Case report

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Dabigatran-induced hemopericardium with tamponade

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Abstract

***Background*: Rapidly changing the pharmacokinetics and pharmacodynamics in critically ill patients with acute kidney injury leads to patients having a high risk of bleeding despite the early cessation of direct oral anticoagulant (DOAC). Bleeding complications can occur at a rare hidden site, the hemopericardium; this type of complication requires point-of-care ultrasound examinations (POCUS) for early detection and the performance of ultrasound-guided drainage as a lifesaving procedure.**

***Case presentation*: An 84-year-old woman with atrial fibrillation who was taking 110 mg bid dabigatran and who presented with obstructive sleep apnea and deteriorated renal function as well as type 2 respiratory failure. The patient was compliant with the dosage of dabigatran (110 mg twice daily), and the last dose was taken a few hours prior to being transferred to the critical care unit. Within 24 hours, the patient was notably lethargic and oliguric. Laboratory examination demonstrated a deterioration in renal function. Serial transthoracic echocardiography demonstrated new mild pericardial effusion that progressively increased for the next 4 hours with signs of early cardiac tamponade. Idarucizumab was administered. The patient underwent successful echocardiography guided pericardiocentesis without complications. A 500 ml of grossly hemorrhagic fluid was removed. The patient recovered to baseline status over the course of one week, with laboratory and clinical resolution of multiorgan failure and no echocardiographic evidence of hemopericardium.**

***Conclusion*: Life-threatening hidden hemorrhagic complications warrant caution in patients receiving DOAC. Our case highlights both a rare bleeding complication of dabigatran, and the effectiveness of idarucizumab, the approved reversal agent. Clinicians should closely monitor patient renal function in the setting of critical care area. Urgent POCUS detected the complication early, and ultrasound guided pericardiocentesis was followed by improved hemodynamic.**

Key words: Dabigatran, hemopericardium, point-of-care-ultrasound.

Introduction

Dabigatran, the first direct oral anticoagulant (DOAC) with a reversal agent, heralded a paradigm shift for the treatment and prevention of thrombosis. Significant bleeding risk is well documented in the literature, (1) but hemopericardium causing hemodynamic instability is still a rare complication of dabigaratn. We present a case of hemopericardium resulting in multiorgan failure related to dabigatran use that was successfully reversed with idarucizumab and was diagnosed early with point-of-care ultrasound (POCUS).

Case presentation

An 84-year-old woman with atrial fibrillation (AF) who was taking 110 mg bid dabigatran and who presented with obstructive sleep apnea with morbid obesity and hypoventilation syndrome, diabetes requiring insulin, hypertension, and diastolic heart failure with severe pulmonary hypertension as discovered by recent echocardiography was transferred to our medical center for further manage-

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ment of acute pulmonary edema and deteriorated renal function as well as type 2 respiratory failure. The patient stated that she started feeling progressively weaker and sleepier, with increasing chronic epigastric pain for a duration of 2 weeks. The patient was compliant with the dosage of dabigatran (110 mg twice daily), and the last dose was taken a few hours before being transferred to the critical care unit. Upon admission, the patient was hemodynamically stable and afebrile. Physical examination revealed significant bilateral lower extremity edema. Laboratory examination noted leukocytosis: the white blood cell count was 18×10^9 cells/l. Renal injury was evident, with a blood urea nitrogen level of 16 mmol/l and a creatinine level of 350 μmol/l, which had increased from baseline levels of 12 μmol/l and 250 μmol/l, respectively, three days prior. Serum potassium was elevated to a level of 5.4 mEq/l. The activated partial thromboplastin time (aPTT) was prolonged to 96.7 seconds. Liver enzyme tests were normal. Electrocardiogram showed rate-controlled atrial fibrillation with no acute changes. Chest X-ray showed probable infiltrates suspected of pneumonia. Intravenous hydration was initiated. Her home dose of dabigatran was continued, and she received her first dose the morning after admission.

Within 24 hours, the patient was notably lethargic and oliguric. Laboratory examination demonstrated a deterioration in renal function, worsening of hyperkalemia, and an acute elevation of transaminases (aspartate aminotransferase level of 635 U/l and alanine transaminase level of 383 U/l). The sepsis workup was negative and demonstrated low procalcitonin levels. The computerized tomographic imaging results of the brain and the abdominal ultrasound results were unrevealing. Serial transthoracic echocardiography demonstrated new mild pericardial effusion that progressively increased for the next 4 hours and decreased the filling of the left ventricle and the dilatation of the inferior vena cava, with a decrease in the inferior vena cava respiratory variation, suggesting elevated right atrial pressure and indicating early cardiac tamponade (**Figure 1**). Dabigatran administration was halted. Within hours, the patient became hemodynamically unstable, with a further deterioration in mental status. The examination noted prominent jugular venous distention, distant heart sounds, and diffuse bilateral wheezes and crackles on auscultation. Repeat laboratory exams demonstrated evidence of multiorgan failure with metabolic acidosis (serum bicarbonate level of 14 mg/dl and lactate level of 4.9 mg/dl) and a significant deterioration in hepatic and renal function (blood urea nitrogen level of 20 mmol/l, creatinine level of 400 μmol/l, aspartate aminotransferase level of 927.5 U/l, and alanine transaminase level of 1955.9 U/l). The electrocardiogram now revealed atrial fibrillation with a rapid ventricular response and the diffuse low voltage across all leads. The trachea was intubated and connected to a ventilator. A repeat transthoracic echocardiogram now demonstrated increasing pericardial effusion with evident coagulum. The patient was subsequently started on norepinephrine for hemodynamic support. Idarucizumab was administered. The patient underwent successful echocardiography guided pericardiocentesis without complications. The aPTT the morning after pericardiocentesis remained normalized at 30.8 seconds. Initially, 500 ml of grossly hemorrhagic fluid was removed in the first 24 hours through the pericardial drain. The cytology results were negative for malignant cells. The blood cell count by volume of the pericardial fluid was greater than 50% of serum, consistent with hemopericardium. The patient recovered to baseline status over one week, with laboratory and clinical resolution of multiorgan failure and no echocardiographic evidence of hemopericardium.

