

Anticoagulation and intraocular haemorrhage in age-related macular degeneration: a probable link?

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Clinical record

An 88-year-old man presented to our emergency department with sudden loss of vision in his right eye. Past ocular history included amblyopia in his right eye and bilateral neovascular age-related macular degeneration (AMD). Previously recorded best corrected visual acuities were 6/120 and 6/18 in his right and left eye, respectively.

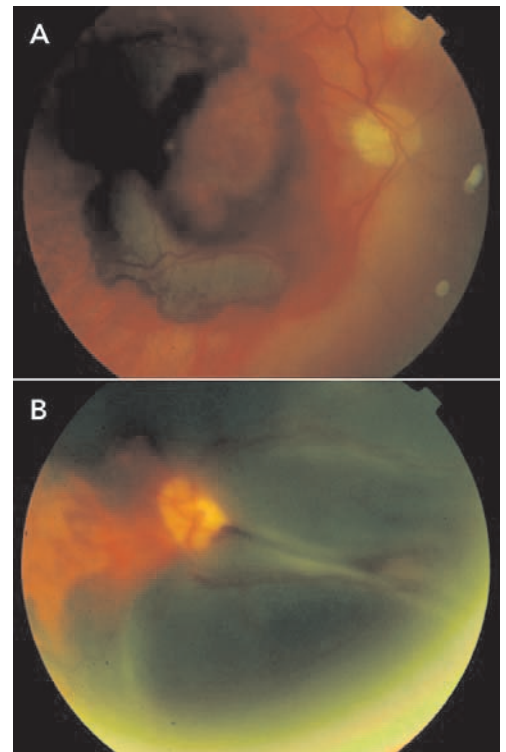
The patient's past medical history included acute myocardial infarction, atrial fibrillation, hypertension, hypercholesterolaemia and polymyalgia rheumatica. He had no history of diabetes, cerebrovascular accident or transient ischaemic attack. His medications included warfarin, aspirin, metoprolol, perindopril and simvastatin. His international normalised ratio (INR) had ranged between 1.3 and 2.3 over the preceding 12 months, with a target of 2.0.

Visual acuity in the right eye was count fingers. Dilated slit lamp examination revealed a large submacular haemorrhage with associated vitreous haemorrhage (Figure A). An electrocardiogram showed atrial fibrillation with a heart rate of 72 beats/min. His blood pressure was 110/80 mmHg. His INR was 2.8. The eye was managed conservatively and, following resolution of the vitreous haemorrhage, vision remained at count fingers.

Four months later, the patient reported sudden loss of vision in his left eye. Visual acuity was light perception, and dilated fundus examination revealed dense subretinal and associated vitreous haemorrhage (Figure B). The patient was still taking warfarin, and his INR at this time was 2.7. As this had been his better eye, he underwent pars plana vitrectomy and clearance of the vitreous haemorrhage. After surgery, his visual acuity was count fingers. After further discussion with the patient's cardiologist, a decision was made to cease warfarin.

A: Fundus photograph of the right eye at presentation, showing macular subretinal and intraretinal haemorrhage. The mild haziness of the photograph is indicative of vitreous haemorrhage.

B: Fundus photograph of the left eye at the time of presentation of visual loss in this eye. Extensive subretinal haemorrhage is seen in the macula. Again, the haziness of the photograph is indicative of vitreous haemorrhage.



This report highlights a potential interaction between a commonly used anticoagulant, warfarin, and an increasingly common ocular condition — AMD. The risk of AMD increases with age, with prevalence reaching 20% of people aged over 75 years in white populations.¹ Neovascular (“wet”) AMD accounts for 10%–20% of cases,² and for 80%–90% of patients who become legally blind from AMD.³ Peripheral vision is typically retained, and most patients are able to maintain a degree of functional independence.

Development of large subretinal and vitreous haemorrhages in neovascular AMD is uncommon. Treatment options are limited and, even with surgical intervention, visual outcomes are in the range of light perception to counting fingers only, with significant loss of paracentral and peripheral vision.⁴ The functional effects are therefore profound.

