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# A Reversal Agent in Time can Save Life- The Role of Idarucizumab in Dabigatran Associated Intracranial Bleed- A Case Report

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## Abstract

Dabigatran is a non-vitamin K antagonist oral anticoagulant (NOAC) whose widespread use for various indications has increased. Intracranial bleed in patients receiving dabigatran is a rare occurrence but can be fatal if reversible agent Idarucizumab is not administered immediately to reverse its effects.

Here we report a case of a 70-year-old lady who was on low dose Dabigatran (110 mg) for chronic deep venous thrombotic disease for 1 year, developed sudden onset of left hemiplegia with altered sensorium. She was evaluated and diagnosed to have right thalamic bleed with intraventricular extension at another center. She presented to our hospital 14 hours after the index event and Injection Idarucizumab 5 g was administered intravenously. An extra ventricular drain was placed on the next day. She had improved clinically without increase in intracranial hematoma and was discharged with mild left hemiparesis. But she developed deep venous thrombosis in the hemiparetic leg 20 days after the stroke and low molecular weight heparin was given for it.

We want to highlight the importance of giving the reversal agent Idarucizumab for dabigatran induced bleed even in late presentation.

## Keywords

Intracranial bleed, Anticoagulants, Hemorrhage, Hemiplegia

## Introduction

With rapid increase in usage of NOACS for various indications, the incidence of life- threatening hemorrhage is bound to increase. But reversal agents are not readily available for all the NOACs in case of bleeding. Idarucizumab is a humanized monoclonal antibody fragment with high affinity for dabigatran and effectively antagonizes its action in a few minutes [1]. Intracranial hemorrhage is a rare, yet deadly complication associated with the use of NOACS in elderly patients. Idarucizumab usage in such patients can decrease the chance of hematoma expansion and mortality associated with the bleed. Here we share our experience about a patient taking NOAC who had an intracranial bleed that was successfully treated with reversal agent Idarucizumab. The knowledge regarding specific reversal agents like Idarucizumab is essential to counter the effects of bleeding associated with NOACS in this current era.

## Case Report

A 70-year-old lady with medical history of hypertension, hypothyroidism and chronic deep venous thrombosis of the right leg was on 110 mg of dabigatran twice a day and aspirin 75 mg once daily. She presented to the emergency department in the morning with sudden onset of left-sided hemiplegia followed

by altered sensorium and vomiting since the previous day evening with NIHSS of 18 and HAS- BLED score of 3. The patient attenders have given her a dose of dabigatran and aspirin after the event thinking it to be an ischemic stroke. She was diagnosed to have intracranial bleed at a local hospital where she received supportive treatment and arrived in our hospital 14 hours after the event. On admission she had high blood pressure of 190/110 mm Hg, Glasgow coma score of 8 and left hemiplegia. Computed tomography (CT) scan of the brain **(**Figure 1**)** showed right thalamic bleed of size 5 x 4.1 x 3 cm with intraventricular extension, perilesional edema with midline shift of 7 mm. Dabigatran and aspirin were discontinued due to the bleed. Her renal parameters (Creatinine of 0.58 mg/dl, eGFR = 97 ml/min/1.73 $m^2$) and prothrombin time with INR (13.2 seconds/1.1) was normal whereas activated partial thromboplastin time (30.9 seconds) was in higher normal range. In view of the intracranial bleed and as the patient was on dabigatran, she was administered Idarucizumab 2 hours after admission in our hospital. Injection Idarucizumab 5 g as two 2.5 g boluses were administered intravenously approximately 16 hours after the onset of symptoms of intracranial bleed. Extra ventricular drain was placed on the next day in view of the midline shift. She was kept on ventilator support due to poor GCS. Repeat CT scan of the brain on third day **(**Figure 1**)** showed 4.4 x 2.8 x 4.5 cm size of right intraparenchymal bleed with no expansion of the hematoma. Patient developed deep venous thrombosis in the hemiparetic leg 20 days later and was started on subcutaneous low molecular weight heparin. She was gradually weaned off from the ventilator and extubated 3 weeks later. Patient received antihypertensives, levothyroxine, antiepileptic, physiotherapy, and other supportive measures while in the hospital. The muscle power improved from 0/5 to 4/5 (NIHSS of 7) and was discharged after 1 month from the index event.

## Discussion

New oral anticoagulants have emerged as an alternative to warfarin in the treatment of venous thromboembolic disease and prevention of thromboembolic events in nonvalvular atrial fibrillation [2].

Dabigatran etexilate (dabigatran) is an oral thrombin inhibitor that reaches its peak plasma concentration within 2 hours of ingestion, with bioavailability of 3-7%, plasma protein binding of 35%, with predominant (80%) renal elimination, 12-17 hours of half-life with normal GFR [3]. Although dabigatran is associated with less serious bleeding than warfarin, life-threatening bleeding can occur. These patients may require urgent surgery/ intervention with increased risk of perioperative bleeding.

Dabigatran was the first direct oral anticoagulants to have its own specific reversal agent -idarucizumab, a monoclonal antibody. Idarucizumab binds dabigatran with an affinity of 350-fold higher than the affinity of dabigatran for thrombin.

