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Case Report

Emergency Open Repair for Ruptured Abdominal Aortic Aneurysm Using Idarucizumab: A Case Report

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ABSTRACT

Background: Idarucizumab is the first specific reversal agent for direct oral anticoagulants. There are only a few reports of the use of idarucizumab.

Case presentation: A 67-year-old man was transported to our hospital complaining of lower abdominal discomfort and dyspnea. His medical history included hypertension and atrial fibrillation treated with dabigatran. Upon arrival, he was alert, with pale skin, and cold sweats with hemodynamic instability. The imaging evaluation revealed a 79-mm abdominal aortic aneurysm and retroperitoneal hematoma. He was diagnosed with a ruptured abdominal aortic aneurysm. We immediately administered 5 g of idarucizumab for the reversal of dabigatran anticoagulation, and emergency open repair of the abdominal aortic aneurysm was performed. Normal intraoperative hemostasis was ultimately achieved. He was finally discharged without any neurological deficit, but left hip disarticulation was needed because of left limb ischemia.

Conclusion: Although idarucizumab would prove useful for patients with a bleeding tendency due to taking dabigatran, it may promote thrombotic events and further studies to clarify the ideal timing for restarting anticoagulation after the administration of idarucizumab are needed.

Introduction

As shown in epidemiological studies in Japan, both the prevalence and incidence of atrial fibrillation (AF) increase over 65 years of age, and more patients are taking anticoagulants [1, 2]. Direct oral anticoagulants (DOACs) are the most effective means of preventing recurrent stroke in patients with AF [3]. Compared to warfarin, DOACs are not associated with a risk of intracranial hemorrhaging, although there is a risk of gastrointestinal bleeding [4-6]. Specific DOAC reversal agents have been needed in patients who experience serious bleeding or undergo urgent surgery or intervention. Idarucizumab rapidly and reliably reverses the anticoagulant effect of dabigatran; however, the effect and adverse events of this agent are unknown. We herein report a case of a well-managed ruptured abdominal aortic aneurysm using idarucizumab.

Case Presentation

A 67-year-old man was transferred to our hospital with complaints of lower abdominal discomfort and dyspnea. He was hemodynamically unstable. His medical history included hypertension, non-valvular atrial fibrillation being treated with dabigatran 150 mg twice a day, and intermittent claudication. He took dabigatran on a regular schedule and had taken a dose 10 hours before arriving.

Upon admission, the patient was alert with pale skin and cold sweats. His vital signs were as follows: pulse rate, 102/minute; and blood pressure, 56/44 mmHg. He responded to a fluid bolus. Abdominal ultrasound showed an extended abdominal aorta. After fluid resuscitation, computed tomography (CT) was performed. Abdominal CT showed a 79×82-mm abdominal aortic aneurysm and retroperitoneal

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hematoma extending toward the right common iliac artery and left external iliac artery. We diagnosed the patient with a ruptured abdominal aortic aneurysm (Figures 1 & 2). A laboratory investigation revealed a hemoglobin level of 12.9 mg/dL, platelet count of 220,000 /μL, prothrombin time of 49.2 sec, international normalized ratio of prothrombin time of 1.44, activated partial prothrombin time of 45.0 sec, fibrinogen of 107.0 mg/dl, blood urea nitrogen of 22.3 mg/dl, and creatinine level of 1.36 mg/dl.

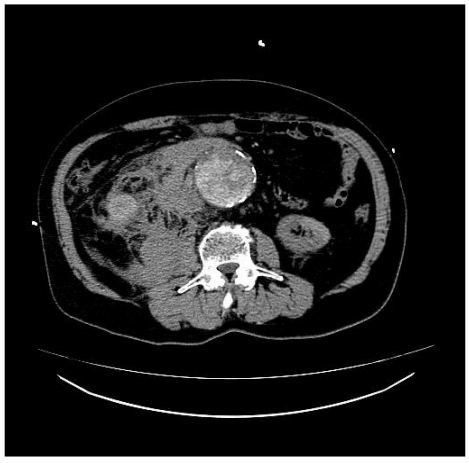

Figure 1: Axial computed tomography showing a ruptured abdominal aorta on the day of admission.

