

Case Report

Cardiac Tamponade Caused by Atrial Lead Perforation or by Spontaneous Hemopericardium in an Edoxaban User

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SUMMARY

Direct oral anticoagulants (DOACs) are widely used to prevent thromboembolic complications in of atrial fibrillation (AF). With aging, symptomatic bradyarrhythmias occurred in a substantial portion of elderly and a permanent pacemaker (PPM) was a curative therapy. A rare but fatal complication of hemopericardium owing to either DOACs or late PPM lead perforation has been documented. However, both etiologies were suspected to happen in a person was not reported before. We introduced a 79-year-old man who presented to our hospital with 2-day progressive dyspnea. His past medical history was significant for AF with use of edoxaban and sick sinus syndrome with a PPM 4 months before admission. He was afebrile and his chest X-ray showed cardiomegaly. Computed tomography revealed massive pericardial effusion and PPM lead perforation into the pericardium space was highly suspected. Since shock developed, emergent pericardiocentesis was administered for cardiac tamponade. The etiology of hemopericardium favored DOACs-related because there was no evidence of other common causes and surgical findings. He was event-free without the use of DOACs in the following one year. It is crucial to diagnose and treat cardiac tamponade promptly in the elder patients with DOACs and implanted a PPM.

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1. Introduction

Direct oral anticoagulants (DOACs), including factor II inhibitor dabigatran, and factor Xa inhibitor apixaban, rivaroxaban, and edoxaban, have been marketed in Taiwan for more than 8 years. DOACs not only provided better outcomes on stroke prevention in patients with non-valvular AF, but reduced bleeding risk, especially in Asians.^{1–4} In addition, DOACs are also effective on thromboembolic events prevention and treatment, such as pulmonary embolism, and deep vein thrombosis.^{5,6} With wide usage of DOACs, more DOACs related complications and safety issues were encountered and discussed.⁷ Hemopericardium related cardiac tamponade is a rare life-threatening complication along with DOACs that required emergent pericardiocentesis to save life.^{8–11} However, hemopericardium caused by late pacemaker lead perforation to pericardium is also a rare complication in patients with pacemaker implantation.¹² A 68-year-old female patient with AF experiencing impending tamponade 2 days after an implantable cardioverter defibrillator implantation without interruption of rivaroxaban had been reported.¹³ To our best knowledge, hemopericardium developed in edoxaban users implanted a permanent pacemaker (PPM) was not reported before.

2. Case report

A 79-year-old man with hypertension, stage 3 chronic kidney disease, and coronary artery disease presented to our emergency department due to worsening dyspnea, which developed within 2 days. Four months before, he was given edoxaban (30 mg, once daily) and amiodarone (200 mg, once daily) for new-onset non-valvular paroxysmal atrial fibrillation, based on a calculated CHA₂DS₂-VASc score of 4 (hypertension, age, and vascular disease) and underwent PPM (Medtronic Astra XT DR MRI X2DR01) implantation for sick sinus syndrome. Both leads of right atrium (RA) and right ventricle (RV) were screw-in leads. At the time of initiation of edoxaban, the patient's serum creatinine level and glomerular filtration rate were 1.91 mg/dL and 34.2 mL/min/1.73 m², respectively. His vital signs were blood pressure 82/60 mmHg, AF with ventricular response rate 83 beats/min, temperature 36 °C, and respiratory rate 20/min. He was in mild respiratory distress. Physical examination showed jugular venous distension and distant heart sounds. Initial workup revealed increased international normalized ratio (INR) as 1.55, anemia (hemoglobin 9.0 g/dL, which was 13.8 g/dL four months ago), and worsened renal function (creatinine 2.6 mg/dL). His electrocardiogram showed AF. Chest X-ray disclosed enlarged cardiac size as a water bottle sign, a pacemaker, and leads of a pacemaker (Figure 1). Chest computed tomography (CT) revealed massive pericardial effusion and the tip of one lead in the RA very close to the

