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Professional paper

Treatment of Submacular Haemorrhage in Patients with Neovascular Age Related Macular Degeneration

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A B S T R A C T

To evaluate the efficacy of the pneumatic displacement of the submacular haemorrhage combined with the intravitreal injection of the tissue plasminogen activator. We present a retrospective clinical case series of nine eyes of nine patients that were treated with the intravitreal injection of the tissue plasminogen activator and expansile gas for the submacular haemorrhage due to the age related macular degeneration. We evaluated visual acuities and complications. Selected patients were additionally treated with the intravitreal bevacizumab injections after the procedure. Mean postoperative followup was 19 weeks. Four (4/9) eyes (44%) received additional treatment with the intravitreal bevacizumab during the postoperative period. Statistical analysis was performed using the Student's paired t-test. The mean visual acuity was 1.77 logMAR preoperatively and 1.06 logMAR postoperatively. After the surgery, 4 or more Snellen lines were gained in 7/9 eyes (78%). The improvement of the visual acuity postoperatively was statistically significant ($p = 0.002$). In 2/9 eyes (22%) the visual acuity did not get better after the procedure. We observed no complications during the follow up period. In our case series, pneumatic displacement of the submacular haemorrhage with the use of the intravitreal tissue plasminogen activator (with or without additional bevacizumab treatment in the selected cases) turned out to be an effective and safe method leading to the improvement of the visual acuity in the majority of cases. To maximise the treatment success, prompt referral to the retinal surgeon is imperative.

***Key words**: submacular haemorrhage, age related macular degeneration, pneumatic displacement, tissue plasminogen activator, bevacizumab, visual acuity*

Introduction

The most common cause of submacular haemorrhage is bleeding from the choroidal neovascularisation associated with the age related macular degeneration (AMD). It can also arise in the context of the posterior segment trauma, pathological myopia, ruptured central retinal artery macroaneurism, polipoidal choroidal vasculopathy, angioid streaks, ocular histoplasmosis and systemic diseases such as coagulopathy[1].

If the haemorrhage involves the fovea, loss of vision is profound and progressive[1–3]. The blood clot will mechanically damage the photoreceptors and prevent the normal metabolic support to the elevated outer retina. In a few days, toxic iron compounds will irreversibly damage the photoreceptors. Therefore, it is sensible that appropriate treatment procedures should be started without delay.

The first successful surgical interventions for submacular haemorrhage with vitrectomy, subretinal injection of the tissue plasminogen activator (t-PA) and retinotomy assisted clot removal were described in the early 1990's[4–6]. In recent years less invasive treatment approaches with the intravitreal t-PA and/or gas injections without vitrectomy have been described[7–17].

During these procedures t-PA is injected into the vitreous and partially enters the subretinal space where thrombolysis is induced. Injected gas bubble (and appropriate positioning) will then apply pressure over the macular area and cause the thrombolysed blood clot to dislocate away from the macula towards the periphery.

Possible complications of this method include retinal t-PA toxicity, intraocular pressure rise, retinal detach-

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ment, endophthalmitis, uveitis, haematovitreous and cataract induction[18–20].

Most recently, additional treatment with antibodies against the vascular endothelial growth factor (anti-VEGF) has been shown to improve the visual outcome in subretinal haemorrhages with active choroidal neovascularization[21–24]. Intravitreal application of anti-VEGF could prevent progression of choroidal neovascularisation and submacular haemorrhage recurrence.

Methods

We present a retrospective clinical case series of nine eyes of nine patients that were treated at the Eye Hospital, University Clinical Centre, Ljubljana, Slovenia, between January 2007 and October 2011. The data were derived from the medical records. The patients ranged in age from 67 to 84 years. Two of them were male and seven were female. All of them suffered from submacular haemorrhage and were treated with the intravitreal injection of t-PA and expansile gas.

They were referred to our hospital as soon as a few hours after the onset of the vision loss and as late as 60 days after the vision loss.

On the day of presentation, patients were prepared according to the procedure protocol in the operating theatre. First, 50 micrograms of t-PA were injected intravitrealy under the topical anesthesia. After a two-hour period of the supine bed rest, 0.3 ccm of SF6 gas was then injected intravitrealy. After the procedure, patients were encouraged to the greatest possible time of face-down positioning for the next three days.