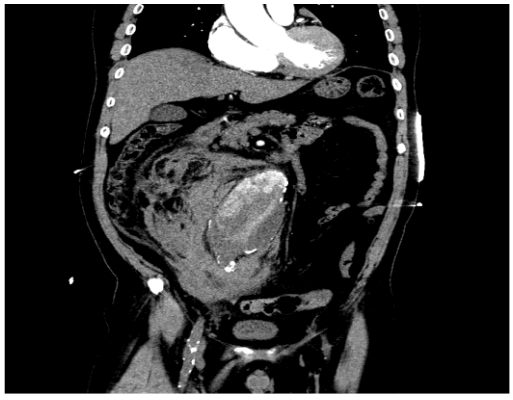

Figure 2: Coronal computed tomography showing a ruptured abdominal aorta on the day of admission.

We administered 5 g of idarucizumab intravenously at 9:20 to reverse dabigatran anticoagulation. He lost consciousness at 9:40 before general anaesthesia started, and his carotid artery was not palpable, so chest compression was started at 9:43. Resuscitative endovascular balloon occlusion of the aorta approached from the left brachial artery was inflated at aortic zone 1. Emergency open repair of the abdominal aortic aneurysm started at 9:48, the abdominal aorta was clamped at 10:00, and he was hemodynamically stable at 10:15, when chest compression ended. Open repair with a Y-shaped graft for the abdominal aorta was performed successfully, and we were able to declamp the aorta with no remarkable change in the hemodynamic status. We did not use any antithrombotic drugs during the operation. The operation ended with open abdominal management to monitor the appearance of the intestinal tract. The operating time was 3 hours 48 minutes, and the blood loss was 1,016 ml.

Just after the initial operation, left limb ischemia was noted, although he was hemodynamically stable. Neither the left dorsal pedis artery nor the posterior tibial artery was palpable. Contrast CT revealed the occlusion of the left external iliac artery, which was distal to the anastomotic region (Figure 3). Open thrombectomy was performed, and several thrombi were removed. Although femoro-femoral bypass surgery was performed on postoperative day 1 (POD 1), left limb ischemia did not improve. Anticoagulation therapy with heparin started on POD 5. On POD 6, the skin of his left limb looked ulcer-like, and enhanced CT revealed left limb ischemia (Figure 4). On POD 8, left hip disarticulation was performed, and he was extubated on POD 9 and discharged after rehabilitation without any neurological deficits.

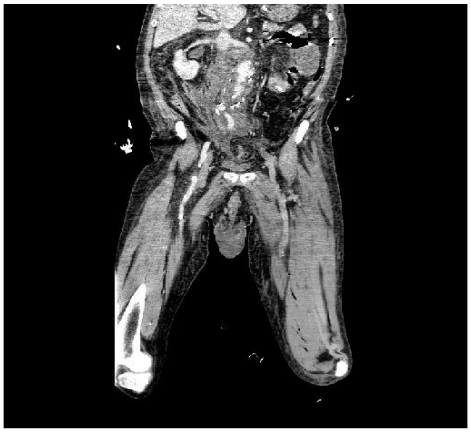

Figure 3: Computed tomography showing left limb ischemia one hour after the initial operation.

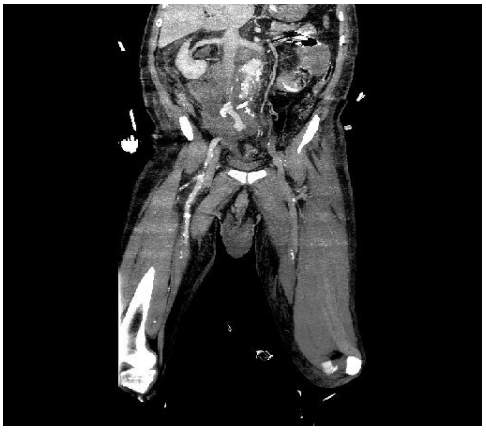

Figure 4: Computed tomography showing left limb ischemia on postoperative day 7.