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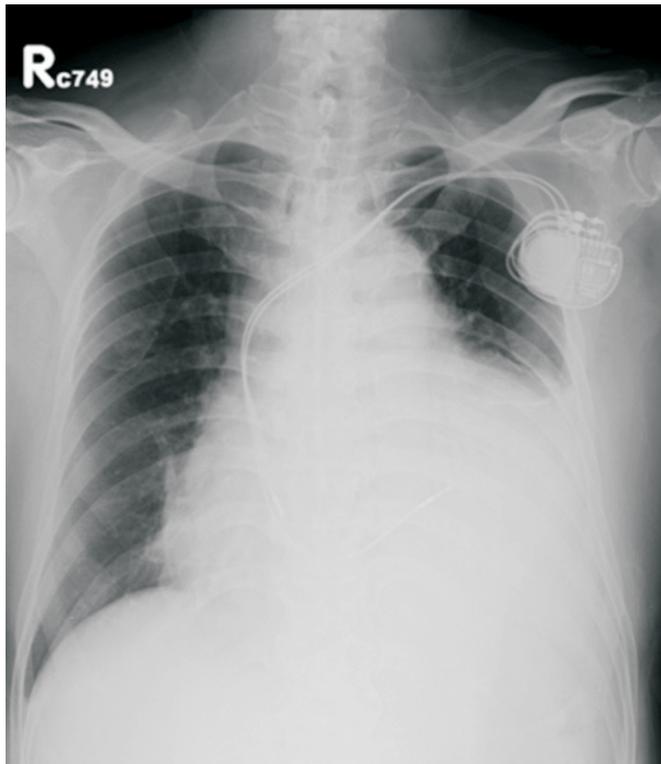


Figure 1. Chest radiography shows cardiomegaly with a water bottle sign and a pacemaker.

pericardium (Figure 2). Diastolic collapse of the RA was shown by echocardiography. Abdomen echogram also showed liver congestion. Impending cardiac tamponade was diagnosed, and cardiogenic shock complicated with acute kidney injury was also impressed. Emergent pericardiocentesis was performed. After drainage of more than 2000 ml bloody fluid, his hemodynamics and symptoms improved quickly. Hemoglobin level of pericardial effusion was 5.2 g/dL and the ratio of hemoglobin between pericardial effusion and plasma was 0.58. Hemopericardium was confirmed. There was no evidence of cancer, infection, or autoimmune disease. After pericardiocentesis, transesophageal echocardiography demonstrated fluid accumulation around RA lead than the other place. Electrophysiological parameters of PPM including impedance and pacing threshold were within normal range in both RA lead and RV lead. Subsequent three-D reconstruction image of cardiac CT was done, and the radiologist described that the RA lead was outside of RA wall with the length of 7 mm protruding to the epicardial fat and mild hemopericardium evenly distributed in pericardial space. However, surgical intervention disclosed abundant epicardial fat surrounding on epicardium of RA but no obvious evidence of lead-related cardiac rupture was observed. Thus, the etiology of hemopericardium was highly suspected edoxaban related. We withheld edoxaban and he was discharged smoothly.

3. Discussion

DOACs may cause a life-threatening situation that physicians should make diagnosis properly and administer treatment promptly. In previous case reports and systemic reviews, dabigatran, apixaban, rivaroxaban and edoxaban had been reported to be associated with hemopericardium, and risk factors included old age, male gender, co-morbidity with hypertension, drug-drug interactions, elevated INR, and impaired renal function.⁸⁻¹¹ Some of these patients were