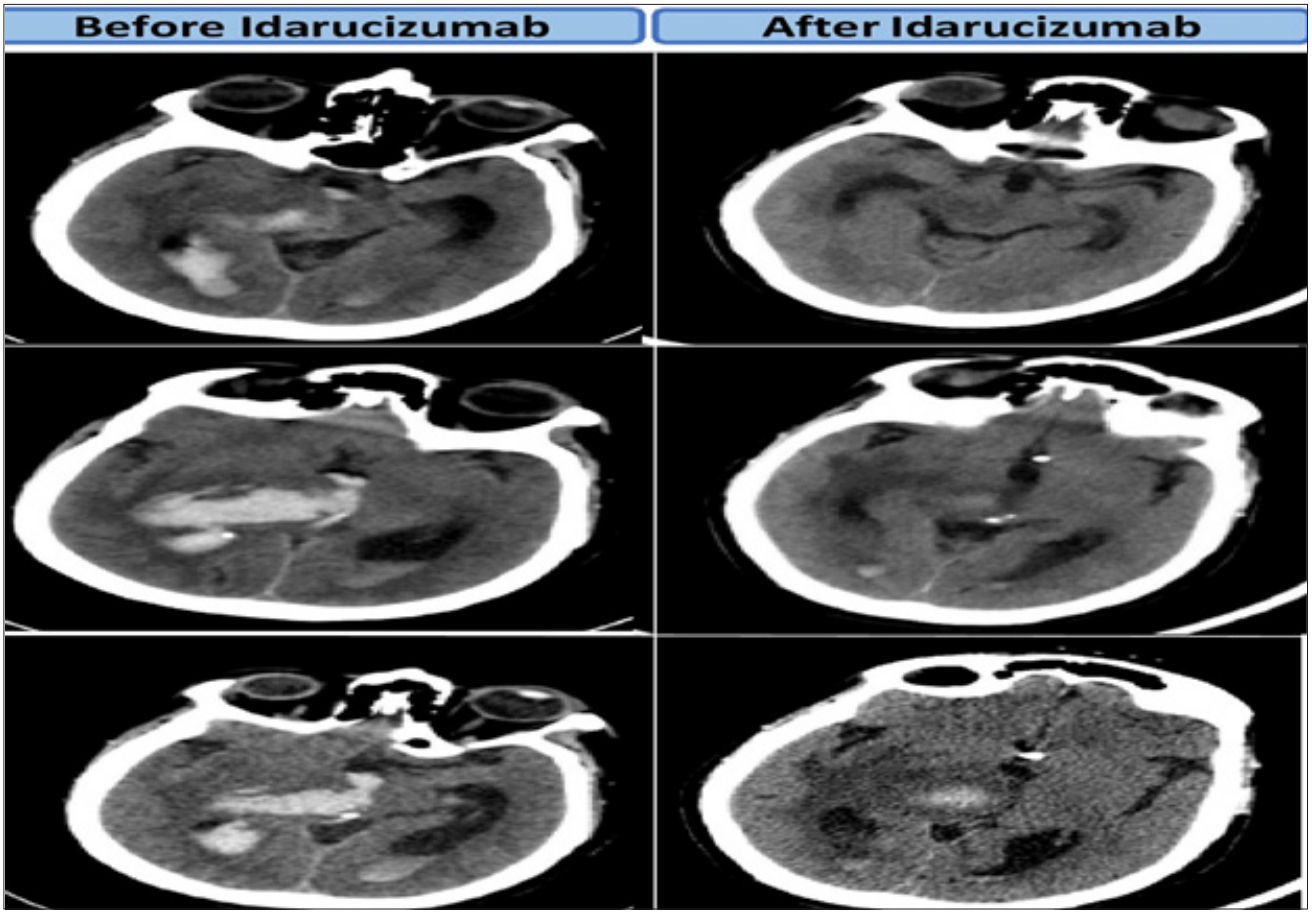


**Figure 1:** CT brain comparing ICH before and after administering Idarucizumab.

Idarucizumab binds unbound, thrombin-bound dabigatran and the active glucuronide metabolites of dabigatran form 1:1 complexes. After binding of dabigatran to idarucizumab, the anticoagulant effects of unbound and protein-bound dabigatran and its active metabolites are neutralized [4]. Indications for using Idarucizumab are emergency surgery/procedures in patients taking dabigatran having acute life-threatening bleeding, [1] or patients with accidental dabigatran overdose [5].

Elderly hypertensive patients on dabigatran are more prone to develop intracranial bleed which is a life- threatening condition. The morbidity and mortality can be reduced with specific reversal agents like Idarucizumab as it can prevent the expansion of hematoma and facilitates the recovery of patients even in late presentation. It is a safe and effective agent whose administration benefit outweighs the risk in elderly hypertensive patients with Dabigatran associated intracranial bleed [6].

## Conclusion

Due to increased use of dabigatran for various conditions, the bleeding incidence especially of intracranial hemorrhage is expected to rise. So, the knowledge, accessibility and prompt usage of reversal agent are crucial chain of events to reduce morbidity and mortality in dabigatran associated major bleed (intracranial bleed). When available, idarucizumab should be used in dabigatran-induced life-threatening bleeding, even if they present late as in our case.

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