CLINICAL IMAGE

Successful use of idarucizumab as a reversal agent for dabigatran in a patient with acute dissected aortic aneurysm

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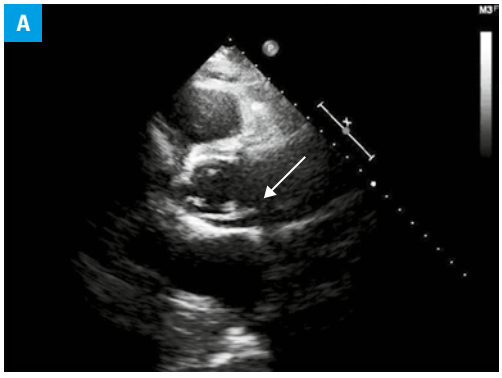
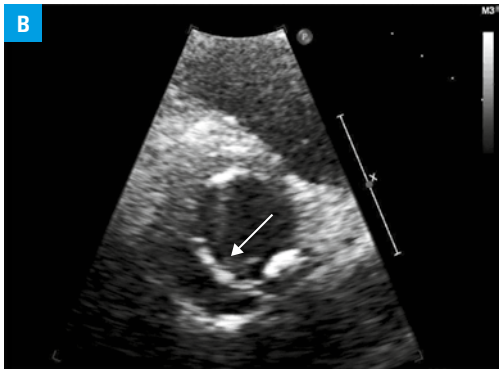
A 66-year-old woman with hypertension, diabetes, chronic kidney disease, and atrial fibrillation treated with dabigatran, a direct thrombin inhibitor licensed for stroke prevention in patients with nonvalvular atrial fibrillation,[1,2] was hospitalized due to severe chest pain. She was in a serious condition (heart rate, 90 bpm; blood pressure, 150/90 mmHg). Auscultation revealed diastolic murmur over the aortic valve. An electrocardiogram showed atrial fibrillation. Laboratory tests revealed elevated thrombin time (93.7 s; reference range, 14–21 s), activated partial thromboplastin time (37 s; reference range, 24–35 s), and glomerular filtration rate (45 ml/min/1.73 m^2). An echocardiogram showed distinct ascending aortic dissection with aortic insufficiency and pericardial effusion (FIGURE 1A–1C). A computed tomography scan revealed an aneurysm of the ascending aorta, aortic arch, and descending and abdominal aorta, with involvement of kidney arteries (FIGURE 1D–1F). A reversal agent for dabigatran, idarucizumab at a dose of 5 g, was administered as intravenous infusion within 15 minutes.





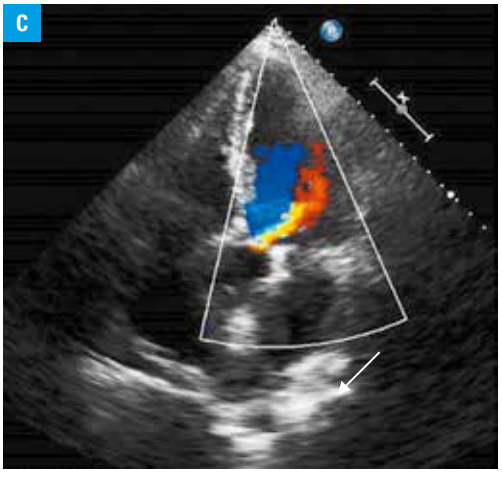


FIGURE 1 **A** – ascending aortic dissection (transthoracic echocardiography, parasternal long-axis view); **B** – ascending aortic dissection (transthoracic echocardiography, parasternal short-axis view); **C** – aortic insufficiency (transthoracic echocardiography, apical 4-chamber view, color Doppler mode)

