

## CASE REPORT

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# Fatal spontaneous intraperitoneal hemorrhage in association with apixaban: A case report

Daniel P Mckenna, Martin Kelly, Terence Murphy

## ABSTRACT

We present the case of an 80-year-old gentleman with a spontaneous intraperitoneal hemorrhage secondary to direct oral anticoagulant (DOAC) medication. As far as we are aware this is the third documented case of spontaneous intraperitoneal hemorrhage in association with direct oral anticoagulants (DOACs) therapy. Previously published cases have also cited apixaban as the associated DOAC. With their increasing prevalence, spontaneous intraperitoneal hemorrhage should be a recognized presentation for the patient in extremis on DOAC therapy.

**Keywords:** Apixaban, Hemorrhage, Intraperitoneal, Spontaneous

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## INTRODUCTION

We present a case of spontaneous intraperitoneal hemorrhage, otherwise known as abdominal apoplexy. Our case centers on a previously independent 80-year-old gentleman admitted post a hip fracture at home. He was commenced on direct oral anticoagulant (DOAC) therapy for newly diagnosed atrial fibrillation as an inpatient. He suffered an in hospital cardiac arrest on day 85 post-surgery. This was as a result of spontaneous intraperitoneal hemorrhage secondary to his DOAC therapy. Given the prevalence of these medications and the requirement for an expedited diagnosis, we believe that awareness of DOAC associated abdominal apoplexy is of utmost importance to those in clinical practice.

## CASE REPORT

Our patient presented to the emergency department with a right sided sub-capital neck of femur fracture following a fall on a wet floor at home. His past medical history was significant for ischemic heart disease requiring percutaneous coronary intervention (PCI), hypertension, and hypercholesterolemia. A new diagnosis of atrial fibrillation on presentation was managed with low molecular weight heparin, in the form of Clexane (Sanofi) 40 mg subcutaneously once daily, perioperatively and DOAC therapy in the form of apixaban postoperatively.

A right-sided hemiarthroplasty was performed three days post-injury and apixaban was commenced two days post-procedure. A subsequent fall postoperatively resulted with an inability to extend his left knee day seven post-hemiarthroplasty. An ultrasound confirmed quadriceps tendon rupture was repaired 14 days after the original fall at home. This repair was completed using a Kessler technique with two 2 Fiberwire (Arthrex) sutures inserted trans-osseously through the patella. Apixaban was restarted two days post-tendon repair. Following

this repair our patient received 72 days of continuous apixaban therapy.

Our patient had a prolonged inpatient stay as a result of slow progress with rehabilitation. A fluctuating delirium resulted post-quadriceps tendon repair with no specific trigger identified. The combination of a contralateral hemiarthroplasty and quadriceps rupture was the primary barrier to progress with physiotherapy. On day 88 post-admission, our patient reported feeling unwell with nonspecific abdominal pain. On examination he was tender in the epigastrium with a Glasgow Coma Score (GCS) of 15/15. At this time his pulse was 72 beats per minute, blood pressure 98/52 mmHg, and oxygen saturations were 96% on room air.

An acute deterioration followed in the next 90 seconds as his GCS fell to 3/15, associated with no pulse. Cardiopulmonary resuscitation was commenced in the form of chest compressions, a total of 7 mg epinephrine, 300 mg amiodarone, and two 200 J shocks for pulseless ventricular tachycardia. Return of spontaneous circulation (ROSC) was achieved 25 minutes post-arrest.

Immediately following ROSC, bloodwork was as follows; hemoglobin 6.8 g/dL, pH 6.9, lactate 9.6 mmol/L, and base excess—25.8 mEq/L. The sudden hemoglobin drop from 14 g/dL one week prior to 6.8 g/dL post-resuscitation prompted an emergency computed tomography (CT) angiogram following ROSC.

The CT angiogram demonstrated a hematoma surrounding the third part of the duodenum with active arterial blush (Figure 1). The hemorrhage originated from the inferior pancreaticoduodenal artery. This subsequently tracked to form perihepatic and peri-splenic hematomas (Figure 2).

Following discussion with the family and assessments by critical care, surgical, and radiological specialists, our patient was felt to have a poor prognosis. He was deemed not suitable for surgical or interventional radiological management. Our patient passed away six hours post-cardiac arrest following a further cardiac arrest in ICU.

