

# Idarucizumab: a quick and effective antidote administered prior to coronary artery bypass surgery and mitral valve annuloplasty in a patient treated with dabigatran

Andrzej J. Sałacki<sup>1,2</sup>, Tomasz Zapolski<sup>2</sup>, Andrzej Wysokiński<sup>2</sup>

<sup>1</sup> 2nd Faculty of Medicine with English Language Division, Medical University of Lublin, Lublin, Poland

<sup>2</sup> Department of Cardiology, Medical University of Lublin, Lublin, Poland

An 86-year-old man with paroxysmal atrial fibrillation was admitted to a cardiac intensive care unit (ICU) due to loss of consciousness following angina pectoris. An electrocardiogram (ECG) in the ambulance demonstrated a complete atrioventricular block. While in the ICU, episodes of severe angina continued, and the patient was hemodynamically unstable with features of pulmonary congestion. His heart rate was 100 bpm and blood pressure—95/65 mm Hg. As anticoagulation therapy, he received dabigatran (110 mg orally twice daily), and the last dose was administered 2 hours before admission. Laboratory tests revealed macrocytic anemia, an international normalized ratio of 1.36, prothrombin time of 15.5 s (reference range, 9.4–12.5 s), activated partial thromboplastin time (APTT) of 34 s (<37 s), brain natriuretic peptide levels of 640 pg/ml (0–100 pg/ml), troponin I levels of 18.5 ng/ml (<0.04 ng/ml), creatinine levels of 1.2 mg/dl, and estimated glomerular filtration rate of 60.4 ml/min/1.73 m<sup>2</sup>. Abnormalities on ECG suggested significant myocardial ischemia (FIGURE 1A–1C). The complete atrioventricular block registered in the ambulance subsided on admission, and the patient developed a sinus rhythm of 100 bpm with right bundle branch block. However, only half an hour after admission, the ECG showed the sinus rhythm of 100 bpm with left bundle branch block. Transthoracic echocardiography revealed decreased contractility with a left ventricular ejection fraction of 35%. Severe mitral regurgitation and the vena contracta at 0.8 cm (FIGURE 1D) were also noted. The patient was administered 600 mg of clopidogrel and 300 mg of aspirin. Subsequently, he underwent coronary angiography, which revealed 3-vessel disease with left coronary artery stenosis (FIGURE 1E–1J). He was consulted by a cardiac

surgeon and was referred for surgery as a life-saving procedure.

As the patient had recently taken dabigatran, he was administered 5 g of idarucizumab in 2 doses (both 2.5 g in 50 ml, administered as a quick 5-minute intravenous bolus, with a 5-minute interval between the doses). Idarucizumab is a fragment of a monoclonal antibody that restores systemic blood coagulation and enables fibrin to be formed again in patients treated with dabigatran etexilate.<sup>1</sup> Following the administration of idarucizumab, the APTT was 37 s and prothrombin time—18 s. After 2 hours, the patient was transferred to a cardiac surgery department to undergo coronary artery bypass surgery and mitral valve annuloplasty. Unfractionated heparin was used during the 6-hour procedure, and protamine sulfate—at the end of surgery. Hemostasis was impaired, which could result from the fact that dual antiplatelet therapy had been implemented. The patient survived the surgery, and extracorporeal circulation lasted 4.5 hours. He was taken off the ventilator after 4 days, and intra-aortic balloon pump was removed after 5 days. The patient was discharged after 16 days of treatment. As anticoagulation therapy, low-molecular-weight heparin was used for a few days, followed by warfarin. During hospitalization, no procoagulant effects were observed.

