Dabigatran-Induced Spontaneous Hemopericardium and Cardiac Tamponade

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Four novel oral anticoagulant agents are currently available for the prevention and treatment of thromboembolic events in patients with nonvalvular atrial fibrillation. We present an unusual case of spontaneous hemopericardium and tamponade in an 87-year-old man with atrial fibrillation who was taking one such agent, dabigatran, as thromboprophylaxis.

Our case highlights both a rare bleeding complication of dabigatran use and the effectiveness of idarucizumab, its newly approved reversal agent. Especially in elderly patients, we recommend that clinicians evaluate risk factors, closely monitor patient status, and consider alternatives to the newer anticoagulants when the risk of bleeding is high. **(Tex Heart Inst J 2017;44(5):370-2)**

Dabigatran, a novel oral anticoagulant, was approved by the United States Food and Drug Administration (FDA) in 2010 for the prevention of embolic events in patients with nonvalvular atrial fibrillation (AF).[1] Hemopericardium has rarely been described in association with the use of oral anticoagulants, including the novel oral anticoagulant agents. We report a case of spontaneous hemopericardium during dabigatran therapy and its reversal with use of the antibody fragment idarucizumab. To our knowledge, this is only the second report of dabigatran-induced spontaneous hemopericardium in the absence of predisposing factors.[2]

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Case Report

In April 2016, an 87-year-old man with well-controlled hypertension and dyslipidemia was admitted to the hospital with worsening dyspnea on exertion. Two months earlier, he had been prescribed dabigatran (150 mg, twice daily) and metoprolol as therapy for AF of unknown duration. A transthoracic echocardiogram (TTE) at that time had shown nothing notable. He subsequently developed progressive edema, renal insufficiency, hypotension, and tachycardia. His medications included dabigatran, furosemide, metolazone, and metoprolol.

His vital signs upon admission were as follows: blood pressure, 90/50 mmHg; heart rate, 112 beats/min; respiratory rate, 18 breaths/min; and oxygen saturation, 95% on room air. His body weight was 81.6 kg (body mass index, 25.83 kg/m^2). He had jugular venous distention with a positive Kussmaul sign and bilateral, pitting lower-extremity edema. No other cardiac or respiratory findings were noteworthy.

Laboratory test results included new anemia (hemoglobin, 9.7 g/dL) and acute kidney injury (increase in creatinine, from 1.0 to 1.9 mg/dL). The estimated creatinine clearance (CrCl) was 33 mL/min. Results of coagulation studies were normal. An electrocardiogram revealed AF with a ventricular rate of 110 beats/min and new low voltage in all leads (Fig. 1). A TTE showed a large pericardial effusion with tamponade physiology and diastolic compression of the right ventricle (Fig. 2A), a severely dilated inferior vena cava without inspiratory collapse (Fig. 2B), and respiratory variation at the tricuspid inflow with >25% increase during inspiration (Fig. 2C). Idarucizumab was administered, after which emergency pericardiocentesis yielded 750 cc of hemorrhagic pericardial fluid. Fluid samples evaluated by gram stain, culture, and cytology were negative. The patient reported immediate resolution of his symptoms. Serial TTEs revealed no reaccumulation of fluid (Fig. 3). The patient was discharged from the hospital in stable condition, without the need for anticoagulation.
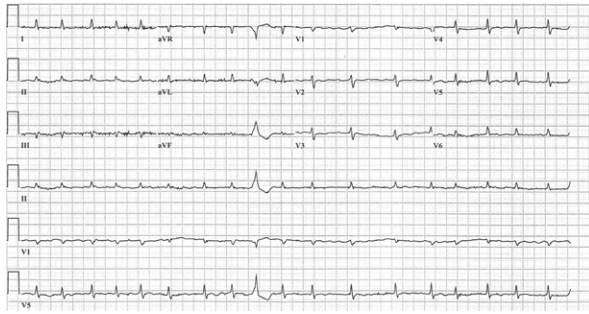
Fig. 1 Electrocardiogram shows atrial fibrillation and low voltage.
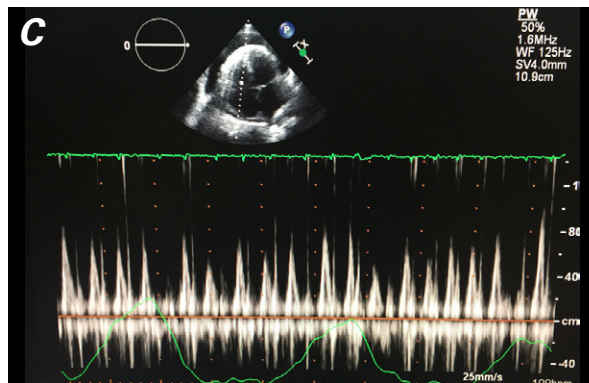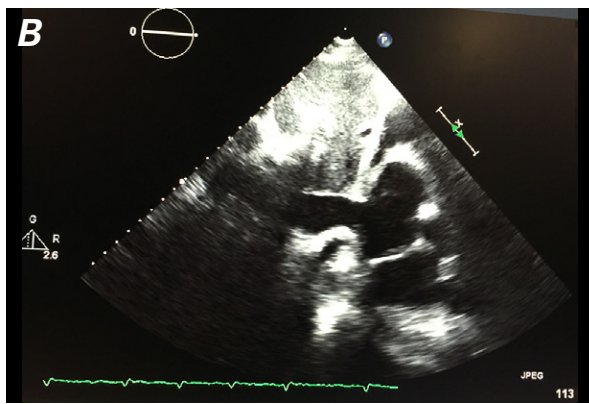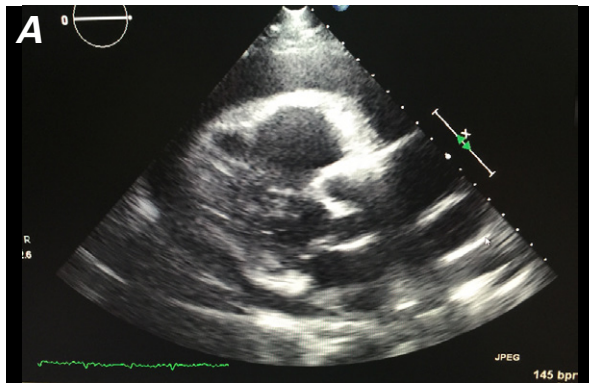
Fig. 2 Transthoracic echocardiograms show A) a large pericardial effusion and diastolic compression of the right ventricle (parasternal long-axis view), and B) a severely dilated inferior vena cava without inspiratory collapse (subcostal view). C) Pulsed-wave Doppler shows respiratory variation at the tricuspid inflow with >25% increase during inspiration (apical 4-chamber view),
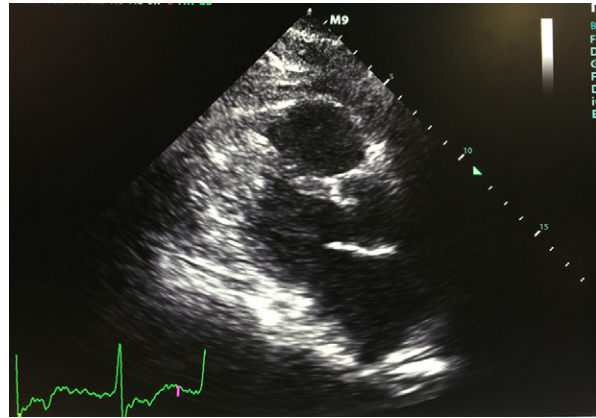
Fig. 3 Transthoracic echocardiogram (parasternal long-axis view) shows resolution of the pericardial effusion.

