Oral anticoagulation medications, such as aspirin, clopidogrel bisulfate, and warfarin sodium, have been associated with the development of vitreous hemorrhage. While many cases of vitreous hemorrhage may resolve spontaneously, nonclearing vitreous hemorrhage may result in significant visual morbidity and require surgical intervention.

Rivaroxaban is an oral anticoagulant increasingly used in the management of atrial fibrillation. It is an oral factor Xa inhibitor administered in a single daily dose. The use of rivaroxaban has been associated with hemorrhagic complications involving the gastrointestinal, intracranial, and urinary systems. Other factor Xa inhibitors include fondaparinux, apixaban, and edoxaban.

We demonstrate an association between rivaroxaban use and spontaneous vitreous hemorrhage. The risk may be particularly serious during the transition period, when more than 1 anticoagulant could be prescribed.

Report of Cases

Case 1
A man in his mid-70s with a medical history of atrial fibrillation was evaluated for an acute vitreous hemorrhage of his right eye. The patient was in the process of transitioning his atrial fibrillation anticoagulation regimen from warfarin to rivaroxaban. His international normalized ratio was therapeutic. His ocular history was remarkable for a retinal detachment in the right eye, which was repaired by an encircling scleral buckle 40 years prior.

On initial examination, his visual acuity measured 20/80 OD and 20/20 OS. Applanation tonometry measured 22 mm Hg in the right eye and 17 mm Hg in the left eye. His anterior segment was within normal limits except for a well-positioned posterior chamber intraocular lens in each eye. The dilated fundus examination of the right eye was limited by a dense vitreous hemorrhage. Superiorly, an encircling scleral buckle was visible with cryotherapy scarring on the crest of the buckle. The dilated fundus examination of the left eye was within normal limits. B-scan ultrasonography of the right eye revealed a vitreous hemorrhage, posterior vitreous separation, and encircling scleral buckle without evidence of retinal tears or detachment.

Given the development of vitreous hemorrhage, the patient elected to discontinue his warfarin treatment while continuing anticoagulation with rivaroxaban for his atrial fibrillation. One month after presentation, the vitreous hemorrhage largely resolved and his visual acuity improved to 20/20 OD. Clinical examination and fluorescein angiography failed to demonstrate any ocular pathology to account for the acute vitreous hemorrhage. He was followed up for another month with no recurrence of vitreous hemorrhage.

Case 2
A man in his late 70s with a medical history of atrial fibrillation was referred for evaluation of an acute vitreous hemorrhage.
Rhage in the right eye. The onset of hemorrhage occurred as his cardiologist was transitioning his anticoagulation regimen from warfarin to rivaroxaban. At the time of presentation, he was taking both 12.5 mg of warfarin and 20 mg of rivaroxaban daily. His international normalized ratio was therapeutic. His ocular history was remarkable for retinal detachment in both eyes, which was repaired by scleral buckling approximately 20 years prior.

On initial examination, his best-corrected visual acuity measured 20/30 OD and 20/25 OS. Applanation tonometry measured 13 mm Hg in the right eye and 15 mm Hg in the left eye. His anterior segment examination was remarkable for subconjunctival hemorrhage temporally in the right eye and a well-positioned posterior chamber intraocular lens in each eye. The posterior segment examination of the right eye revealed a vitreous hemorrhage inferiorly and an encircling scleral buckle with cryotherapy superotemporally. A posterior segment examination of the left eye was notable for an encircling scleral buckle and cryotherapy scars. B-scan ultrasonography of the right eye demonstrated a vitreous hemorrhage inferiorly, posterior vitreous separation, and an encircling scleral buckle without evidence of retinal tears or detachment.

The patient discontinued warfarin treatment but continued rivaroxaban anticoagulation for his atrial fibrillation. One month later, his visual acuity improved to 20/20 OD and the vitreous hemorrhage largely resolved. Fluorescein angiography of the right eye demonstrated no evidence of neovascularization. The patient was followed up for 3 months without any recurrence of vitreous hemorrhage.

Case 3
A man in his mid-80s with a medical history of coronary atherosclerosis and atrial fibrillation was referred for evaluation of a vitreous hemorrhage of the right eye. The patient’s cardiologist had previously initiated 20 mg of rivaroxaban anticoagulation once daily for atrial fibrillation while maintaining 75 mg of clopidogrel anticoagulation every other day for coronary artery disease. The patient’s international normalized ratio was therapeutic.

On initial examination, his visual acuity measured 20/30 OD and 20/40 OS. Applanation tonometry measured 19 mm Hg OD and 10 mm Hg OS. His anterior segment examination was significant for a well-positioned posterior chamber intraocular lens in the right eye and 2+ nuclear sclerosis in the left eye. The posterior segment examination of the right eye was notable for the vitreous hemorrhage precluding a clear view posteriorly. A dilated fundus examination of the left eye was remarkable only for a posterior vitreous separation. B-scan ultrasonography was performed in the right eye, which demonstrated a vitreous hemorrhage, posterior vitreous separation, and no evidence of any retinal tears or detachment.

The patient’s cardiologist was notified of the vitreous hemorrhage and discontinued clopidogrel treatment while maintaining anticoagulation with rivaroxaban. Two months after presentation, the vitreous hemorrhage mostly resolved and visual acuity improved to 20/25 OD. Clinical examination did not demonstrate any evidence of neovascularization. There was no recurrence of vitreous hemorrhage at his last follow-up, 5 months after his initial presentation.

Conclusions
Rivaroxaban anticoagulation may be associated with spontaneous vitreous hemorrhage. In all cases, an acute vitreous hemorrhage occurred shortly after rivaroxaban treatment was initiated. The vitreous hemorrhage resolved spontaneously in all cases and subsequent clinical and angiographic assessments did not reveal any ocular pathology to account for the hemorrhage. Our case series was inherently limited by its small size. Larger-scale studies will be instructive.

Rivaroxaban anticoagulation has been increasing in popularity and it is often used as a replacement for warfarin anticoagulation in the management of atrial fibrillation. Compared with warfarin, rivaroxaban offers distinct advantages in dosage and monitoring. Warfarin requires routine coagulation monitoring and dose adjustments to optimize and maintain anticoagulation. In contrast, rivaroxaban has consistent and predictable pharmacokinetics and is administered as a standard dosage without the need for coagulation monitoring or dose adjustments. In 2014, rivaroxaban accounted for approximately $1.5 billion in sales, which represented a 76% increase compared with 2013.

As more patients with atrial fibrillation are transitioned from warfarin to rivaroxaban anticoagulation, ophthalmologists should be cognizant of the potential risk of vitreous hemorrhage.
Drafting of the manuscript: Both authors. Critical revision of the manuscript for important intellectual content: Hwang. Administrative, technical, or material support: Both authors. Study supervision: Hwang.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

REFERENCES