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Case Report

Use of idarucizumab for dabigatran reversal in cardiac tamponade during atrial fibrillation ablation: A case report

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ABSTRACT

It is known that the efficacy of catheter ablation for atrial fibrillation (AF) is high, but cardiac tamponade may occur in 1–2% cases. Even in such cases, fatal condition can be avoided by appropriate drainage, but reversal of anticoagulation therapy might also be necessary. Here, we report a case of use of idarucizumab for cardiac tamponade during AF ablation. Although the drainage with pericardial centesis should be selected, we could not perform because echo free space was too thin at least at the precordial or apical side of the ventricle. Fortunately, dabigatran reversal by idarucizumab suppressed cardiac tamponade progress and the patient recovered without undergoing any invasive procedures. The pericardial drainage must be the principal therapy for cardiac tamponade, but reversal of anticoagulant might be helpful for patients' recovery. It might be thought that dabigatran, the only direct oral anticoagulant with a specific reversal agent, should be the safest choice in case of risk for bleeding complications such as AF ablation.

<**Learning objective:** Cardiac tamponade is one of the complications of catheter ablation for atrial fibrillation (AF). In such cases, fatal condition can be avoided by appropriate drainage, but reversal of anticoagulation therapy might be necessary. Drainage with pericardial centesis was not selected because echo free space was too thin. Dabigatran reversal by idarucizumab suppressed cardiac tamponade progress. It was thought that dabigatran would be the safest choice in case of bleeding complications during AF ablation.>

Introduction

Pulmonary vein isolation (PVI) has become the most popular choice for the treatment of atrial fibrillation (AF) [1]. While the efficacy of catheter ablation is high, cardiac tamponade may occur in 1%–2% cases [2]. Even in such cases, fatalities can be avoided by appropriate drainage, however, reversal of anticoagulation therapy may be necessary as it is usually uninterrupted to avoid cerebral infarction [3]. We employed periprocedual anticoagulation with uninterrupted dabigatran, shown to be a superior protocol by the RE-CIRCUIT trial [4]. We also prepared idarucizumab, a humanized antibody recombinant that targets dabigatran, for emergent reversal of dabigatran. Here, we describe a case of cardiac tamponade during AF ablation successfully recovered by using idarucizumab to reverse the anticoagulant effect of dabigatran.

Case report

A 72-year-old male with symptomatic paroxysmal AF was scheduled to undergo a PVI procedure. His body weight was 64.6 kg and serum creatinine was 1.09 mg/dL, with creatinine clearance calculated as 55.45 mL/min. His CHA_2DS_2-VASc for Atrial Fibrillation Stroke Risk score was 1 point. Periprocedual anticoagulation using dabigatran etexilate 150 mg bid was prescribed for the 12 weeks preceding the PVI procedure. On the day of the procedure, the patient took 150 mg of dabigatran in the morning, approximately 5 h prior to venous access for the PVI procedure. The

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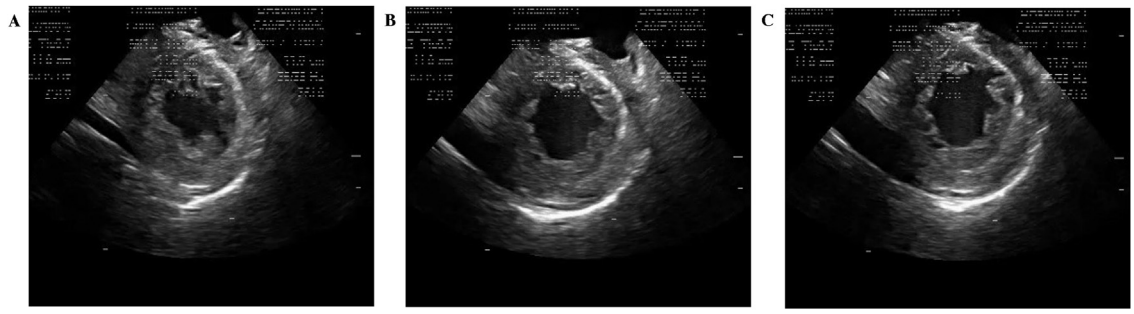

Fig. 1. Time course of changes to the echo-free space. Changes in pericardial effusion during atrial fibrillation (AF) ablation over time. Panel A shows a little echo-free space prior to AF ablation. Panel B shows an iatrogenic increase in pericardial effusion after AF ablation. The echo-free space is increased to 10 mm. Panel C shows pericardial effusion after administration of 60 mg of protamine. The echo-free space is increased from 10 to 12 mm.

activated clotting time (ACT) was controlled to maintain a value of 300–400 s by heparin injection. The transseptal puncture was repeated three times to insert three catheters into the left atrium (LA) using intracardiac echo (ICE) catheter and fluoroscopic guidance. The anatomy of the LA was reconstructed using the EnSite NavX mapping system (St. Jude Medical, Inc., St. Paul, MN, USA) combined with computed tomography imaging prior to the PVI procedure. The aim of the PVI procedure was to achieve ipsilateral extensive PVI for both sides using a 4-mm tip irrigation catheter as a contact force-sensing catheter (TactiCath Quartz, Abbott, St. Paul, MN, USA), using a double lasso technique. Radiofrequency energy was set at 25 W and delivered at a 400 force–time integral at each site. Contact between the catheter tip and the endocardium was confirmed by 10–20 g contact force.