Discussion

Atrial fibrillation is the most prevalent cardiac arrhythmia in the U.S., affecting an estimated 5.2 million Americans in 2010.[3] More than 80% of these patients have an indication for oral anticoagulation[4] to reduce the risk of stroke. The novel oral anticoagulants include dabigatran, which inhibits thrombin; and rivaroxaban, apixaban, and edoxaban, which inhibit factor Xa. These agents are as effective as warfarin in preventing the primary endpoints of stroke and systemic embolism and lowering the risk of major bleeding.[1,5,6] Of importance, these new agents have reduced the rate of intracranial hemorrhage in comparison with vitamin K antagonists[1,5,7,8] but are consistently associated with a higher risk of gastrointestinal bleeding.[7-9]

Our report highlights a rare case of dabigatran-induced hemopericardium and tamponade in a patient who had no clinical evidence of pericarditis, trauma, or renal failure.[10] Spontaneous hemopericardium without tamponade has occurred in patients who took dabigatran,[2] rivaroxaban,[11] and apixaban.[12] Warfarin-associated spontaneous hemopericardium is very rare, and reported cases have been in the context of coagulopathy,[13-16] cardiac surgery,[17] or pericarditis.[18,19]

Several cases of dabigatran-induced hemopericardium have been reported.[2,10,20,21] Dy and Shiltz[10] reported 2 such cases, with cardiac tamponade in the presence of acute renal failure. Both patients had a CrCl of <30 mL/min. Because approximately 80% of the drug is cleared renally, the FDA recommends that dabigatran doses be decreased to 75 mg twice daily, to maintain a CrCl of 15 to 30 mL/min. Our patient had a CrCl >30 mL/min on presentation, so it is unlikely that impaired dabigatran metabolism contributed to his hemopericardium. In one randomized trial,[9] a dabigatran dose of 110 mg, twice daily, was associated with a lower risk of bleeding than that with warfarin use in patients <75 years of age, and it yielded a similar risk of bleeding in those >75

years old. Conversely, standard dabigatran dosing of 150 mg, twice daily, in patients >75 years old was associated with a trend toward a higher risk of bleeding. Our 87-year-old patient was taking the higher dose, because dabigatran is not available in the 110-mg formulation in the U.S. Caution should be exercised in initiating elderly patients on the higher dose of dabigatran, and the use of an alternative agent might be safer for them.

In October 2016, the FDA approved an antibody fragment, idarucizumab, for dabigatran reversal.[22] There are no FDA-approved antidotes or reversal agents for factor Xa inhibitors. We gave our patient idarucizumab before pericardiocentesis, and we noted no further clinical bleeding or fluid accumulation.

Spontaneous hemopericardium can occur even with appropriate use and dosing of novel oral anticoagulant agents, especially in elderly patients. We recommend that clinicians evaluate patient age, bleeding and fall risks, and renal function before prescribing the newer agents, and that they consider alternatives when the risk of bleeding is high.

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