Letter to the Editors

Spontaneous hyphaema in a patient on warfarin treatment

Alessandro Bagnis¹, Silvio Lai¹, Michele Iester¹, Luca Bacino² & Carlo Enrico Traverso¹¹*Centro di Ricerca Clinica e Laboratorio per il Glaucoma e la Cornea, Clinica Oculistica, DiNOG, University of Genova, Genova*²*Unità Operativa di Cardiologia, Ospedale San Paolo, Azienda Sanitaria Locale 2 Savonese, Savona, Italy*

We report a case of spontaneous hyphaema with no apparent predisposing cause except the assumption of an excessive warfarin dosage leading to over-anticoagulation; a literature search performed in Medline revealed only one case of spontaneous hyphaema resulting from warfarin therapy and no other ocular cause [1]. In case of overdosing, the incidence of warfarin-related hyphaemas could be higher, and it should be taken into account in clinical practice.

A 72-year-old woman presented complaining of blurred vision and discomfort in her right eye of 1 day's duration. She had been taking 5 mg of warfarin sodium daily for atrial fibrillation for 2 years; she denied any other systemic disorder except hypertension and the history was negative for eye disease or treatment. The International Normalized Ratio (INR)/dosing was stable and the INR was regularly monitored every 3–4 weeks. The patient's compliance with the regimen was good; two episodes of self-limiting subconjunctival haemorrhage during the previous 12 months were reported. There was no recent illness and no new concurrent medications. Slit-lamp examination of the right eye revealed diffuse haeme within the anterior chamber and a 2-mm layered hyphaema. No iris abnormalities were present. Gonioscopy was unremarkable and dilated fundus examination was within normal limits for age. The left eye was normal. Haematological evaluation disclosed prolonged activated partial thromboplastin time of 73.4 s (normal range 26–36 s) and INR of 5.56 (normal range 0.80–1.20).

By the consent of the patient's haematologist, warfarin was discontinued until a subsequent haematological evaluation 3 days later. At that time she was asymptomatic and visual acuity was normal (best corrected visual acuity 1.0 decimels, or 20/20 snellen). The anterior chamber had cleared completely; minimum blood was visible on the iris surface and within the anterior iris stroma at 6 o'clock position. Gonioscopy and fundus examination were still negative for ocular abnormalities. Warfarin was reintroduced at

a dose of 2.5 mg/day and the INR monitored 3 days later; the ocular bleeding has not recurred up to now. The use of the Naranjo probability scale revealed that the adverse event was possibly due to warfarin therapy (final score 4).

Most spontaneous hyphaemas are associated with iris abnormalities, but this condition has been reported to occur from a variety of ocular causes (Table 1). Nunziata has reported a case of bilateral hyphaema in which no predisposing condition could be identified [2].

Table 1

Possible causes of hyphaema

Ocular conditions	
Iris abnormalities	Inflammatory/infectious diseases
• Microhaemangiomas	• Uveitis
• Malign/benign tumours	• Microbial cheratitis
• Neovascularization	• HZV infection
• Persistent pupillary membrane	
Other ocular causes	Surgery (late complication)
• Pseudoexfoliation syndrome	• Swan syndrome
• Retrolental fibroplasias	• UGH syndrome
• Persistent hyperplastic primary vitreous	• Iris supported IOL
• Retinoschisis	
• Acute primary closed-angle glaucoma	
Systemic conditions	
Haematological alterations	Rheumatological disorders
• Sickle cell disease	• Reiter's syndrome
• Acute lymphoblastic/myelocytic leukaemia	• Ankylosing spondylitis
• Lymphomas	

Spontaneous hyphaemas have been linked to many ocular and extraocular conditions (see text for details). HZV, herpes zoster virus; UGH, uveitis-glaucoma-hyphaema; IOL, intraocular lens.

Various systemic conditions have been associated with spontaneous hyphaemas: haematological alterations such as sickle cell disease, acute lymphoblastic and myelocytic leukaemia, lymphomas, juvenile xanthogranuloma, histiocytosis X and many rheumatological disorders causing uveitis, such as Reiter's syndrome or ankylosing spondylitis (Table 1).

Warfarin is the most commonly used drug for outpatient anticoagulation therapy and its main side-effect is bleeding; theoretically, this can occur in all organs, including the eye. Ocular bleeding can occur as subconjunctival, vitreal, retinal or choroidal haemorrhages; bloody tears have been also reported [3].

Cases of bleeding within the anterior chamber in non-operated eyes and linked to warfarin therapy in eyes with predisposing abnormalities have been previously reported by Greenfield and coworkers [4]. Aspirin and *Ginkgo biloba* also have been linked with spontaneous hyphaema [5, 6].

Ocular haemorrhages in warfarinized patients can be sight-threatening events, but often they are clinically benign and resolve without any sequelae. However, they may be the only indication that the patient is at risk for major bleeding episodes linked to over-anticoagulation. A number of studies have shown what amounts to an exponential increase in haemorrhagic complications as the INR increases to >5.0 [7].

Patients on warfarin therapy should be instructed to notice any change in their quality of vision; should any intraocular bleeding be diagnosed by the ophthalmologist, patients require immediate blood work and consultation with their primary care provider.

REFERENCES

- 1 Koehler MP, Sholiton DB. Spontaneous hyphema resulting from warfarin. *Ann Ophthalmol* 1983; 15: 858–9.
- 2 Nunziata RB. Idiopathic spontaneous hyphemas. *Ann Ophthalmol* 1990; 22: 472–4.
- 3 Bodack MI. A warfarin-induced subconjunctival hemorrhage. *Optometry* 2007; 78: 113–8.
- 4 Greenfield DS, Liebmann JM, Ritch R. Hyphema associated with pupillary dilation in a patient with exfoliation glaucoma and warfarin therapy. *Am J Ophthalmol* 1999; 128: 98–100.
- 5 Kageler WV, Moake JL, Garcia CA. Spontaneous hyphema associated with ingestion of aspirin and ethanol. *Am J Ophthalmol* 1976; 82: 631–4.
- 6 Schneider C, Bord C, Misse P, Arnaud B, Schmitt-Bernard CF. Spontaneous hyphema caused by *Ginkgo biloba* extract. *J Fr Ophthalmol* 2002; 25: 731–2.
- 7 Ansell J, Hirsh J, Dalen J, Bussey H, Anderson G, Poller L, Jacobson J, Deykin D, Matchar D. Managing oral anticoagulant therapy. *Chest* 2001; 119: 22S–38S.

RECEIVED

26 February 2008

ACCEPTED

23 May 2008

PUBLISHED *OnlineEarly*

16 July 2008

CORRESPONDENCE

Alessandro Bagnis MD, Clinica Oculistica Università di Genova, Azienda Ospedaliera Universitaria San Martino, Viale Benedetto XV 10, 16132 Genova, Italy.
E-mail: alebagnis@libero.it