·Letter to the editor·

Natural evolution and surgical outcome of massive subretinal haemorrhage in a patient with neovascular age-related macular degeneration on warfarin therapy

Zhe Liu[1], Chuan-Bin Sun[2], Chao-Yang Hong[1], Miao-Qin Wu[1], Ke Yao[2]

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[1]Eye Center, Zhejiang Provincial People's Hospital; Eye Institute of Zhejiang Province, Hangzhou 310014, Zhejiang Province, China
[2]Eye Center, Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, Zhejiang Province, China
Correspondence to: Miao-Qin Wu. Eye Center, Zhejiang Provincial People's Hospital; Eye Institute of Zhejiang Province, Hangzhou 310014, Zhejiang Province, China.doctorwumq@yahoo.com.cn

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Dear Sir,

I am Dr Zhe Liu, from the Eye Center of Zhejiang Provincial People's Hospital in Hangzhou, Zhejiang Province, China. I write to present a case report of massive subretinal haemorrhage in a patient with neovascular age-related macular degeneration (AMD) on warfarin therapy.

Anticoagulants or antiplatelet agents have been commonly used to prevent thrombosis in cardiovascular diseases. Massive subretinal haemorrhage is a rare but blindness-causing complication of anticoagulation therapy [1-5]. Many studies have revealed poor surgical outcomes of massive subretinal haemorrhage in patients with neovacular age-related macular degeneration (AMD) on warfarin therapy [1-6]. However, little is known, to our knowledge, about the natural evolution of massive subretinal haemorrhage in cases receiving warfarin therapy.

A 63-year-old man was referred to us from a cadiologist for sudden visual loss in his right eye. He was diagnosed with arthritis and rhematic heart disease 30 years ago, performed of mechanical valve prosthesis 3 years ago, after which he took Warfarin 3mg once daily, and kept a therapeutic International Normalized Ration (INR) about 2. Neovascular AMD with subretinal yellowish exudate was found in his right eye 6 months ago by an ophthalmic consultation.

Initial examination showed his INR was 2.0, visual acuity was light perception in the right eye, and 1.0 in the left eye. Intraocular pressures were 18.6 mmHg and 17.5mmHg in the right and left eye, respectively. Slit-lamp examination revealed a normal anterior segment in both eyes. Ophthalmoscopy found a massive inferior subretinal hemorrhage with macular involved in the right eye (Figure 1A). B-mode ultrasonography confirmed the massive subretinal hemorrhage in his right eye (Figure 1B). To avoid the continuation of intraocular haemorrhage, his cadiologist suggested to stop warfarin therapy and down regulated INR to 1-1.5. Unfortunately, this did not help to prevent further intraocular bleeding, the subretinal hemorrhage was progressively enlarged and finally his visual acuity dropped to no light perception. One week later, his INR was lower than 1.0, and Warfarin 2mg per day was advised by the cardiologist to avoid thrombosis. Another 6 days later, the patient complained of severe pain in the right eye accompanied with an intraocular pressure of 60 mmHg. Slit-lamp examination revealed an extremely shallowed anterior chamber (Figure 1C) and highly elevated hemorrhagic retinal detachment which nearly touched the natural lens. B-mode ultrasonography confirmed a massive subretinal haemorrhage much more enlarged than before (Figure 1D).

The patient was diagnosed with massive subretinal haemorrhage complicated by secondary acute angle-closure glaucoma in the right eye. Although maximal dose of mannitol 20% and acetazolamide, combined with methypredisolone 80 mg invtravenous injection, were used, the elevated IOP in his right eye was still out of control, and severe ocular pain lasted. The patient then underwent phacoemulcification, pars plana vitrectomy with subretinal tissue plasminogen activator (t-PA) injection, retinotomy, and silicone oil tamponade in the right eye. Due to the highly elevated retina was nearly touched the lens,

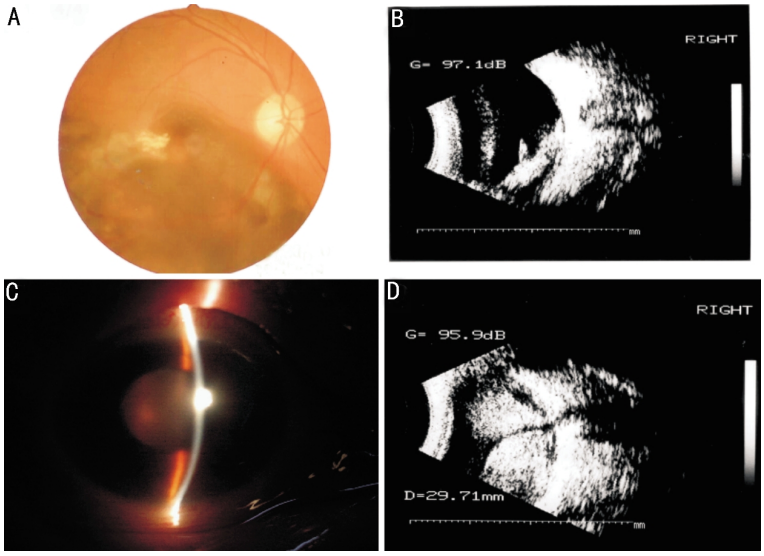

Figure 1 A: Color fundus photograph revealed a massive subretinal haemorrhage (MSH) in the right eye; B: B-mode ultrasonogrphy showed theMSH; C: Slit-lamp examination showed an extremly shallowed anterior chamber and highly elevated MSH nearly touched to lens-iris diagram; D: B-mode ultrasonogrphy comfirmsed the MSH was much more enlarged than before