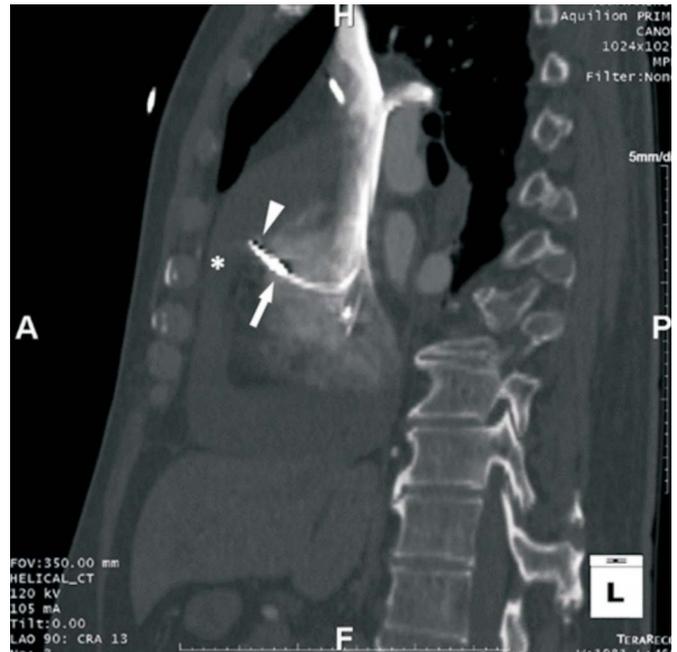


Figure 2. Reconstruction CT demonstrates massive pericardial effusion (*) with a water bottle sign and the tip of right atrial lead (arrow) outside RA wall (arrowhead).

asked to withdrawal DOACs after emergent pericardiocentesis.

It's important to differentiate the etiology of hemopericardium in our patient. According to the literature review, pacemaker leads dislocation also can cause hemopericardium, whereas late pacemaker-related complications, including hemopericardium, are more difficult to identify. Common etiologies including infection, malignancy, autoimmune disease, myocardial infarction related mechanical complication, aortic dissection, or trauma, which contributes to pericardial effusion, were excluded, and we had to figure out whether DOACs or PPM leads-related perforation resulted in hemopericardium. Initially, the chest X ray and the first time CT implied the tip of RA lead very close to the pericardium. Electrophysiological parameters of a pacemaker, including impedance and pacing threshold, provide limited information to detect leads perforation. Normal parameters do not exclude a perforation because most of the electrode may contact with the atrial myocardium resulting in no change in the lead parameters.¹⁴ Besides, screw leads is an independent predictor of a perforation.¹⁵ Thus, three D reconstruction cardiac CT image showed that the RA lead perforation to pericardium was highly suspected. It is important to balance the pros and cons of medical treatment and surgical intervention. After discussing with a heart team, we decided to operate because of the low surgical risk of the patient by EURO score.¹⁶ However, no evidence of PPM lead perforation to the pericardium was found during the operation. The discrepancy of image and surgery result may be explained by the RA lead penetrated the myocardium and the tip was within epicardial fat. In the literature review, unrecognized asymptomatic perforation of PPM or implantable cardiac defibrillator, especially atrial lead, was a common phenomenon on CT images.¹⁷ Hence, in our patient, edoxaban induced hemopericardium complicated with impending cardiac tamponade was favored.

Stroke prevention in this patient is very crucial, but should we consider resuming DOACs or implanting the left atrial appendage (LAA) occlusion? Once DOACs-related major bleeding was diagnosed, he/she had to stop anticoagulation completely and be exposed to the risk of thromboembolic events incidentally. Restarting

of DOACs after major bleeding events is debated. In the patients who had contraindication to long-term anticoagulation for AF, percutaneous LAA occlusion may be considered as Class of Recommendation IIb.¹⁸ Thus, we withheld DOACs in this patient because of significant bleeding risk and potential for recurrent hemopericardium. He was event-free in the following year.