At the end of the PVI procedure, a decrease in movement of heart silhouette in the fluoroscopy was noted. The ICE catheter was quickly reinserted into the cardiac chamber, revealing a pericardial effusion of 10 mm posterior to the left ventricle (Fig. 1, Panels A and B). Fortunately, the PVI procedure was completed at this point. The quality of the PVI was confirmed by complete disappearance of PV electrograms and findings using the EnSite NavX system. Within the following 10 min, the systemic blood pressure dropped to 56/38 mm Hg. Transthoratic pericardial puncture and drainage of pericardial effusion was planned immediately, but the transthoratic echocardiogram showed a very thin echo-free space (<2–3 mm) on the precordial side of the heart, including the epigastric view. Under careful and close observation, conservative therapies were continued while preparing for emergent surgery. To reverse the effect of heparin, 60 mg of protamine was administered, as well as an intravenous saline bolus injection, and continuous catecholamine injection was started with small dose (0.0025 mg/kg/min). This usage of catecholamine might be avoided by considering increase of bleeding, but we used it very carefully because the degree of pericardial effusion was relatively limited at least at this time. Through these therapies, further drop in systemic blood pressure was prevented, but the echo-free space in ICE recording slowly increased from 10 to 12 mm (Fig. 1, Panels B and C). Finally, we decided to use idarucizumab to reverse the effects of dabigatran. This decision was made because the bleeding was considered to still be active, even after reversal using heparin. Throughout this time course, drainage using pericardial centesis was ready at any time, but it was not chosen because the echo-free space on the precordial side of the heart was still thin. A surgical approach was also considered but it became unnecessary because a gradual improvement in the systemic blood pressure was observed. After standard use of idarucizumab (5 g administered as two boluses within 5 min), there was no increase in echo-free space, and systemic blood pressure was gradually increased. The time course of the blood pressure and coagulation parameters are shown in Fig. 2. We decreased the dose of catecholamine gradually along the time course, and we could stop catecholamine within 17 h by 8:00 am next morning. The patient showed a standard and smooth clinical course after idarucizumab administration, and we restarted dabigatran 150 mg bid two days after the procedure. We observed gradual decrease of pericardial effusion by repeated echocardiogram and confirmed complete vanishment of pericardial effusion in one week.

Discussion

The PVI procedure is powerful but might be associated with bleeding and thromboembolism in some cases. When considering the risk of massive bleeding, such as cardiac tamponade, reducing the anticoagulation effect in the perioperative state is preferential, however, reduction or reversal of anticoagulation is known to produce a high-risk state for thromboembolism [5]. In accordance with the meta-analysis of warfarin therapies, uninterrupted warfarin exhibits minimal risk for thromboembolism without increasing the risk of bleeding [6]. Among the direct oral anticoagulants (DOACs), dabigatran has provided the most variety of studies dealing with the perioperative state of the PVI procedure. As a result, dabigatran exhibited noninferiority or even superiority to uninterrupted warfarin, which was recently confirmed by the RE-CIRCUIT trial [4]. Therefore, we employed a protocol using uninterrupted dabigatran in the PVI procedure.

However, if bleeding and cardiac tamponade complications occur, reversal of anticoagulation may have to be considered. The results from the RE-CIRCUIT trial showed that uninterrupted dabigatran was associated with a significant reduction in the major bleeding event rate compared with international normalized ratio (INR)-adjusted warfarin in the setting of AF ablation [4]. However, the result from the RE-CIRCUIT, AXAFA-AFNET 5, and VENTURE-AF trials showed that dabigatran, apixaban, and rivaroxaban were noninferior in cardiac tamponade event rate to INR-adjusted warfarin in the setting of AF ablation [4,7,8]. In the present case, although the precise mechanisms of cardiac tamponade were unclear, the speed of bleeding was speculated to be relatively slow because the patient showed a gradual decrease in systemic blood pressure. In the case of cardiac tamponade, pericardial drainage should be the principal therapy. We also tried to do that but it was difficult as the echo-free space was too thin, at least at the precordial or apical side of the ventricle. We used smaller dose of catecholamine in this case which should be avoided because cardiac tamponade was considered as a main factor for hypotension. The catecholamine was used very carefully with small dose under close observation because the degree of pericardial effusion was relatively limited in the echocardiogram. As a result, further drop of systemic blood pressure was prevented, so that the other factors, such as increased vagal tone, might be included as the