Acute cardiac conditions requiring surgical treatment very rarely necessitate the use of idarucizumab. In RE-VERSE AD™, a phase III trial evaluating the efficiency and safety of dabigatran reversal with idarucizumab before urgent surgical treatment, only 2 of the 39 patients had cardiac disease (dissecting aortic aneurysm in one patient and cardiac tamponade in the other). Among the 90 study participants, thrombotic

## Correspondence to:

Andrzej J. Sałacki, MD,  
Katedra i Klinika Kardiologii,  
Uniwersytet Medyczny w Lublinie,  
ul. Jaczewskiego 8, 20-954 Lublin,  
Poland, phone: +48 81 724 41 51,  
e-mail: andrzej.salacki@umlub.pl

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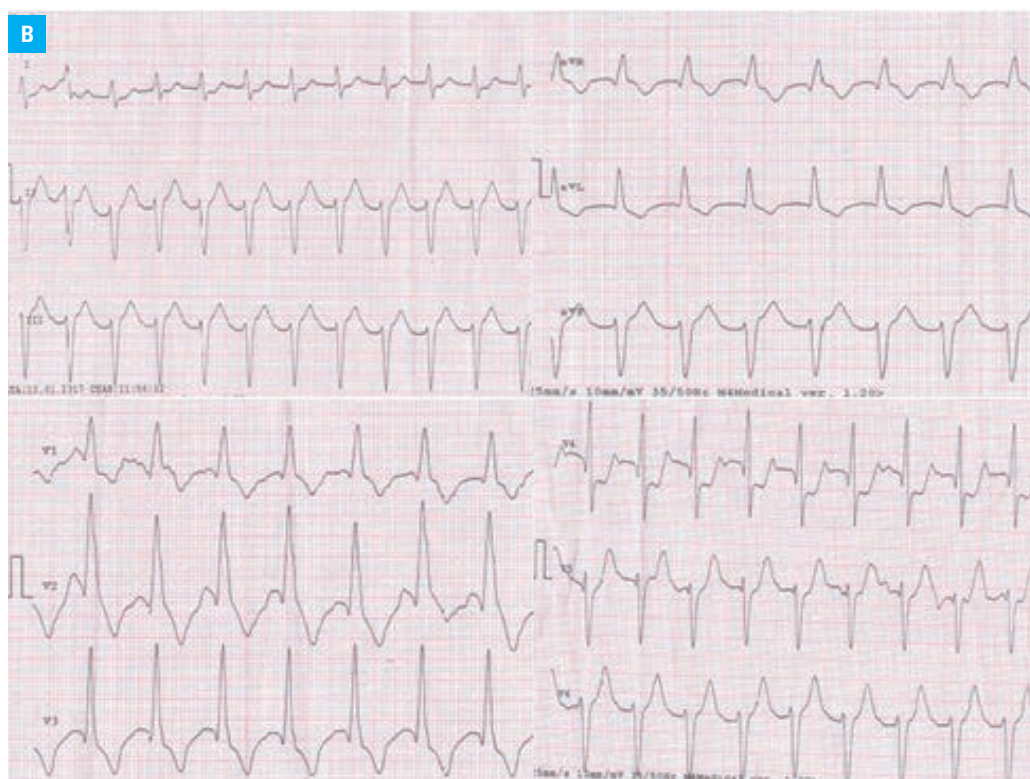
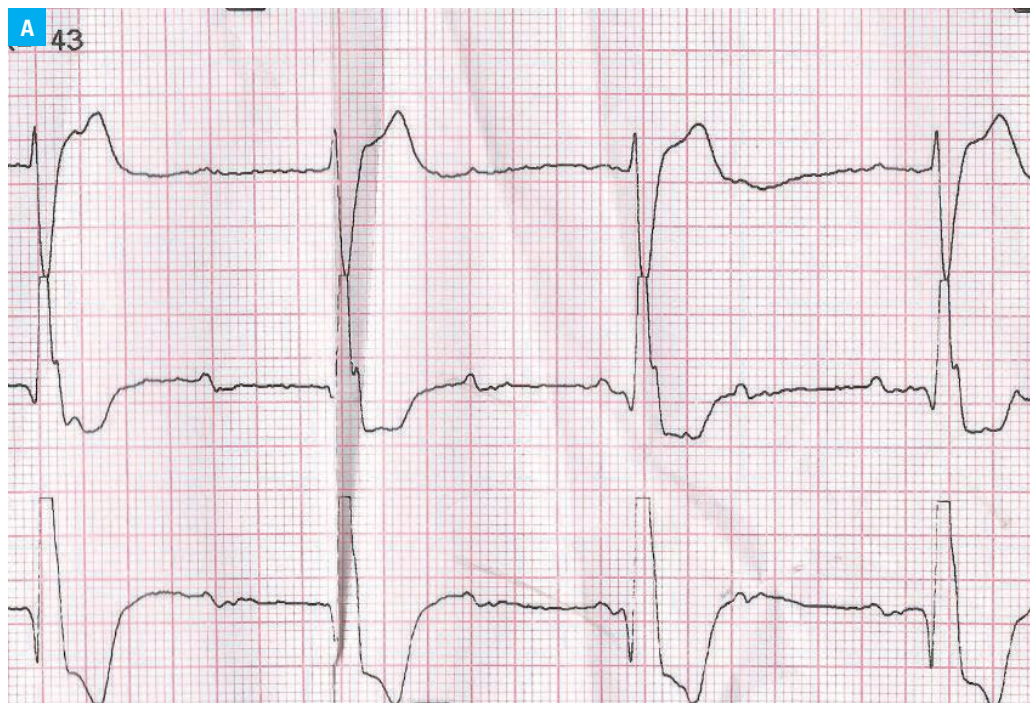
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**FIGURE 1**