They were appointed to the regular follow up visits one week and four weeks after the procedure, and electively thereafter. We evaluated visual acuities (VA) and complications. For the statistical analysis, VA at presentation and four weeks after the procedure were compared. Statistical analysis using the Student's paired t-test was performed.

Selected patients with active choroidal neovascularisation and without significant macular fibrosis as shown on subsequent fluorescein angiography were additionally treated with the intravitreal bevacizumab injections in the weeks after the procedure.

Results

The results and patients' characteristics are shown in Table 1.

The mean age of patients included in our study was 74,78 years, seven of them were female and two were male. In five eyes the hemorrhage had occurred in the right eye and in four eyes the left eye was affected. Pa-

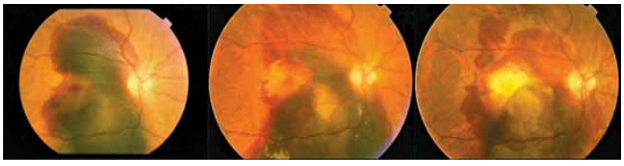


Fig. 1. Patient No. 2: at presentation, 4 weeks post procedure, 40 weeks post procedure.

Fig. 2. Patient No. 3: at presentation, 4 weeks post procedure, 34 weeks post procedure.

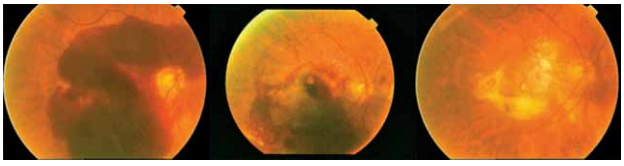


Fig. 3. Patient No. 4: at presentation, 1 week post procedure, 27 weeks post procedure.

TABLE 1
PATIENTS' CHARACTERISTICS

Patient	Age	Sex	Eye	VA at presentation (logMAR)	Duration of symptoms (days)	VA 4 weeks after the procedure (logMAR)	Gain of VA (logMAR)	Comments
1. CA	70	F	L	1.60	3	0.40	1.20	
2. NI	80	F	L	1.60	7	1.60	0.00	
3. ZB	82	F	R	3.00	4	2.00	1.00	bevacizumab
4. DF	67	M	R	1.60	3	0.50	1.10	bevacizumab
5. BM	67	F	R	0.80	4	0.40	0.40	bevacizumab
6. ZJ	75	F	L	0.70	7	0.30	0.40	
7. PL	79	F	L	3.00	6	1.60	1.40	
8. JP	84	F	R	2.00	60	2.00	0.00	
9. ZK	69	M	R	1.60	1	0.70	0.90	bevacizumab

VA – visual acuity

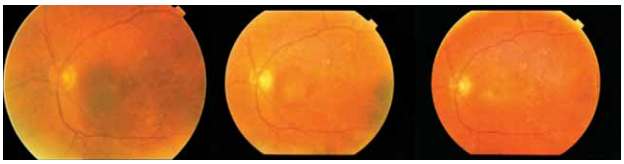


Fig. 4. Patient No. 8: at presentation, 1 week post procedure, 9 weeks post procedure.

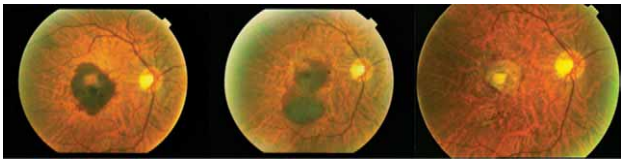
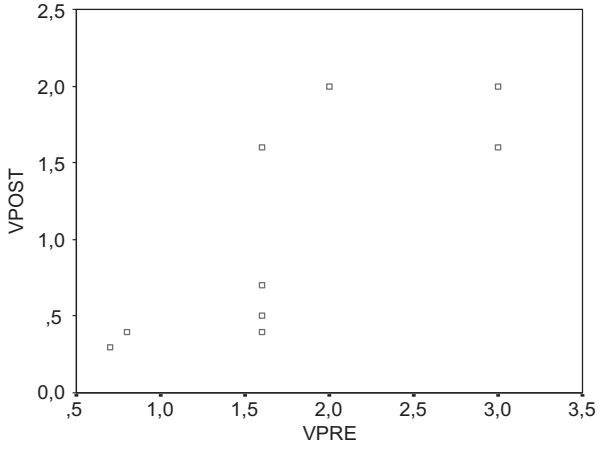


