Published in final edited form as:

Ophthalmic Surg Lasers Imaging Retina. 2016 January 1; 47(1): 78–80. doi: 10.3928/23258160-20151214-13.

Bilateral Spontaneous Hyphema, Vitreous Hemorrhage and Choroidal Detachment with Concurrent Dabigatran Etxilate Therapy

Kevin Wang^{1,2} and Justis P. Ehlers^{1,3}

¹Ophthalmic Imaging Center, Cole Eye Institute, Cleveland Clinic

²Case Western Reserve School of Medicine

³Vitreoretinal Service, Cole Eye Institute

Abstract

A 79 year old woman was referred for rapid onset of painless bilateral vision loss. Anterior segment exams revealed bilateral spontaneous hyphema and fibrin accumulation. Observation of the posterior chamber by B-scan ultrasound showed vitreous hemorrhage and choroidal detachment bilaterally. No evidence of additional intraocular inflammation was present. Laboratory work-up for hematologic abnormalities was unremarkable. These hemorrhagic events were suspected to be a complication from taking the novel anti-coagulant, dabigatran etexilate. She initially underwent non-surgical therapy, which included immediate cessation of dabigatran, and administration of topical and systemic steroids. The lack of response to medical therapy in the left eye led to surgical treatment of vitreous and persistent subcapsular hemorrhage via pars planar vitrectomy with capsulectomy.

Keywords

Spontaneous hyphema; vitreous hemorrhage; dabigatran

Introduction

Dabigatran etexilate (Pradaxa, Boehringer, Ingelheim Germany) is a competitive thrombin inhibitor that was approved in 2010 for prevention of embolic stroke in patients with atrial fibrillation. In contrast to warfarin, dabigatran does not require frequent laboratory monitoring of clotting status as it does not impact many of the same hematologic parameters. Additionally it is not metabolized by CYP450 resulting in fewer concerns regarding drug-drug and drug-food interactions. However, these benefits also makes the management of dabigatran-induced bleeding complications more challenging. Monitoring anticoagulation status is more difficult in dabigatran patients because necessary tests such as thrombin and ecarin clotting time are often unavailable to clinicians. Also, unlike vitamin K

Corresponding Author: Justis P. Ehlers MD, 9500 Euclid Ave/i32, Cleveland, OH 44195. ehlersj@ccf.org; Phone: 216-636-0183.

Financial Disclosures:

KW: None; **JPE:** Biopogen (C, P), Thrombogenics (C, R), Synergetics (P), Genentech (R), Leica (C), Zeiss (C), Alcon (C);

antagonists for warfarin, reversal agents for dabigatran are not readily available to treat severe hemorrhagic complications. Ocular hemorrhagic complications present unique concerns in dabigatran patients. In this report, we present a case of bilateral spontaneous hyphema, vitreous hemorrhage, and associated choroidal hemorrhages associated with concurrent dabigatran use.

Case

A 79 year old female presented with rapid onset of painless bilateral vision reduction. Previous ocular surgeries included laser iridotomy and phacoemulsification with posterior chamber intraocular lens (PCIOL) implants in both eyes several years prior. Her past medical history was significant for hypertension, congestive heart failure, atrial fibrillation, and coronary artery disease. Oral medications she was taking included dabigatran 150mg twice daily for atrial fibrillation which was initiated within the preceding 12 months.

On presentation visual acuity was 20/400 in the right eye and 20/500 in the left eye. Intraocular pressure was within normal limits. Anterior segment exam revealed hyphema and fibrin accumulation (Figure 1A–B). Although fibrin was present, the predominant cell type present appeared to be red blood cells rather than white blood cells. Visualization of the posterior segment exam of both eyes was limited by vitreous hemorrhage. B-scan ultrasound revealed bilateral vitreous hemorrhage and choroidal detachments. Ultrasound biomicroscopy confirmed well-positioned intraocular lenses with associated intracapsular hemorrhage without iris contact. Laboratory evaluation revealed no hematologic abnormalities. No significant abnormalities were identified. Given the spontaneous bleeding, dabigatran was immediately discontinued in consultation with the patient's cardiologist. Initial treatment included topical prednisolone and atropine. Following minimal response, the patient was also placed on a trial of oral prednisone 40 mg daily with minimal slow response (Figure 1C–D).

Following one month of medical therapy, the right eye experienced slow improvement to 20/150 with moderate persistent hemorrhage and improving choroidals. The left eye worsened to 20/600 with persistent hyphema and vitreous hemorrhage, though the choroidal detachments improved. Given the persistent hemorrhage, the patient underwent pars plana vitrectomy with capsulectomy for vitreous hemorrhage and persistent subcapsular hemorrhage. The retina was unremarkable. The ophthalmic status remained stable without recurrent hemorrhage for approximately 1 month postoperatively and the patient was subsequently lost to follow-up.

