TPA	**NON FAV**	**NON FAV**
12.	32	M	OS	2	6/24	6/9	SMALL	GAS + I/V TPA	FAV	FAV
13.	55	M	OS	30	6/180	6/24	MASSIVE	PPV + S/R TPA + GAS	FAV	FAV
14.	31	M	OS	7	FC 0.5 M	FC 1 M	MASSIVE	GAS	**NON FAV**	**NON FAV**
15.	38	M	OD	7	6/18	6/6	MEDIUM	GAS	FAV	FAV
16.	35	M	OD	5	6/60	6/24	SMALL	GAS	FAV	FAV
17.	36	F	OD	17	6/60	6/12	SMALL	GAS + I/V TPA	FAV	FAV
18.	33	F	OS	8	6/60	6/9	SMALL	GAS + I/V TPA	FAV	FAV
19.	24	M	OD	1	FC 1 M	6/36	MEDIUM	GAS + I/V TPA	FAV	FAV
20.	25	M	OD	3	6/60	6/12	SMALL	GAS	FAV	FAV

SMH: Submacular hemorrhage; BCVA: Best corrected visual acuity; M: Male; F: Female; FC: Finger counting; M: Meter; DD: Disc diameter; TPA: Tissue plasminogen activator; I/V: Intravitreal; PPV: Pars plana vitrectomy; S/R: Subretinal, FAV: Favorable; NON FAV: Non-favorable.
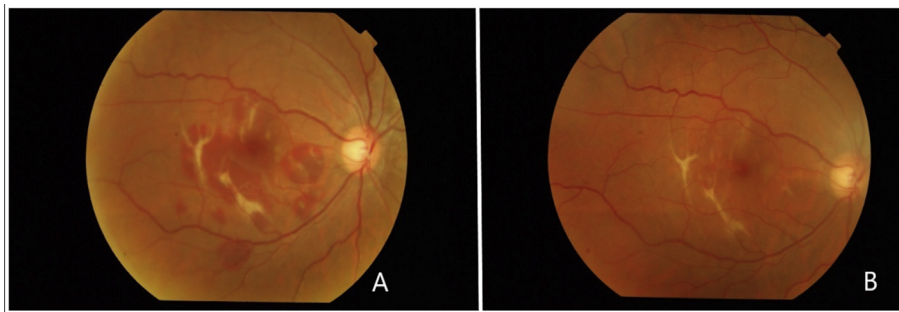

Fig. 1. A: Fundus photograph of right eye showing small submacular hemorrhage (SMH) of 2 weeks duration and juxtafoveal choroidal ruptures. B: Postoperative fundus photograph of the same eye, showing complete resolution of the SMH following intravitreal gas + recombinant tissue plasminogen activator (r-tpa).

One patient treated between 14 and 30 days also showed an unfavorable functional outcome secondary to macular scar, and one patient showed an unfavorable anatomical outcome. However, the correlation between the duration of the SMH and anatomical and functional was not found to be statistically significant [anatomical outcome ($P = 0.43$) and functional outcome ($P = 0.81$)].

Twelve out of thirteen patients with a baseline best corrected visual acuity (BCVA) of >6/60 showed a favorable functional outcome, and five out of seven patients with BCVA <6/60 showed an unfavorable functional outcome. This correlation was statistically significant ($P = 0.007$).

Discussion

Blunt trauma is a potential cause of SMH leading to severe vision loss.[7] An irreversible loss of vision may occur in these cases secondary to long standing SMH or underlying causes such as macular scarring or a choroidal rupture passing through the macula.[8,9]

Long standing SMH is said to cause photoreceptor damage secondary to iron toxicity, fibrin meshwork contraction,[10] and reduced nutrient flux,[11−13] with subsequent macular scarring. Therefore, an early displacement of the SMH is advocated. Various treatment options are available for the displacement of the SMH including pneumatic displacement alone or with intravitreal r-tpa, PPV with intravitreal or subretinal r-tpa, and intravitreal gas tamponade and postoperative positioning.

In 1991, Peyman et al. first reported the visual outcomes of r-tpa assisted SMH removal.[1] In their series, 60% of patients achieved an improvement in BCVA of two or more lines. Wilson Heriot in 1996 described a minimally invasive technique comprising an intravitreal injection of r-tpa and gas tamponade to promote the lysis of the macular hemorrhage, a procedure which attempted to replace a surgical intervention for draining SMH.[14] In our series, 15 out of 20 patients with

post-traumatic SMH underwent displacement of the hemorrhage using intravitreal r-tpa and gas tamponade, and four patients were treated with gas alone and one patient with PPV along with subretinal r-tpa and gas tamponade. We observed a favorable anatomical outcome with complete displacement of hemorrhage in 18 eyes and a favorable functional outcome with a visual gain of ≥2 Snellen's line in 16 eyes. An unfavorable functional outcome was seen in four patients which were due to choroidal rupture passing through the macula in two patients and macular scarring in two patients.

