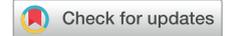


# Combined left atrial appendage closure and ablation in a patient with hemophilia B, paroxysmal atrial fibrillation, and transient ischemic attack



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## Introduction

Hemophilia B is an X-linked hereditary bleeding disorder characterized by deficiency in factor IX. Affected individuals may experience either spontaneous or procedure-related bleeding but are also paradoxically at risk for thrombotic events.<sup>1</sup> Owing to reduced mortality from bleeding and viral infections, affected individuals now have a longer life expectancy.<sup>2</sup> Hemophilia-affected patients may present with age-related cardiovascular diseases such as atrial fibrillation (AF) and ischemic heart disease, much like the general population. These conditions pose a challenge for physicians because guidelines have not been published and anticoagulation is generally contraindicated in these individuals. We present a patient with hemophilia B, symptomatic paroxysmal AF, and transient ischemic attack (TIA) where pulmonary vein isolation (PVI) and left atrial appendage (LAA) occlusion were performed with replacement factor IX and short-term warfarin therapy.

## Case report

A 60-year-old woman with hereditary factor IX deficiency, paroxysmal AF, and sick sinus syndrome status post pacemaker implantation was seen in the office. She had a history of prolonged bleeding as a child for 12 days following a tooth extraction. She reported a recent episode of amaurosis fugax, consistent with a TIA. She had been followed for paroxysmal AF, with daily palpitations that had not been adequately controlled with antiarrhythmic medication. Her pacemaker was a St Jude Identity DR pacemaker, which corroborated daily episodes of AF lasting minutes to occasionally hours,

with an overall burden of 3%. The atrial sensitivity was set at 0.5 mV; atrial sensing was 2.7–4.6 mV and atrial threshold was 0.75 V at 0.4 ms. The mode switch detection rate was 180 beats/min, and AF suppression was programmed off.

The embolic event gave her a CHADS<sub>2</sub>-VASc score of 3, putting her at a significant risk for recurrent cerebral events. Given her factor IX deficiency and susceptibility for bleeding, long-term anticoagulation was not an option. After discussion with the patient and consultation with a hematologic specialist, the decision was made to perform a combined LAA occlusion using the Watchman device (Boston Scientific, Marlborough, MA) and PVI with the use of perioperative recombinant factor IX.

The patient's baseline factor activity level was 15%, consistent with mild factor IX deficiency. Replacement was calculated to achieve an activity level of 30% to safely maintain her on warfarin. The patient started warfarin 4 days prior to the procedure, with a goal international normalized ratio (INR) of 2–3. Factor IX was infused at 20 units/kg every other day starting at preoperative day 3. Preoperatively, factor IX was infused 82 units/kg 30 minutes prior to the procedure. On the day of the procedure, the INR was 1.76. In the lab, heparin bolus and infusion prior to transseptal puncture was performed per the usual protocol, with a goal activated clotting time of 350–400 s. The patient's presenting rhythm was sinus. Occlusion of the LAA was performed first, followed by PVI. Successful Watchman placement was confirmed without residual flow. PVI was then performed with wide antral lesion sets using radiofrequency ablation, the CARTO mapping system (Biosense Webster, Irvine, CA), and an irrigated force sensing ablation catheter. Entrance and exit block was confirmed in all veins. Transseptal dwell time was 3 hours 18 minutes. At the conclusion of the case, protamine was administered to reverse the heparin effect, and adequate hemostasis was achieved. On postoperative day 1, the patient received 67 units/kg factor IX, then resumed every-other-day dosing at 20 units/kg.

We performed follow-up transesophageal echocardiogram at an abbreviated interval of 30 days, which demonstrated a

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## KEY TEACHING POINTS

- Patients with hemophilia are living longer and represent a small but growing pool of patients at risk for atrial fibrillation. While long-term anticoagulation is contraindicated in this group, these patients still carry risk for thrombotic events associated with atrial fibrillation.
- The use of standardized factor replacement protocols that can normalize levels of the deficient factor and temporary use of intraprocedural and periprocedural anticoagulation are feasible. In appropriate patients, this may allow for safe ablation of atrial fibrillation, as well as left atrial appendage closure in patients with high long-term risk for thromboembolism.
- Left atrial ablation and appendage closure may be safely performed with concomitant factor replacement and warfarin treatment in patients with hemophilia B.

well-sealed device with no leak. Recombinant factor IX and warfarin were discontinued at this time. Antiplatelet medications were rationalized at this point but it was felt her bleeding risk was too high. At 6-month follow-up she was doing well, with no complications, and pacemaker interrogation confirmed no further episodes of AF.