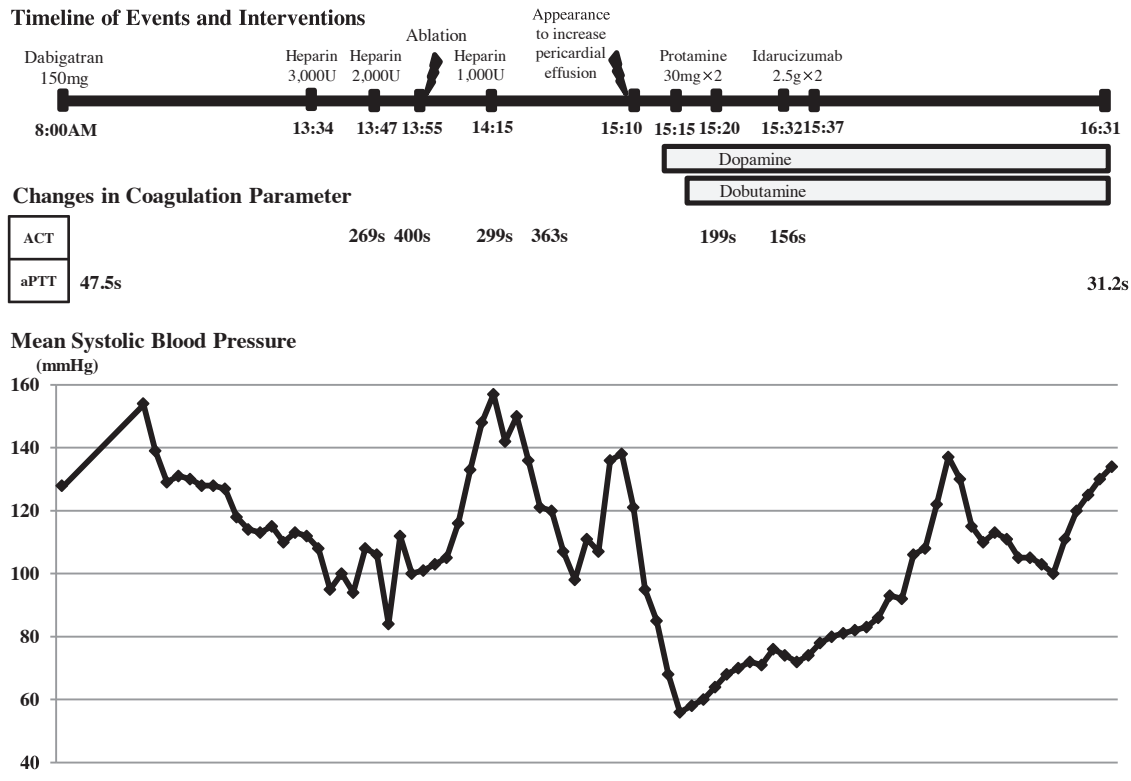

Fig. 2. Time course of events and interventions. Time course of blood pressure, coagulation marker, and administered drug before and during atrial fibrillation (AF) ablation. AF ablation was performed using uninterrupted dabigatran 300 mg (twice a day) via oral administration. The activated clotting time (ACT) during AF ablation was controlled between 300–400 s, but was increased with iatrogenic pericardial effusion. ACT was shortened to 199 s by administration of 30 mg of protamine, further shortening the ACT to 156 s by administration of 30 mg of protamine; however, the pericardial effusion was increased further. Activated partial thromboplastin time (aPTT) with dabigatran oral administration was extended to 47.5 s, but was shortened to 31.2 s after administration 5 g of idarucizumab.

mechanisms of hypotension. Again, we do not mean the use of idarucizumab permitted us to use catecholamine and we consider that the result in this case was one lucky phenomenon. In the next step, idarucizumab was used to reverse the effects of dabigatran as it was previously demonstrated to reverse the effects within 5 min in the RE-VERSE AD trial [9]. We kept ready for pericardial centesis at any time depending on the patient's condition, but the increase in pericardial effusion was stopped after idarucizumab usage. This result does not change the importance of pericardial drainage as the principal therapy for cardiac tamponade, but it may indicate the usefulness of anticoagulant reversal in case of bleeding. In the present case, although precise time-sequential monitoring of coagulation activity was not performed, the increase in echo-free space was prohibited following treatment with idarucizumab, therefore, its use was considered effective to stop the bleeding. Probably, the monitoring of coagulation and idarucizumab activities might be ideal to discuss about its usefulness in this case, but such step was not available because this was a clinical and emergent case. However, sufficient effect should be speculated by referring to clinical studies of idarucizumab in optimal infusion. Although the use of idarcizmab resulted in better clinical outcome without any invasive procedure in this case, we have to emphasize that the importance of principal procedure, i.e. pericardial drainage in this case, would not be affected by DOAC reversal. However, it should be true that the presence of therapeutic choice for specific and strong reversal for anticoagulant may give us safer situations in various procedures. It might be thought that dabigatran, the only DOAC with a specific reversal agent, currently represents the safest choice in case of risk for bleeding complications such as AF ablation.

Conflict of interest

The authors declare no conflicts of interest associated with this manuscript.

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