In the elder society, the prevalent rate of AF that requires DOACs treatment and cardiac arrhythmias that need PPM implantation is growing. However, the rare complication of hemopericardium caused by the above events is fatal to the elderly, whose organ function may be poorly preserved. The mechanisms by which hemopericardium with DOAC were related to renal insufficiency and drug-drug interaction. The DOACs concentrations would accumulate in renal dysfunction and concomitant use of amiodarone by inhibition of P-glycoprotein/ABC11 metabolism in edoxaban and P-glycoprotein inhibitors/CYP3A4 in rivaroxaban and apixaban.^{19–21} Prompt diagnosis and emergent pericardiocentesis are critical for the patient. Besides, surgical risk should be carefully evaluated if suspected PPM lead perforation to the pericardium. We should take more attention to patients who have permanent pacemaker implantation in DOACs treatment, especially in the elderly.

Disclosure

To the best of our knowledge, the named authors have no conflict of interest, financial or otherwise.

References

- Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361:1139–1151.
- Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011;365:981–992.
- Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365:883–891.
- Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2013;369:2093–2104.
- Büller HR, Prins MH, Lensin AW, et al. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. *N Engl J Med*. 2012;366:1287–1297.
- Bauersachs R, Berkowitz SD, Brenner B, et al. Oral rivaroxaban for symptomatic venous thromboembolism. *N Engl J Med*. 2010;363:2499–2510.
- Villines TC, Peacock WF. Safety of direct oral anticoagulants: Insights from postmarketing studies. *Am J Med*. 2016;129:S41–S46.
- Asad ZUA, Ijaz SH, Chaudhary AMD, et al. Hemorrhagic cardiac tamponade associated with apixaban: A case report and systematic review of literature. *Cardiovasc Revasc Med*. 2019;20:15–20.
- Jelani QU, Gordon R, Schussheim A. Dabigatran-induced spontaneous hemopericardium and cardiac tamponade. *Tex Heart Inst J*. 2017;44:370–372.
- Menendez D, Michel J. Hemopericardium with tamponade following rivaroxaban administration and its attenuation by CYP3A4 inhibitors. *Proc (Bayl Univ Med Cent)*. 2016;29:414–415.
- Tsai TY, Leu HB, Lo LW, et al. Spontaneous hemopericardium complicated with hemothorax in a patient receiving edoxaban therapy: A case report. *Acta Cardiol Sin*. 2019;35:342–344.
- Refaat MM, Hashash JG, Shalaby AA. Late perforation by cardiac implantable electronic device leads: Clinical presentation, diagnostic clues, and management. *Clin Cardiol*. 2010;33:466–475.
- Tsai CT, Liao JN, Chao TF, et al. Uninterrupted non-vitamin k antagonist oral anticoagulants during implantation of cardiac implantable electronic devices in patients with atrial fibrillation. *J Chin Med Assoc*. 2019;82:256–259.
- Sadamatsu K. Complication of pacemaker implantation: An atrial lead perforation. In: Das MK, ed. *Modern Pacemakers - Present and Future*. 2011:333–342.
- Mahapatra S, Bybee KA, Bunch TJ, et al. Incidence and predictors of cardiac perforation after permanent pacemaker placement. *Heart Rhythm*. 2005;2:907–911.
- Nashef SA, Roques F, Michel P, et al. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg*. 1999;16:9–13.
- Hirschl DA, Jain VR, Spindola-Franco H, et al. Prevalence and characterization of asymptomatic pacemaker and ICD lead perforation on CT. *Pacing Clin Electrophysiol*. 2007;30:28–32.
- January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2019;74:104–132.
- Steffel J, Giugliano RP, Braunwald E, et al. Edoxaban vs. warfarin in patients with atrial fibrillation on amiodarone: A subgroup analysis of the engage AF-TIMI 48 trial. *Eur Heart J*. 2015;36:2239–2245.
- Vranckx P, Valgimigli M, Heidebuchel H. The significance of drug-drug and drug-food interactions of oral anticoagulation. *Arrhythm Electrophysiol Rev*. 2018;7:55–61.
- Conen D. Edoxaban and amiodarone: Interactions on multiple levels. *Eur Heart J*. 2015;36:2210–2211.