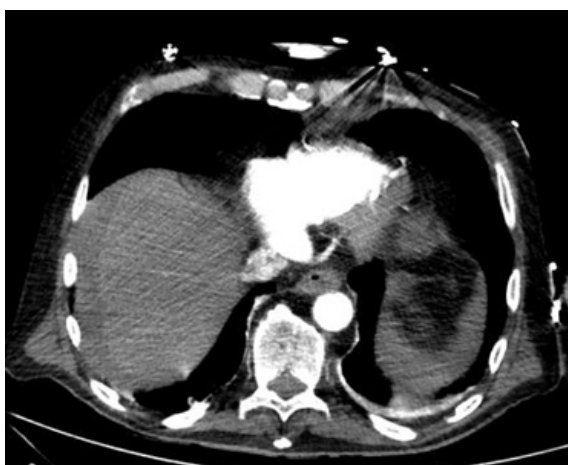


Figure 1: This axial image of the CT angiogram demonstrates a hematoma surrounding the third part of the duodenum with active arterial blush.



Figure 2: This axial CT image illustrates that the hemorrhage seen in Figure 1 has tracked to form perihepatic and peri-splenic hematomas.

## DISCUSSION

Idiopathic spontaneous intraperitoneal hemorrhage (ISIP) also known as abdominal apoplexy is a rare cause of cardiovascular compromise with 30% of cases having no identifiable cause as in our case [1]. Causes can be divided in relation to their anatomical location or their underlying disease pathology. For cases of ISIP associated with coagulopathy, an iliopsoas hemorrhage is the most common site [2].

Given the low incidence, it presents a diagnostic challenge when using history and clinical examination alone. This is ever more challenging when a patient presents with cardiac arrest on the ward as in our case. The risk factors identified in our patient for ISIP were his cardiovascular history and DOAC therapy. We acknowledge that our case is one without an exact etiology for this hemorrhage, which as aforementioned is not uncommon. However, we do believe the DOAC therapy to be a contributory factor in this patient's mortality. As such, awareness of abdominal apoplexy is important for those managing patients on DOACs.

In terms of diagnosis, the modality of choice is an abdominal CT angiogram [3]. This can be used to localize the source of hemorrhage and determine the most appropriate treatment algorithm, be it surgical or angiographic management.

Direct oral anticoagulants are a class of anticoagulants primarily used for stroke prevention in non-valvular atrial fibrillation [4]. Unlike rivaroxaban, apixaban, and dabigatran have been shown to have a safer bleeding profile than the traditional oral anticoagulant of choice, warfarin [5]. In hemorrhage prevention, care should be taken in patients with chronic kidney disease or those at risk of acute kidney injury given the renal clearance of these medications.

Spontaneous hemorrhage in association with rivaroxaban has previously given rise to cardiac

tamponade [6] and spontaneous vitreous hemorrhage [7]. Cases of atraumatic splenic hemorrhage have been noted with apixaban, dabigatran, and rivaroxaban [8].

A literature search of PubMed and Google Scholar was performed on 21st April 2024. The terms “intra peritoneal hemorrhage,” OR “retroperitoneal hemorrhage,” OR “intra peritoneal haemorrhage,” OR “retroperitoneal haemorrhage,” AND “spontaneous” were searched. Studies where a DOAC was the only known contributing factor were included. Hemorrhages associated with underlying disease pathology and/or trauma were excluded. Interestingly for the two case reports found apixaban was the associated anticoagulant [9, 10].

Based on this search, ours is the third case of abdominal apoplexy in association with apixaban. Given the prevalence of the medication we recommend the consideration of ISIP in those patients with acute abdominal pain on a DOAC medication.

## CONCLUSION

This case report of fatal idiopathic spontaneous intraperitoneal hemorrhage in association with apixaban is a reminder to the risks associated with anticoagulation. As in our case, most patients commenced on DOAC therapy are elderly and vulnerable to hemodynamic compromise. Bearing in mind the widespread use of DOACs, this is a differential diagnosis that may need more consideration going forward.

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## Author Contributions

Daniel P Mckenna – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Martin Kelly – Conception of the work, Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Terence Murphy – Conception of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

## Guarantor of Submission

The corresponding author is the guarantor of submission.

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## Consent Statement

Written informed consent was obtained from the patient for publication of this article.

## Conflict of Interest

Authors declare no conflict of interest.

## Data Availability

All relevant data are within the paper and its Supporting Information files.

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