Previous studies have demonstrated an association between the use of anticoagulant medication, particularly warfarin, and large intraocular haemorrhages among patients with neovascular AMD.^{5,6} The largest of these, a retrospective case–control study comprising 100 patients, found that those with massive intraocular haemorrhage were 11.6 times more likely to be taking anticoagulant medication.⁶ Among these patients, INR ranged from 3.0 to 4.0. Patients with massive haemorrhage were twice as likely to be taking aspirin, although the significance of this

finding is less certain, as the lower limit of the 95% confidence interval was less than 1. No patient was taking anticoagulants and aspirin concurrently.⁶

In our patient, the role of concurrent aspirin therapy is unclear, as there is no evidence in the literature to support or refute the hypothesis that concurrent antiplatelet therapy may have contributed to the development of haemorrhage. However, both instances of haemorrhage were noted to occur at times when his INR was high compared with those recorded over the previous 12 months. Our patient was taking aspirin at all times during this period. Although it is possible that intraocular haemorrhage may have occurred purely as a result of his underlying neovascular AMD, the temporal relationship between the development of the haemorrhages and the high INRs strengthens the case for the implication of warfarin therapy as a contributing factor. Application of the Naranjo probability scale⁷ indicates that this adverse drug event was probable (Naranjo score, +5).

The association between anticoagulant therapy and intraocular haemorrhage is of key importance for several reasons. Firstly, massive intraocular haemorrhage is an important diagnosis to consider in an anticoagulated patient who presents with loss of vision, and who has a background of neovascular AMD. Secondly, patients with neovascular AMD in one eye are at risk of

Lessons from practice

- Patients with neovascular age-related macular degeneration (AMD) have a small but significant risk of intraocular haemorrhage, which may be increased in severity if patients are taking anticoagulant medication.
- The outcomes of intraocular haemorrhage are poor, with significant deterioration in paracentral and peripheral vision, and subsequent implications for ability to maintain functional independence.
- When considering anticoagulation therapy for patients with neovascular AMD, liaison between the general practitioner, cardiologist and ophthalmologist will ensure that an appropriate risk–benefit evaluation is made.
- If patients who take anticoagulant medication develop signs of neovascular AMD, it is essential that the ophthalmologist liaise with the GP and/or cardiologist to ensure that the need for anticoagulation, and the target international normalised ratio, are carefully reviewed. ◆

developing neovascular AMD in the second eye,⁸ and therefore at risk of developing large intraocular haemorrhages in both eyes if long-term anticoagulation is continued.

There are several clinical situations in which the indication for anticoagulation is relative. There are key roles for the ophthalmologist, cardiologist, and general practitioner to ensure that an appropriate risk–benefit evaluation is made before initiating anticoagulant therapy for patients with neovascular AMD. Patients taking anticoagulants who develop neovascular AMD, and in particular those with neovascular AMD who are taking anticoagulants and who develop intraocular haemorrhage in one eye, should have their therapy carefully re-evaluated.

Importantly, awareness of the poor outcomes of intraocular haemorrhage in neovascular AMD, the role of anticoagulants as a risk factor, and effective communication between health profes-

sionals may help reduce the incidence of this devastating complication.

Competing interests

None identified.

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References

- 1 Klein R, Klein BE, Tomany SC, et al. Ten-year incidence and progression of age-related maculopathy: the Beaver Dam eye study. *Ophthalmology* 2002; 109: 1767-1779.
- 2 Ambati J, Ambati BK, Yoo SH, et al. Age-related macular degeneration: etiology, pathogenesis, and therapeutic strategies. *Surv Ophthalmol* 2003; 48: 257-293.
- 3 Ferris FL, Fine SL, Hyman L. Age-related macular degeneration and blindness due to neovascular maculopathy. *Arch Ophthalmol* 1984; 102: 1640-1642.
- 4 Bressler NM, Bressler SB, Gragoudas ES. Age-related macular degeneration. *Surv Ophthalmol* 1988; 32: 375-413.
- 5 El Baba A, Jarrett WH, Harbin TS, et al. Massive hemorrhage complicating age-related macular degeneration. *Ophthalmology* 1986; 93: 1581-1592.
- 6 Tilanus MA, Vaandrager W, Cuyppers MH, et al. Relationship between anticoagulant medication and massive intraocular hemorrhage in age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol* 2000; 238: 482-485.
- 7 Naranjo CA, Busto U, Sellers EM, et al. A method of estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30: 239-245.
- 8 Sarraf D, Gin T, Yu F, et al. Long-term drusen study. *Retina* 1999; 19: 513-519.

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