Discussion

We experienced a case of a ruptured abdominal aortic aneurysm that resulted in successful patient management with good bleeding control using idarucizumab. This is the first report of a case of open repair for a ruptured abdominal aortic aneurysm after the administration of idarucizumab. Idarucizumab was effective for achieving bleeding control, but we struggled to manage acute limb ischemia after the operation.

Warfarin has long been the first-line therapy for stroke prevention in patients with atrial fibrillation. However, DOACs have been on the market since 2011, and the recommended first-line therapy was changed to DOAC in the 2013 atrial fibrillation guideline in Japan [7-10]. While specific reversal agents for warfarin and heparin have been available for some time, such agents for DOACs were lacking until idarucizumab was

developed. Idarucizumab, a monoclonal antibody fragment, has been licensed for rapid and specific reversal of the anticoagulant effect of dabigatran since 2015 in the USA and was introduced to the market in September 2016 in Japan [11]. It is approved for dabigatran reversal in patients who have life-threatening bleeding or are undergoing urgent surgery or intervention. Immediately after the intravenous administration of 5 g of idarucizumab, the concentration of unbound dabigatran is reduced to the lower limit of quantification within 5 minutes, regardless of the bodyweight or dose of dabigatran. Idarucizumab binds dabigatran with an affinity that is 350 times as high as that observed with thrombin. It has a half-life of approximately 45 minutes and is cleared renally [12].

Pollack *et al*. showed that the rate of thrombotic events after the administration of idarucizumab was 4.8% at 30 days and 6.8% at 90 days [13]. All the events, such as deep vein thrombosis, pulmonary embolism, acute myocardial infarction, and stroke that happened within 72 h after its administration occurred in patients in whom anticoagulant therapy had not been started again.

In the initial operation, although our patient needed chest compression for pulseless electrical activity due to hypovolemic shock, intraoperative bleeding was well controlled. However, despite open thrombectomy and femoro-femoral bypass were performed, left hip disarticulation was still needed. We presume that acute thrombosis due to abdominal aortic aneurysms influenced this thrombotic event. The patient had been aware of swelling in his left thigh and intermittent claudication for three days before hospital admission. These symptoms are signs of thromboembolism, that can affect postoperative acute limb ischemia [14-16].

Patients with renal impairment reportedly show a decreased clearance and prolonged initial half-life of idarucizumab [17]. In our case, the patient had renal impairment perioperatively, so the relationship between the reversal of dabigatran and thrombotic events is likely. The ideal timing for restarting anticoagulation after surgery or interventions is still unclear. While some reports have been published, high-quality evidence of perioperative antithrombotic in open repair of ruptured abdominal aortic aneurysm is lacking [18, 19]. In the study by Chinien *et al.*, patients receiving systemic heparin showed lower perioperative mortality than those not receiving it. Although no significant difference was noted between the heparin and the no-heparin group, fewer patients had thrombectomy after receiving heparin (8% vs. 12%) [19]. These principles and our present experience suggest that we should restart anticoagulation early for patients who have undergone abdominal aortic repair after idarucizumab administration. Further studies to clarify the ideal timing for restarting anticoagulation in patients administered idarucizumab are warranted in order to develop the appropriate management approach.

Conclusion

We encountered a patient taking dabigatran for AF, who had a ruptured abdominal aortic aneurysm. After idarucizumab was administered, emergency open repair of the abdominal aortic aneurysm was performed successfully.

We expect idarucizumab to prove for patients with a bleeding tendency due to taking dabigatran, but it may promote thrombotic events. Further studies to clarify the ideal timing for restarting anticoagulation after the administration of idarucizumab are needed.

Conflicts of Interest

None.

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