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CASE REPORT
Unclassified rare cardiovascular diseases and disorders

Safety of pulmonary vein isolation in atrial fibrillation patients treated with dabigatran when idarucizumab is available (RCDD code: VIII)

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Abstract

Patients with atrial fibrillation (AF) are at increased risk of stroke and systemic thromboembolism and prevention of such episodes is ensured by choosing appropriate anticoagulation. In paroxysmal drug-refractory AF, catheter ablation is the recommended choice of treatment. The decision on whether to stop administration of oral anticoagulant before catheter ablation procedures is often unclear. We present the case of a 67-year-old hypertensive woman with a 5-year history of symptomatic, drug-refractory paroxysmal AF, who was admitted for pulmonary vein isolation (PVI) and was anticoagulated with dabigatran. After successful transseptal puncture, an intravenous injection of 10 000 units of heparin was administered. Radiofrequency ablation was initiated at the left pulmonary trunk. After the second application of radiofrequency ablation, a drop in arterial blood pressure to 70/50 mmHg was observed. Urgent echocardiography revealed the presence of fluid within the epicardial surface of the left ventricular apex up to 19 mm, behind the right ventricle and right atrium up to 11 mm. Subsequently, all catheters were removed from the left atrium, and 50 mg of protamine sulfate, dopamine, and intravenous fluids were immediately administered. Idarucizumab was urgently delivered to the catheterisation laboratory and was available during patient hospitalisation in the intensive care unit. However, prior to patient discharge, echocardiography revealed only a trace amount of fluid in the pericardium and the use of idarucizumab was not indicated. Interruption of anticoagulation treatment with dabigatran before ablation is not required. Idarucizumab increases the safety of PVI in patients treated with dabigatran. JRCD 2018; 3 (8): 281–283

Key words: rare disease, atrial fibrillation, ablation, pulmonary vein isolation, anticoagulation, dabigatran

Background

Patients with atrial fibrillation (AF) who are at substantial risk of stroke and systemic thromboembolism require appropriate anticoagulation [1]. The CHA_2DS_2-VASc score and biomarker-based approaches were developed to aid in the assessment of stroke risk in patients with AF [2]. According to current European Society of Cardiology guidelines and international expert consensus, patients with paroxysmal AF and failure of pharmacologic therapy to improve symptoms in class IA are recommended to undergo catheter ablation [3, 4]. It was previously shown that cryoballoon ablation was noninferior to radiofrequency ablation with regard to efficacy and overall safety in this clinical indication [5].

Case presentation

A 67-year-old hypertensive woman with a 5-year history of symptomatic (European Heart Rhythm Association [EHRA] symptom scale of III), drug-refractory paroxysmal AF, was admitted for pulmonary vein isolation (PVI). She had a CHA_2DS_2-VASc score of 2 and was anticoagulated with dabigatran 150 mg twice daily. The patient received her last dose of dabigatran the evening before

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Table. Selected concerns, indications and contraindications for use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Based on references [3, 7] and/or summaries of product characteristics (SmPCs)

	Dabigatran	Rivaroxaban	Apixaban
Mechanism of action	Oral direct thrombin inhibitor	Oral direct factor Xa inhibitor	
Selected contraindications / interactions / non-recommended use	Mechanical heart valves or moderate-to-severe mitral stenosis; St. John's wort use; creatinine clearance <15 ml/min or dialysis; Child-Pugh category C.		
	Dronedarone use; creatinine clearance <30 ml/min (in the US, but not in Europe, dabigatran 75 mg twice a day has been approved for patients with a creatinine clearance 15–29 ml/min); ulceration of the digestive tract.	Dronedarone use in patients receiving rivaroxaban should be avoided. Rivaroxaban should not be used in patients with Child-Pugh category B.	
Dose in atrial fibrillation	150 mg twice daily or 110 mg twice daily	20 mg once daily or 15 mg once daily	5 mg twice daily or 2.5 mg twice daily
Selected indications for reduced dose	Age ≥80 years or combining with verapamil. In younger patients ≥75 years, those with creatinine clearance ≤50 ml/min, gastro-oesophageal reflux disease, gastritis, esophagitis or at increased risk of bleeding consider individually.	Creatinine clearance <50 ml/min	Creatinine clearance <30 ml/min or at least two of: age ≥80 years and/or serum creatinine ≥1.5 mg/dl (133 µmol/l) and/or body weight ≤60 kg.
Safety concerns	Assess kidney function at least yearly (together with haemoglobin and liver function), in patients ≥75 years or frail at least every 6 months, if creatinine clearance ≤60 ml/min recheck interval = creatinine clearance / 10		
Specific reversal agent	Available (idarucizumab)	Not yet approved and not yet available (andexanet alpha)	