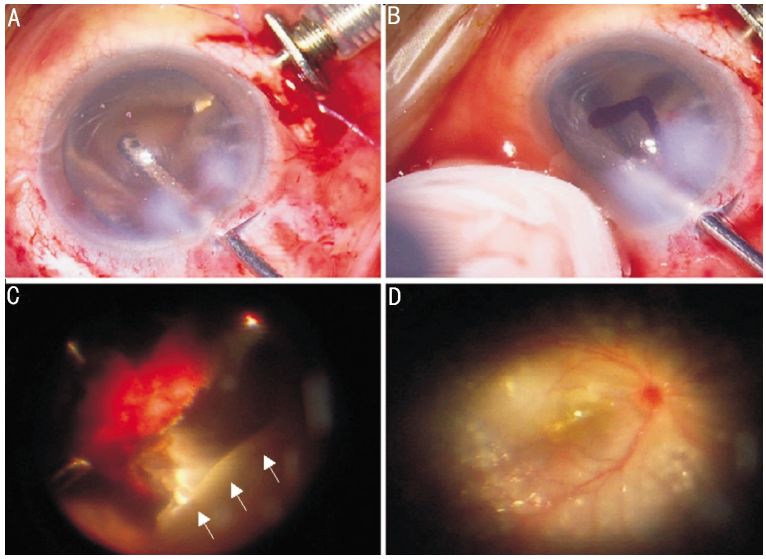

Figure 2 A: Photograph of the right eye during vitrectomy after phacoemucification, the highly elevated retina could be seen directly by the operating microscope B: 30 minutes after subretinal injection of tissue plasminogen activator for clot dissolution, brown-colored blood flowed out through the incised hole in detached retina; C: A peripheral 360º retinotomy was performed for additional clot removal, the black arrows showing the incised and overturned peripheral retina; D: Postoperative photograph revealed a reattached retina with exudative macular degeneration in the right eye, fresh laser photoagulation spots were clearly seen in this case

vitrectomy probes were first put through the corneal incision. t-PA was diluted to 40mg in 0.1mL buffered saline solution and injected into the subretinal space via a 28-gauge translocation needle through the corneal incision (Figure 2A). After 30 minutes for clot dissolution, a large amount of brown-colored blood flowed out through the incised hole in the detached retina (Figure 2B). Pars plana vitrectomy was then performed after reposition of the retina, peripheral 360º retinotomy was done for the residual clot removal (Figure 2C). Then, laser retinopexy is performed aroud the retinotomy and peripheral retinotomy, and silicone oil was injected into the vitreous cavity (Figure 2D). No fresh intraocular haemorrhage during operation was found, and ocular pain was relieved right after operation. Unfortunatly, although subretinal haemorrhage was completely drained off, no visual improvement was achieved during 6 months' follow-up.

It is well known that anticoagulation therapy is apt to cause intraocular hemorrhage, however,massive subretinal haemorrhage associated with warfarin therapy rarely occurrs [1-6]. Due to the poor prognosis of massive subretinal haemorrhage, it is of great importance to understand its

mechanism and natural evolution.

Literature published revealed massive subretinal haemorrhage associated with Warfarin therapy mainly occurred in neovascular AMD cases[1-6], which indicated that fragility of abnormal new ocular blood vessels is a main cause of massive subretinal haemorrhage. Tilanus et al reported that high INR (more than 3) was more likely to produce massive subretinal haemorrhage in neovascular AMD cases on Warfarin therapy [4], which indicated that a higher INR might be a risk factor for massive subretinal haemorrhage. In our study, massive subretinal haemorrhage occurred even though the INR was in a "appropriate" range, which implied that INR might not be a good indicator of massive subretinal haemorrhage in AMD cases on warfarin therapy.

Both cardiologists and ophthalmologosts are sometimes in the dilemma between bleeding and thrombosis when anticoagulants or antiplatelet agents are used for cardiovascular disease cases. Whether anticoagulation therapy should be stopped or reduced dose is still under discussion. Some researchers recommend an immediate injection of Vitmin K and lower dose of wafarin to reverse high INR [1]. In our case, due to the patient's INR was only 2.0 when visual loss occurred in his right eye, the cardiologist recommended a cease of warfarin without Vitmin K injection. Unfortunately, the subretinal haemorrhage progressively enlarged and led to a visual result of no light perception. The anterior movement of lens-iris diagram pushed by extremely elevated subretinal haemorrhage, combined with the inflammatory anterior rotation of ciliary body, probally are the main causes of angle closure glaucoma in our case [7].

Subretinal injection of t-PA, combined with vitrectomy and retinotomy is effective in draining off massive subretinal haemorrhage. However, the prognosis of massive subretinal haemorrhage is poor, even though a successful surgery is performed in these cases. The possible explanation exists in that the blood in subretinal space may cause severe damage to photoreceptors via iron toxicity and separating photoreceptors from the retinal pigment epithelium by fibrin clot [6]. Animal models have already proved that irreversible retinal damage due to experimental subretinal haemorrhage occurred rapidly [8].

Conflict of interest There is no conflict of interest.

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