Fig. 5. Patient No. 9: at presentation, 1 week post procedure, 9 weeks post procedure.

tients presented to our clinic as early as a few hours and as late as two months after the hemorrhage had occurred.

VA before the procedure ranged form 0,7 logMAR to 3 logMAR and the mean VA was 1.77 (±0.81) logMAR. After the procedure, displacement of submacular haemorrhage from the fovea centralis was achieved in seven of nine eyes. Mean postoperative followup lasted 19 weeks. The range of VA postoperatively was from 0.3 logMAR to 2 logMAR with a mean of 1.06 (±0.73) logMAR. Mean improvement of the VA turned out to be 0.71 (±0.52) logMAR, or more than 4 lines according to the decimal VA expression system. Postoperatively, improvement of the VA was achieved in 7/9 eyes (78%) (Graph 1). The improvement was statistically significant (p = 0.002). However, in 2/9 eyes (22%) no gain in the VA was detected. We observed no complications of the procedure during the follow up period.



Graph 1. Relationship between the patients' visual acuities at presentation and 4 weeks after the procedure.
VPRE – visual acuity at presentation
VPOST- visual acuity 4 weeks after the procedure

Additionally, 4/9 eyes (44%) received supplementary treatment with intravitreal bevacizumab during the postoperative period.

Discussion

Multiple treatment possibilities have been proposed for the treatment of the submacular haemorrhage duo to the AMD: observation, anti-VEGF injections, photodynamic therapy, vitrectomy with or without t-PA, pneumatic displacement with or without t-PA, RPE patch surgery and macular translocation[22,25,26]. There remains no consensus on the optimal treatment[26].

The procedure we performed has been well described in the literature with most eyes achieving improvement of the visual function[7–17]. In 7/9 eyes of the patients under the examination, the gain in the VA was observed, as well. Moreover, the procedure is minimally invasive and can be managed under the topical anesthesia. On the other hand, in 2/9 eyes no improvement of the VA was observed. This was the consequence of the scar tissue formation under the retina in the macular area.

In our case series, no eyes had VA better than 20/100 before the procedure. After the surgery VA 20/60 or better was achieved in four eyes (44%). We believe that this moderate improvement in vision is significant since these patients are at risk of the vision loss to the fellow eye due to the AMD.

The value of the early intervention is especially important in the modern age of the anti-VEGF therapy. The possibility to treat the underlying choroidal neovascularisation offers further potential for the visual rehabilitation if the haemorrhage is managed as soon as possible.

However, it has to be taken into account, that the number of patients included in the study was small. To get more representative findings, the group of examinees should be enlarged.

Conclusion

In our case series, pneumatic displacement of the submacular haemorrhage with the use of the intravitreal t-PA (with or without additional bevacizumab treatment in selected cases) turned out to be an effective and safe method leading to the improvement of the VA in the majority of cases.

To maximise the chances for the treatment success, prompt referral to the retinal surgeon is imperative.

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TRETMAN SUBMAKULARNOG KRVARENJA U PACIJENATA SA NEOVASKULARNOM MAKULARNOM DEGENERACIJOM-AMD

SAŽETAK

Razmatra se efikasnost primjene zraka i intravitralne aplikacije-plazminogen aktivatora, na stanje mrežnice, devet očiju u devet pacijenata. U ovoj aplikaciji analiziraju se moguće komplikacije i stanje vida. Također se razmatra efikasnost intravitrealne aplikacije bevacizumab, nakon ovih primjenjenih metoda u vremenu od devetnaest tjedana. Analiza oštrine vida bila je preoperativno 1,77 logMAR, a postoperativno 1,06 logMAR, što je statistički značajno. U toku ovog postupka nisu zabilježene komplikacije.