## Discussion

Traditional concepts of hemophilia protecting against thromboembolism are being challenged with the growing number of aging hemophilia patients.<sup>1</sup> The availability of recombinant factor replacement has increased the life expectancy of hemophilia patients, which also increases the lifetime likelihood of developing AF.<sup>2</sup> Our hemophilic patient suffered a TIA in the setting of paroxysmal AF, despite minimal traditional risk factors. Without modifying her risk, the likelihood of a recurrent thromboembolic event was high. Long-term oral anticoagulation is contraindicated in factor IX deficiency owing to patients' bleeding propensity, regardless of factor level. While recombinant factor replacement during oral anticoagulation therapy is possible, the frequency of intravenous infusion and cost make long-term use prohibitive.

An alternative approach to management of thromboembolic risk owing to AF in hemophilia may be an LAA closure. This approach has been previously reported in hemophilia A.<sup>3</sup> As the majority of emboli in AF emanate from the LAA, closure may provide similar protection to anticoagulation in patients who are poor candidates for long-term anticoagulation. The Watchman device has been found to provide comparable long-term stroke risk reduction to warfarin in

patients with AF.<sup>4,5</sup> Although the long-term stroke reduction associated with LAA occlusion is unknown in patients with hemophilia, our patient did not have viable alternatives to reducing her risk.

US guidelines recommend 45 days of warfarin post Watchman placement; the consensus statement on AF recommends 2 months of anticoagulation postablation.<sup>6</sup> The postprocedural period following both AF ablation and Watchman placement may be a time of high embolic risk, owing to tissue damage from ablation, an inflammatory milieu, and the presence of the Watchman device that has not yet undergone complete endothelialization. Patients that discontinue anticoagulation in the early postablation period appear to have an elevated risk of stroke.<sup>7</sup> However, there are no randomized studies comparing postprocedural anticoagulation regimens, and the post-AF ablation guidelines are based on consensus opinion. Given the challenges of frequent factor replacement, the patient's concerns about anticoagulation, and the costs involved, we decided on a 30-treatment protocol with factor IX and warfarin. Factor IX was dosed based on the patient's factor IX activity, with warfarin treatment for a goal INR of 2–2.5. While this approach was safely pursued in this case, more experience is necessary to determine the optimal postablation anticoagulation duration.

Given the patient's symptomatic paroxysmal AF, we opted to pursue PVI at the same time as LAA closure. The single procedure would achieve a 2-fold endpoint, while exposing her to the risks of anticoagulation only once. AF ablation in hemophilia has been previously reported.<sup>8</sup> We considered the safety of combined ablation and appendage closure with the knowledge that embolization of the Watchman device following combined AF ablation and LAA closure has been reported.<sup>9</sup> As our patient was primarily in sinus rhythm with an AF burden of 3%, termination of persistent AF to normal sinus rhythm, which might alter atrial contractility, was not a primary concern. We placed the Watchman device prior to ablation to avoid edema that might alter the anatomy of the LAA ostium, possibly leading to a change in Watchman position as the edema resolved.

This proved a successful and safe strategy for our patient with hemophilia, AF, and TIA requiring management of thromboembolic risk. Further studies in the small but growing group of patients with hemophilia and AF are needed to determine how to best treat this complex combination of conditions.

## Conclusion

In patients with hemophilia and AF, short-term factor replacement and warfarin therapy allows for correction of the coagulation cascade and performance of left atrial ablation and appendage closure using standard anticoagulation protocols. This may be a safe alternative option for patients with AF and hemophilia with symptomatic AF and at high risk of stroke.

## References

1. Ritchie B, Woodman RC, Poon MC. Deep venous thrombosis in hemophilia A. *Am J Med* 1992;93:699–700.

2. Franchini M, Mannucci PM. Co-morbidities and quality of life in elderly persons with haemophilia. *Br J Haematol* 2010;148:522–533.
3. Cheung VT, Hunter RJ, Ginks MR, Schilling RJ, Earley MJ, Bowles L. Management of thromboembolic risk in persons with haemophilia and atrial fibrillation: is left atrial appendage occlusion the answer for those at high risk? *Haemophilia* 2013;19:e84–e86.
4. Reddy VY, Sievert H, Halperin J, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation. A randomized clinical trial. *JAMA* 2014; 312:1988–1998.
5. Reddy VY, Doshi SK, Kar S, et al. 5-Year outcomes after left atrial appendage closure: from the PREVAIL and PROTECT AF Trials. *J Am Coll Cardiol* 2017; 70:2964–2975.
6. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOL-AECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm* 2017;14:e275–e444.
7. Noseworthy P, Yao X, Deshmukh A, et al. Patterns of anticoagulation use and cardioembolic risk after catheter ablation for atrial fibrillation. *J Am Heart Assoc* 2015;4:9.
8. Lin J, Iqic P, Hoffmayer K, Field M. Patients with hemophilia: unique challenges for atrial fibrillation management. *HeartRhythm Case Rep* 2015; 1:445–448.
9. Gabriels J, Beldner S, Khan M, Zeitlin J, Jadonath R, Patel A. Embolization of Watchman device following a hybrid radiofrequency ablation of atrial fibrillation and Watchman implantation procedure. *JCE* 2017;28:835–836.