We found no correlation between the size of the SMH and the final anatomical and functional outcome. This was similar to what has been reported by the other authors.[15,16] As mentioned, a small hemorrhage centered at the fovea maybe associated with a worse visual acuity than a larger thin SMH not covering the fovea. Glatt and Machemer in their experimental study found that irreversible retinal damage occurred within 24 h and a total loss of photoreceptors after seven days.[17] However in humans, SMH has been treated after eight days with some improvement in vision. In our study, eyes with duration of SMH less than seven days had a significantly higher probability of achieving favorable anatomical outcome compared to eyes with SMH more than a week duration of the hemorrhage. The eyes with a baseline visual acuity >6/60 showed a more favorable functional outcome. We were unable to compare the results between the different modalities of treatment, as the number of patients in each group were inadequate.

On review of literature, Kamei et al. have reported a favorable visual outcome in 86% of their patients; however, they advocated the use of perfluorocarbon liquid (PFCL) to displace the SMH after subretinal injection of r-tpa through a small retinotomy.[18] Lewis et al. reported good visual outcome in 83% of their patients with an underlying cause of AMD treated within two weeks of onset of SMH.[19] Hattenbach et al. in their series of SMH secondary to AMD showed complete displacement of blood from the fovea in 81% of the eyes and final visual improvement by two lines in 30% with 50 mg/0.1 ml of r-tpa and 0.5 ml of 100% sulfur hexafluoride gas. 67% of the eyes with SMH less than 14 days duration exhibited an improvement of visual acuity compared to 30% where the hemorrhage was more than 14 days in duration. They found no relation between the size of the hemorrhage and the final visual acuity.[16]

Kumar et al. performed a retrospective chart review on ten eyes of ten patients with SMH secondary to wet AMD treated with 23-gauge PPV, followed by submacular injection of r-tpa (12.5 µg/0.1 ml), bevacizumab (2.5 mg/0.1 ml), and air (0.3 ml).[20] They found that this modified technique aids in the effective displacement of thick SMH with simultaneous treatment of the underlying CNVM. Rishi et al. in their series of 46 eyes which included SMH secondary to various causes such as AMD, IPCV, retinal artery macro aneurysm (RAM), high myopia, and post-trauma in ten eyes found no difference in terms of favorable anatomical or functional outcomes between different treatment modalities (intravitreal r-tpa and

gas, gas alone, and PPV with subretinal r-tpa and gas); however, they found eyes with a median duration of SMH less than 7.5 days had a significantly higher probability of achieving favorable anatomical outcome compared to eyes with SMH >14.5 days duration.[15] However, the duration of SMH did not influence the functional outcome. They also found that the size of the SMH did not affect anatomical or functional outcome. Ohji et al. were the first to report the displacement of SMH with gas alone in five eyes secondary to AMD and RAM.[21] In this series, the authors concluded that the final outcome does not depend on the size and duration of SMH. However, it has been reported that the visual recovery after gas alone is lower in comparison to using r-tpa as the movement of the clot without prior lysis results in irreversible damage along the photoreceptors layer and is not very effective for large thick SMH.[16,22] However, we need to keep in mind the toxic damage caused by r-tpa itself. This damage results from the administration of doses greater than 100 µg either through a single injection or after re-injecting smaller doses leading to toxicity, which would be cumulative and dose dependent. The toxicity is said to be primarily due to L-arginine, the commercial vehicle for r-tpa.[23,24]

In comparison to already reported cases, our series includes cases of SMH secondary to blunt trauma only. On review of literature, we found only anecdotal case reports of post-traumatic SMH treated by intravitreal ranizumab by Salim et al.[7] where they have postulated that the anti-inflammatory property of anti-vascular endothelial growth factor (anti-VGEF) may play a role. Heras-Mulero et al. have reported one case of post-traumatic SMH treated by PPV with intravitreal r-tpa and gas.[25] Rishi et al. in their series have not separately analyzed the anatomical and functional outcomes in post-traumatic SMH cases.[15] To the best of our knowledge, this is the largest retrospective case series analyzing the functional and anatomical outcomes of post-traumatic SMH.

The drawbacks of our study are that it is of a retrospective design, relatively small size with unequal distribution between different modalities of treatment, and selective bias of one modality as the majority of the patients were treated with intravitreal r-tpa and gas. Optical coherence tomography (OCT) analysis of SMH is important to prognosticate and to guide the treatment but a number of our study patients were managed at peripheral centers where there is unavailability of OCT machine. Lack of OCT parameters is a major drawback of our study.

In conclusion, minimally non-invasive procedure including intravitreal r-tpa and gas appear to be effective in the displacement of post-traumatic SMH. However, one needs to keep in mind that factors other than density, size, and the duration of SMH such as choroidal rupture, RPE atrophy, macular scarring, and post-traumatic optic neuropathy may have an influence on the final visual outcome in post-traumatic SMH patients which may not play a role other etiologies of SMH. As the number of patients in our study is limited, we propose a larger prospective study to confirm the results.

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