Electrocardiograms showing complete atrioventricular block (A) and right bundle branch block (B)



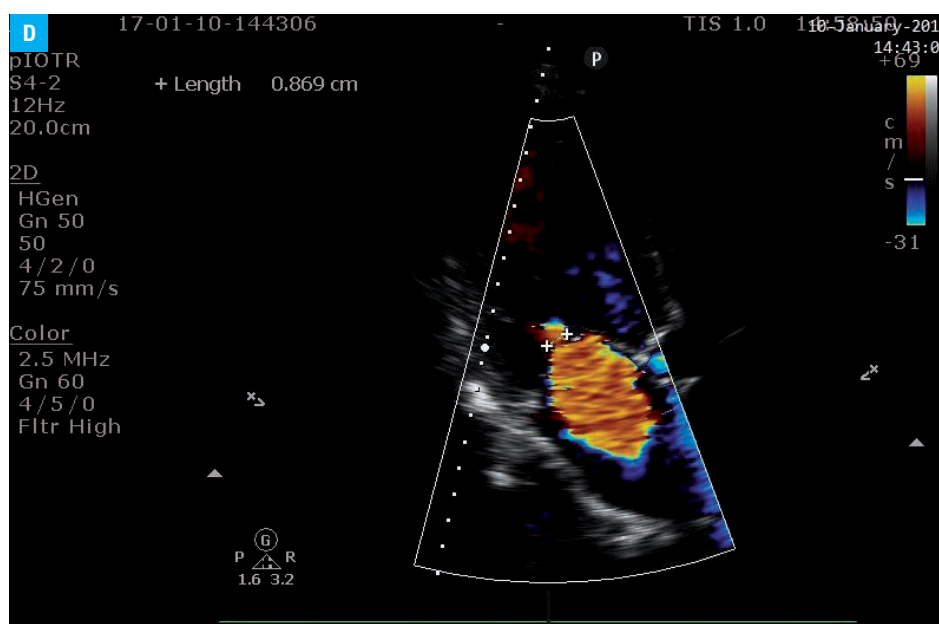
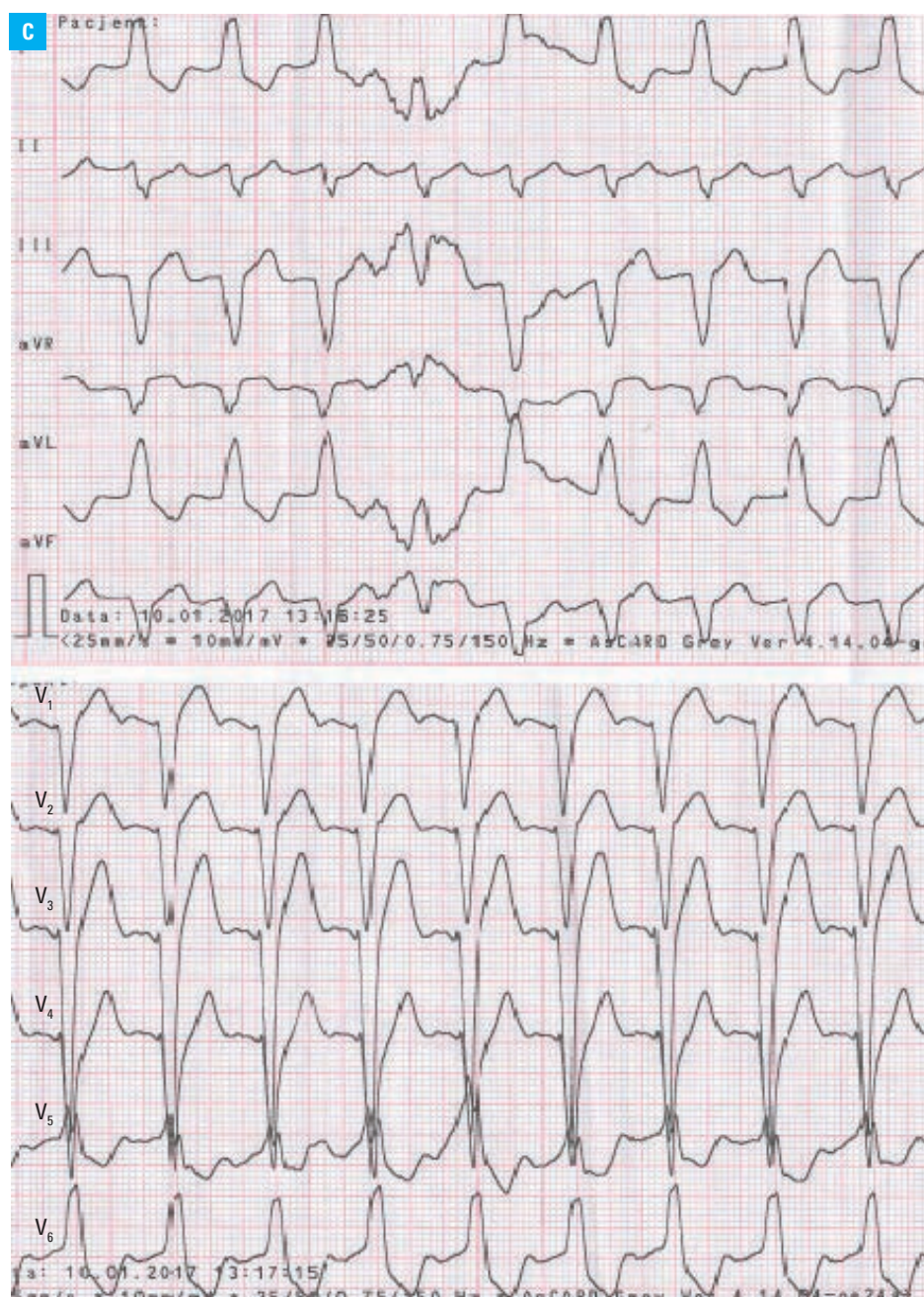
events were reported only in 5; however, none of them received anticoagulation therapy at that time. In the present case, no thrombotic complications were observed after the surgery; however, the results of RE-VERSE AD™ indicate a risk of thrombotic events in patients not receiving anticoagulation therapy and suggest reintroduction of the therapy as soon as possible.<sup>2,3</sup> The use of idarucizumab has been reported in patients treated with dabigatran and requiring an urgent surgery due to an acute dissecting aortic aneurysm or life-threatening bleeding.<sup>4,5</sup> However, to our knowledge, this is the first report

of a patient with 3-vessel disease, left coronary artery stenosis, and severe mitral regurgitation who was referred for an urgent cardiac surgery as a life-saving procedure and who received idarucizumab as an effective antidote for dabigatran.