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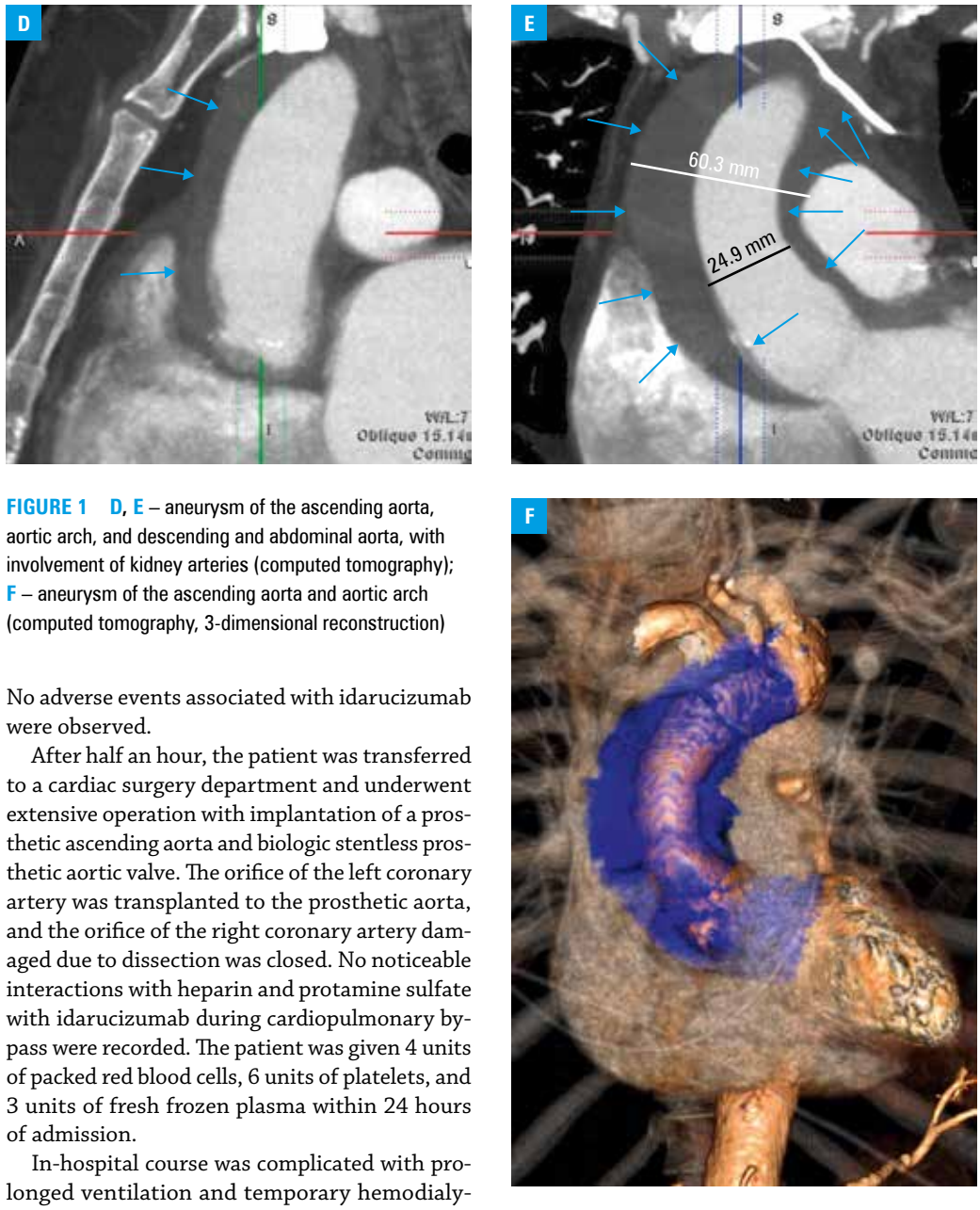

FIGURE 1 **D**, **E** – aneurysm of the ascending aorta, aortic arch, and descending and abdominal aorta, with involvement of kidney arteries (computed tomography); **F** – aneurysm of the ascending aorta and aortic arch (computed tomography, 3-dimensional reconstruction)

No adverse events associated with idarucizumab were observed.

After half an hour, the patient was transferred to a cardiac surgery department and underwent extensive operation with implantation of a prosthetic ascending aorta and biologic stentless prosthetic aortic valve. The orifice of the left coronary artery was transplanted to the prosthetic aorta, and the orifice of the right coronary artery damaged due to dissection was closed. No noticeable interactions with heparin and protamine sulfate with idarucizumab during cardiopulmonary bypass were recorded. The patient was given 4 units of packed red blood cells, 6 units of platelets, and 3 units of fresh frozen plasma within 24 hours of admission.

In-hospital course was complicated with prolonged ventilation and temporary hemodialysis. Parenteral anticoagulation was initiated 24 hours later (enoxaparin, 2 × 70 mg subcutaneously). After 20 days of hospitalization, the patient was transferred to a rehabilitation department in hemodynamically stable condition. Dabigatran treatment was reinitiated on discharge.

To our knowledge, this is the first report of a patient with dissected aortic aneurysm, who received a specific antidote monoclonal antibody, idarucizumab, as a reversal agent for dabigatran, just before major cardiac surgery.[3] The patient participated in the RE-VERSE AD study[4] testing the use of idarucizumab and was enrolled as a surgical patient requiring urgent intervention.

Idarucizumab, a monoclonal antibody fragment, binds dabigatran with an affinity that is 350-fold higher than that observed for thrombin.[5] Consequently, idarucizumab binds free and thrombin-bound dabigatran, and immediately neutralizes its anticoagulation activity.[4] The dabigatran–idarucizumab complex is eliminated by the kidneys within several hours. Dabigatran therapy may be reinitiated after 24 hours from antidote administration.

The efficacy and safety of idarucizumab were demonstrated in patients with severe bleeding or who required urgent surgery.[4] In practice, idarucizumab should be used in patients with life-threatening bleeding or bleeding affecting critical organs, major bleeding despite local treatment, or in cases of high risk of bleeding recurrence due to dabigatran overdose or reduced elimination rate. The antidote should be also considered when there is a need for urgent surgery/intervention associated with high risk of bleeding.[4,5]

Among 36 patients in the RE-VERSE AD study[4] who underwent the procedure, normal intraoperative hemostasis was reported in 33, and mildly or moderately abnormal hemostasis was reported in 2 patients and 1 patient, respectively. In the case of our patient, the cardiac surgeon reported normal hemostasis.

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