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Case Report

Use of Idarucizumab for dabigatran reversal: Emergency department experience in two cases with subdural haematoma

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ABSTRACT

Introduction: Idarucizumab is the first effective humanized monoclonal antibody fragment developed specifically as a reversal agent for dabigatran, a Direct Oral Anticoagulant. Despite recent trials demonstrating reversal of clinically relevant bleeding, there is a paucity of data on use outside the trial setting. This manuscript describes the use of Idarucizumab to reverse dabigatran in two patients presenting to the emergency department of a major tertiary hospital with acute traumatic subdural haematomas (SDH).

Methods: Patients were identified through retrospective review of medication dispensing systems and electronic medical records.

Results: Two cases of Idarucizumab use were identified. Case 1 was of a 63-year-old male who presented following a motorcycle crash. Case 2 was of a 77-year-old male who presented with a 3-week history of ataxia and recurrent falls. Both patients were taking dabigatran for atrial fibrillation (AF). CT Brain revealed acute SDH with clinical indications for urgent surgical evacuation. Serum dabigatran levels were obtained on arrival in the emergency department with levels of 155 ng/ml and 110 ng/ml (reference range 117–275 ng/ml). Idarucizumab for dabigatran reversal was commenced; Case 1 received 5 g Idarucizumab as an intravenous bolus dose, while Case 2 received 5 g Idarucizumab as two 2.5 g intravenous infusions. Serum dabigatran levels for Cases 1 and 2 were 0 ng/ml at 75 min and 340 min post Idarucizumab administration respectively. Both patients proceeded to craniotomy with evacuation of the SDH. There was no extension of the SDH in either case. Anticoagulation was withheld until outpatient clinic review, and both patients transferred for rehabilitation prior to discharge home.

Conclusion: Idarucizumab was clinically effective for reversing dabigatran, resulting in undetectable serum levels, and should be considered in patients presenting to hospital with clinically significant bleeding associated with dabigatran therapy.

Introduction

In-hospital mortality in the setting of disorders of coagulation and traumatic brain injury (TBI) has been reported to be approaching 50% [1] Timely normalization of coagulopathy has also been associated with improved outcomes [2] Dabigatran, a direct thrombin inhibitor, is a novel anticoagulant. Patients treated with dabigatran who present with major bleeding or need urgent

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Table 1
Case 1 laboratory data.

Laboratory markers (reference ranges)	Admission	Post Idarucizumab Administration (T = 75 min from administration)
Dabigatran (117–275 ng/ml)	155	0
PT* (10.6–15.3 s)	17.4	14.1
APTT* (26–38 s)	63	35.5
INR* (0.9–1.3)	1.4	1.1
TCT* (14–24 s)	133.4	18.1

surgical intervention are at risk of severe complications due to the anticoagulation effects [3] Idarucizumab is the first effective humanized monoclonal antibody fragment developed specifically as a reversal agent for dabigatran [4–6] The Therapeutic Goods Administration approved the use of Idarucizumab in Australia in June 2016.

Early studies in healthy young patients and those between 45 and 80 years old with mild to moderate renal impairment have demonstrated idarucizumab rapidly reverse the anticoagulant effects of dabigatran and achieve haemostasis without pro-thrombotic effects. However, the safety and efficacy in patients with serious bleeding or who require urgent surgery is not known.

This case series documents the use of Idarucizumab to reverse dabigatran in patients presenting to the emergency department of a major tertiary hospital with acute traumatic subdural haematomas (SDH).

Methods

Patients were identified through retrospective review of medication dispensing systems and electronic medical records. Two cases were identified from 1/1/2016 to 1/6/2016 and informed consent to present this report obtained. The study was approved by The Alfred Hospital Research and Ethics Committee.

Results

Two cases were identified for inclusion. Case 1 was of a 63-year-old male who was transferred from a regional centre following a motorcycle crash. He had a history of atrial fibrillation for which he was prescribed dabigatran. Computed tomography (CT) imaging following the crash showed a SDH with mass effect. Fresh Frozen Plasma and a 3-factor prothrombin complex concentrate were administered prior to transfer. Upon arrival at our centre, and following analysis of laboratory data and multi-disciplinary medical team discussions, a decision to administer Idarucizumab was made. Laboratory results are listed in Table 1 and a timeline of events in Fig. 1. A single 5g-bolus dose of Idarucizumab was administered. The patient proceeded to the operating theatre where he underwent a craniotomy and evacuation of the SDH. Surgery was successful and haemostasis was achieved. Post-operative complications involved residual dysphasia, which resolved within 2 weeks post discharge. There was evidence of residual SDH on CT scans performed at 2 and 4 weeks post the crash but with no acute component. Anticoagulation was withheld and the patient was discharged into the care of his local medical officer who was advised to restart anticoagulation if there had been no extension of SDH on a follow-up CT scan to be performed 6 weeks post crash.

Case 2 was of a 77-year-old male who presented with an ataxic gait and recurrent falls, increasing in frequency in the preceding 3 days. He had a history of atrial fibrillation for which he was prescribed dabigatran. CT imaging revealed an acute on chronic SDH. Laboratory investigations confirmed active anticoagulation (Table 2) and a timeline of events outlined in Fig. 2. Multi-disciplinary medical discussions resulted in a decision to administer Idarucizumab. The patient was prescribed a 5 g dose of Idarucizumab, administered as two 2.5 g bolus doses spaced 5 min apart. No other blood products were administered to achieve haemostasis. The patient proceeded to the operating theatre for a frontoparietal mini craniotomy and evacuation of the SDH. The post-operative course was uncomplicated but routine CT follow-up at 4 weeks showed some residual SDH, although the patient was asymptomatic. A decision was made to remain off anticoagulation until a repeat CT was performed in 8 weeks time. CT scans performed seven months

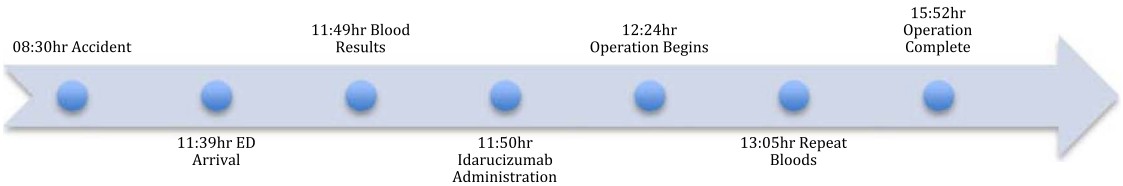

Fig. 1. Case 1 Timeline.