the procedure. On admission, her international normalised ratio (INR) was 1.36 (normal range 0.9–1.3), activated partial thromboplastin time (APTT) 66.3 seconds (normal range 25–37 seconds), and prothrombin time (PT) 15.5 seconds (normal range 13–17 seconds). The electrocardiogram (ECG) showed AF with fast ventricular rate in the range of 130–180 per minute. Prior to ablation, thrombi in the left atrium were excluded via transoesophageal echocardiography. Using a transfemoral approach under Ensite navigation (St. Jude Medical, St. Paul, Minnesota, USA), diagnostic catheters (Hagmed, Rawa Mazowiecka, Poland) were placed in the apex of the right ventricle and coronary sinus. Subsequently, successful transseptal puncture using fluoroscopy and invasive blood pressure monitoring was performed, followed by an intravenous injection of 10 000 units of heparin. With the use of the Ensite system and pulmonary vein ablation catheter (PVAC) (Medtronic, Minneapolis, Minnesota, USA), electroanatomical mapping of the left atrium was performed (Figure Panel A) and radiofrequency ablation was initiated at the left pulmonary trunk. After the second application of radiofrequency ablation, a drop in arterial blood pressure to 70/50 mmHg was observed. Urgent echocardiography revealed presence of fluid within the epicardial surface of the left ventricular apex up to 19 mm (Figure Panel B) and behind the right ventricle and right atrium up to 11 mm (Figure Panel C), indicating moderate pericardial effusion. The patient reported weakness and dyspnoea. Subsequently, all catheters were removed from the left atrium, and 50 mg of protamine sulfate, dopamine, and intravenous fluids were immediately administered. Idarucizumab was urgently delivered to the catheterisation laboratory and was accessible during patient hospitalisation in the intensive care unit. The overall procedure time was 100 minutes; total fluoroscopy exposure was 3 minutes and 45 seconds (335.9 cGy cm^2). Prior to discharge, echocardiography revealed only a trace amount of fluid in the pericardium (Figure Panel D). Because of this, there was no indication for the use of idarucizumab.

Discussion and review of literature

Consideration of indications and contraindications for anticoagulation is crucial in patients with AF, and non-vitamin K antagonist oral anticoagulants play an increasing role in the treatment of patients with AF (Table) [3, 6, 7]. The decision on whether to interrupt oral anticoagulant treatment before cardiovascular implantable electronic device implantation and catheter ablation procedures is often unclear. These are generally considered as interventions with low bleeding risk, unless a complex anatomical setting is present or complex procedures are performed, respectively. However, complex left-sided ablations, including PVI, are regarded as interventions with a high bleeding and increased thromboembolic risk [7]. The current EHRA Practical Guide on the use of non-vitamin K antagonist oral anticoagulants (NOAC) recommends catheter ablation in patients who have been therapeutically anticoagulated with NOAC, generally without interruption or with a short cessation period of such treatment, depending on several factors, including CHA_2DS_2-VASc score, creatinine clearance, operator experience, and routine use of heparin before the first transseptal puncture [7]. Performance of catheter ablation during the use of dabigatran was tested in the Randomized Evaluation of Dabigatran Etexilate Compared to Warfarin in Pulmonary Vein Ablation: Assessment of an Uninterrupted Periprocedural Anticoagulation Strategy (RE-CIRCUIT) trial [8]. In this trial, patients received dabigatran at the usual time in the morning on the day of ablation and was associated with fewer bleeding complications than uninterrupted

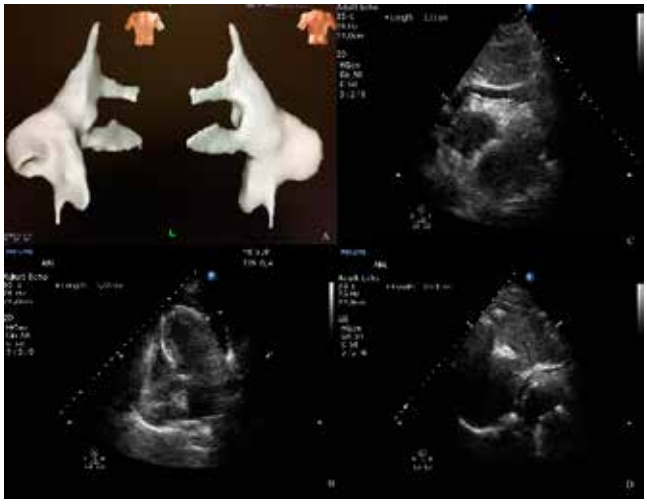

Figure. A. Electroanatomical map of the left common pulmonary trunk. B. Moderate pericardial effusion in the region of the left ventricular apex. C. Moderate pericardial effusion behind the right atrium and right ventricle. D. Follow-up echocardiography

warfarin [8]. On the other hand, in cases of bleeding, measurement of the anticoagulant effect of the oral direct inhibitor of thrombin, may be required [9]. However, measurement of dabigatran plasma concentration is not widely available in all hospitals. Therefore, APTT may be useful in the assessment of the relative degree of anticoagulation with dabigatran. In patients receiving 150mg of dabigatran twice daily the median trough APTT is ~1.5 times higher than the level observed in controls, while a ratio of >2.5 may indicate supratherapeutic levels [9].

Moreover, a reversal agent for dabigatran (idarucizumab) is currently available, while a reversal agent for factor Xa inhibitors will likely be available in daily clinical practice in the near future [10, 11]. Idarucizumab was successfully tested in patients with serious bleeding and in those who require urgent procedures [10]. In the Reversal Effects of Idarucizumab on Active Dabigatran (RE-VERSE AD) study, idarucizumab was given in two separate bolus infusions, no more than 15 minutes apart (total of 5 g of idarucizumab), to patients in whom the median time since last intake of dabigatran was 15.4 hours (in 36% of patients, the last intake was <12 hours, while in 6% of patients this time was ≥48 hours) [10].

There are published reports which show the importance of idarucizumab in specific urgent medical situations [12–14]. However, this case report and review of the literature highlight the potential clinical utility of idarucizumab in cardiology during catheter ablation. Pericardial effusion during pulmonary vein isolation occurs in < 1% of cases, however, if present, could lead to cardiac tamponade and death [15]. Therefore, the choice of an optimal anticoagulant agent is crucial.

Conclusion

There is no necessity to interrupt anticoagulation treatment with dabigatran before AF ablation if idarucizumab is available. Idarucizumab increases the safety of PVI in patients treated with dabigatran.

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