Discussion

This case report has two significant results: first, the importance of point-of-care ultrasound in the early detection of underlying causes of shock and, second, the unpredictable changes in DOACs in terms of pharmacodynamics and pharmacokinetics in critically ill patients in the absence of direct monitoring of drug activity.

The superiority of DOACs over vitamin K antagonists is well documented and has led to an increase in its use in nonvalvular AF due to its predictable pharmacokinetics and pharmacodynamics, its effective anticoagulant effects, and the absence of the need for coagulation monitoring. (1) However, in the absence of routine laboratory coagulation monitoring, it makes it difficult and delays dosage adjustments in patients with acute renal impairment and severe liver impairment in critical care units. The thrombin clotting time, prothrombin time, and aPTT are not useful for coagulopathy with dabigatran since the drug is highly sensitive. (2) High clinical suspicion of hemorrhagic complications from DOAC is needed in the setting of critical care units, and the early withholding of the drug may prevent hemorrhagic complications.

Connolly, et al reported that the prevalence of significant bleeding was 2.71% per year in a group receiving dabigatran (110 mg bid) and was 3.11% per year in a group receiving dabigatran (150 mg

bid); the prevalence of life-threatening bleeding in those receiving 110 and 150 mg of dabigatran twice daily was 1.22% and 1.45%, respectively. (3) Hemopericardium is a rare complication of dabigatran therapy, and several cases of dabigatran-induced hemopericardium have been reported. (4-7) Dy and Shiltz reported two such cases with cardiac tamponade in the presence of acute renal failure. (8) Our case involved the development of hemopericardium with tamponade in the context of acute kidney injury, as the drug effect in the kidney is prolonged, and additional complications are expected because 85% of the drug is excreted from the kidney.

A structured ultrasound protocol in shock patients that evaluates the heart, inferior vena cava, abdomen, aorta, and lungs can provide rapid and valuable information in order to guide clinicians to better differentiate among the etiologies of shock. (9) The heart, particularly the pericardium, is the first organ to be evaluated in most ultrasound protocols in shock patients. (9) This was helpful in our case because the patient had morbid obesity and was taking bilevel positive airway pressure. Early intervention was performed with echocardiography guided pericardiocentesis.

Conclusion

Dabigatran etexilate is an oral anticoagulant that has been increasingly used in daily practice. However, life-threatening hidden hemorrhagic complications warrant caution. Our case highlights both a rare bleeding complication of dabigatran, and the effectiveness of idarucizumab, the approved reversal agent. Clinicians should evaluate bleeding risk factors and closely monitor renal function in patients in the setting of critical care units, especially in elderly patients. Urgent POCUS detected the complication early, and ultrasound-guided pericardiocentesis was followed by improved hemodynamic.

Competing of interest

Authors declare no potential conflicts of interest with respect to the case report, authorship, and/or publication of this article.

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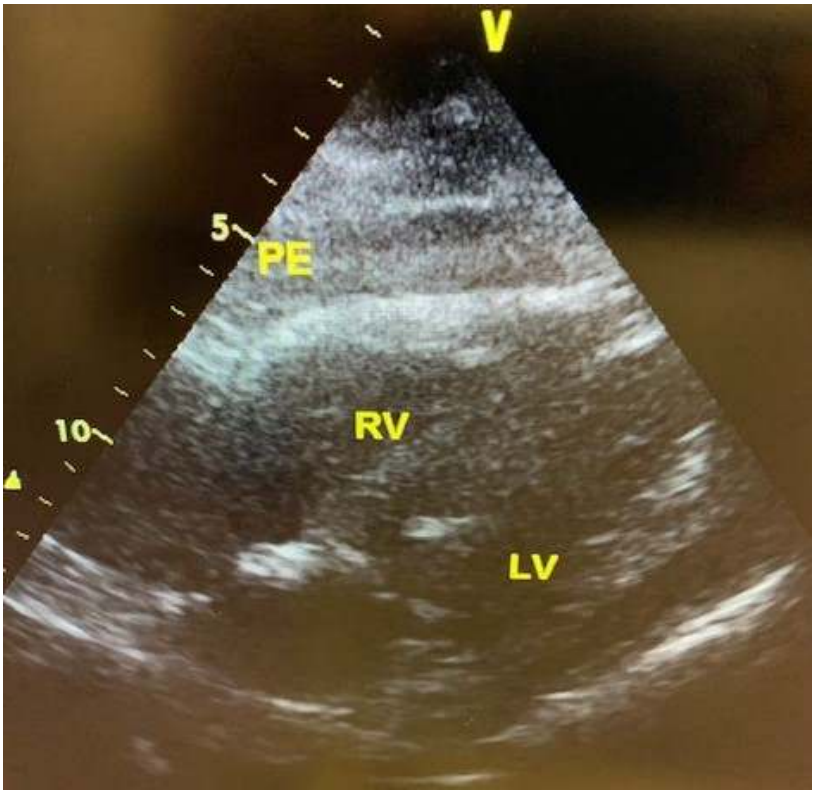
Contribution

ZB wrote the article, OM and MJ shared in the discussion and with TZ shared in collecting the data and revision of the manuscript.

Figure 1. Echocardiography in left parasternal view



Legend: LV=left ventricle; RV=right ventricle; PE=pericardial effusion.

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