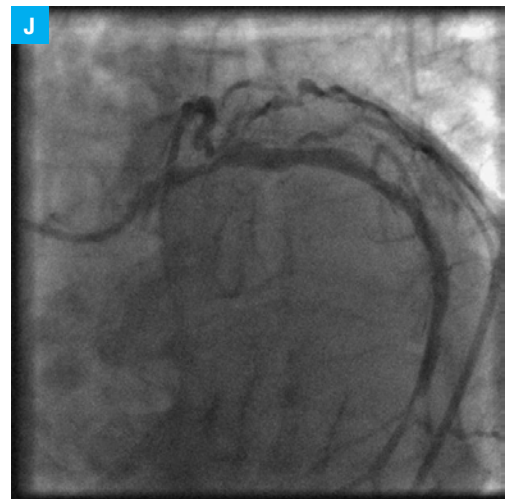
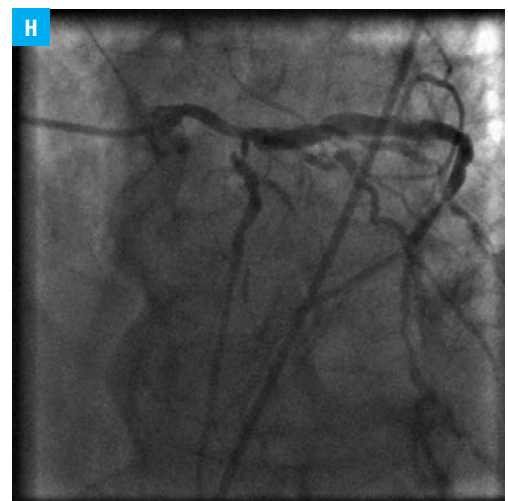
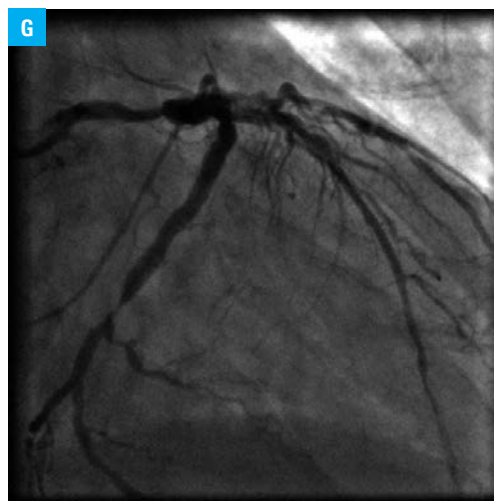


**FIGURE 1**

**C** – an electrocardiogram showing complete left bundle branch block;  
**D** – severe mitral regurgitation on transthoracic echocardiography (apical 2-chamber view)



**FIGURE 1** Coronary angiography images:  
**E** – right coronary artery ostial stenosis and occlusion in the middle segment (presentation: LAO 41°, CRA 0°); **F** – right coronary artery occlusion in the middle segment (presentation: RAO 25°, CRA 5°); **G** – left main stenosis in the distal part and circumflex branch stenosis in the middle segment (presentation: RAO 22°, CRA 1°); **H** – left anterior descending branch stenosis in the proximal segment (presentation: LAO 34°, CRA 27°); **I** – circumflex branch stenosis in the middle segment (presentation: LAO 34°, CRA 27°); **J** – left main stenosis in the distal part, protruding to the bifurcation with the left anterior descending and circumflex branches (presentation: LAO 34°, CAU 21°)



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