Discussion

The emergence of novel anticoagulants, such as dabigatran, may present new challenges and potential unique hemorrhagic complications. In this report, bilateral spontaneous hyphemas, vitreous hemorrhages, and choroidal detachment occur in a patient during concurrent dabigatran use. Even with cessation of medication, the hemorrhage persisted over several weeks with poor clearance. There was minimal response to topical and systemic steroid challenges. Bilateral spontaneous hyphema are extremely rare events often associated with

various anterior chamber abnormalities or ocular trauma [1–4]. In our review of the literature, only one other case of anticoagulant-induced bilateral spontaneous hyphema was identified and it was associated with warfarin use [5]. Rare dabigatran-related ocular hemorrhagic complications have been reported, specifically subconjunctival hemorrhage and choroidal hemorrhage [6, 7].

The absence of a reversal agent for dabigatran-induced bleeding events makes managing complications difficult. While hemodialysis [8, 9] and idarucizumab [10, 11] may be effective methods for treatment, these treatment options are relatively invasive or not readily accessible. Current guidelines for management of dabigatran-induced bleeding only describes general supportive therapies such as transfusions of fresh-frozen plasma or packed red blood cells if necessary [12].

With dabigatran and other direct thrombin inhibitors increasing in use, recognizing their potential role in hemorrhagic complications is critical. In the RE-LY and RE-COVER randomized control trials, the safety and efficacy of dabigatran was compared to warfarin in patients with atrial fibrillation or acute venous thromboembolism [13, 14]. The RE-LY study revealed higher incidences of adverse bleeding events in elderly patients and patients with chronic kidney disease [13]. While most hemorrhagic complications were gastrointestinal or urogenital in origin, intraocular bleeding was observed as a rare event in 0.63% of patients taking dabigatran in the RE-COVER study [14]. Taken together, these studies suggest careful surveillance of concomitant medications and underlying medical conditions are vital to assessing potential risk factors in complex cases.

Acknowledgments

Financial Support: NIH/NEI K23-EY022947-01A1 (**JPE**); Ohio Department of Development TECH-13-059 (**JPE, SKS**); Research to Prevent Blindness (**Cole Eye Institutional**);

References

1. Borne MJ, et al. Juvenile xanthogranuloma of the iris with bilateral spontaneous hyphema. *J Pediatr Ophthalmol Strabismus*. 1996; 33(3):196–7. [PubMed: 8771527]
2. Vijayalakshmi P, et al. Bilateral spontaneous hyphema in juvenile xanthogranuloma. *Indian J Ophthalmol*. 2006; 54(1):45–6. [PubMed: 16531672]
3. Shimada Y, Horiguchi M, Okubo T. Bilateral spontaneous hyphema with uveitis in a young girl. *J Pediatr Ophthalmol Strabismus*. 2004; 41(2):114–5. [PubMed: 15089069]
4. Mason GI, Ferry AP. Bilateral spontaneous hyphema arising from iridic microhemangiomas. *Ann Ophthalmol*. 1979; 11(1):87–91. [PubMed: 420480]
5. Dharmasena A, Watts GM. Bilateral spontaneous hyphaema: case report and review of literature. *J Thromb Thrombolysis*. 2013; 36(3):343–5. [PubMed: 23378149]
6. Nguyen TM, et al. Subconjunctival hemorrhage in a patient on dabigatran (Pradaxa). *Am J Emerg Med*. 2013; 31(2):455e3–5. [PubMed: 23000334]
7. Kang TS, Lord K, Kunjukunju N. Spontaneous choroidal hemorrhage in a patient on dabigatran etexilate (Pradaxa). *Retin Cases Brief Rep*. 2014; 8(3):175–7. [PubMed: 25372432]
8. Chang DN, Dager WE, Chin AI. Removal of dabigatran by hemodialysis. *Am J Kidney Dis*. 2013; 61(3):487–9. [PubMed: 23219111]
9. Wanek MR, et al. Safe use of hemodialysis for dabigatran removal before cardiac surgery. *Ann Pharmacother*. 2012; 46(9):e21. [PubMed: 22872748]
10. Pollack CV Jr, et al. Idarucizumab for Dabigatran Reversal. *N Engl J Med*. 2015

11. Glund S, et al. Safety, tolerability, and efficacy of idarucizumab for the reversal of the anticoagulant effect of dabigatran in healthy male volunteers: a randomised, placebo-controlled, double-blind phase 1 trial. *Lancet*. 2015
12. Wann LS, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (update on dabigatran): a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2011; 57(11): 1330–7. [PubMed: 21324629]
13. Connolly SJ, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009; 361(12):1139–51. [PubMed: 19717844]
14. Schulman S, et al. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med*. 2009; 361(24):2342–52. [PubMed: 19966341]

Figure 1.

Anterior segment photos at initial diagnosis (A, B) and 2 weeks after initial medical treatment (C, D). Prominent contracted fibrin and hyphema are visible in both eyes at presentation (A, B). Following initial medical therapy, fibrin begins to improve but the blood remains 2 weeks later (C, D).