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Jessica Barnes

MedStar Union Memorial Hospital

Zayd Alhaddad

MedStar Union Memorial Hospital, zayd.alhaddad@medstar.net

Robert Paz

MedStar Union Memorial Hospital

Christopher Haas

MedStar Union Memorial Hospital

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Atraumatic Splenic Rupture on Direct Oral Anticoagulation

Barnes Jessica ^a, Alhaddad Zayd ^{a,*}, Paz Robert ^b, Haas Christopher ^{a,c}

^a MedStar Health Internal Medicine Residency Program, USA

^b MedStar Health, Hospitalist Medicine, USA

^c Georgetown University Medical Center, USA

Abstract

Direct Oral Anticoagulants have become a popular go to treatment option for patients with atrial fibrillation, deep vein thrombosis, or pulmonary embolism. This case report follows a 58 year old woman who developed atraumatic splenic rupture, a rare but recognized complication of direct oral anticoagulation use.

Keywords: Splenic rupture, Apixaban, Pulmonary embolism

1. Introduction

Apixaban is a direct factor Xa inhibitor whose popularity has increased since it was demonstrated non-inferior to warfarin for stroke prevention in patients with atrial fibrillation as well as for management of venous thromboembolism, with a decreased risk of major bleeding, in the ARISTOTLE and AMPLIFY trials, respectively.¹⁻³ Despite the reduced bleeding risk, atraumatic splenic rupture has been increasingly recognized as a complication of apixaban use. The literature categorizes splenic rupture into two broad categories: traumatic vs. atraumatic. Atraumatic splenic rupture (ASR) can further be broken down into atraumatic-pathologic or atraumatic-idiopathic; drug-associated rupture would be included in the former.⁴ The incidence of ASR has been reported to be 3.2%.⁵ Case series have found between 7.2% and 50% of ASR cases to be related to drug related causes.^{4,6,7} More specifically, 33% of the drug related ASR cases have been found to be due to anticoagulant use.⁶ Here we discuss a case of atraumatic splenic rupture in a 58-year-old female on apixaban for deep vein thrombosis (DVT).

2. Case presentation

A 58-year-old female with a history of venous thromboembolism on apixaban presented to the emergency department with a two-week history of progressive right flank and hip pain associated with ambulation. She reported no antecedent trauma or heavy lifting prior to symptoms development and noted no additional swelling, discoloration, bruising, or decreased functional capacity during this time. Given the persistence of her symptoms and lack of response to over-the-counter pain medications, she presented for further evaluation. Additional medical history was notable for bipolar disorder, schizophrenia, and breast cancer treated with lumpectomy, radiation, and anastrozole.

In the emergency department, the patient was hemodynamically stable with a preserved heart rate (97 beats per minute), mild hypertension (149/88 mmHg), and preserved saturations on room air. Physical examination was unremarkable, without evidence of abdominal, flank, or costovertebral tenderness, rash, or ecchymoses. There was no associated musculoskeletal tenderness and range of motion at the hip was preserved. Laboratory diagnostics demonstrated mild leukopenia [3.1 k/uL

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* Corresponding author.
E-mail address: zayd.alhaddad@medstar.net (A. Zayd).

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(Reference range 4 k/uL - 10.8 k/uL)], hyponatremia [131 mmol/L (reference range 137 mmol/L-145 mmol/L)], and a normal hemoglobin [11.9 gm/dL (reference range 11 gm/dL- 14.5 gm/dL)]. Urinalysis was unremarkable. Diagnostic imaging included a Computed tomography scan (CT) with contrast of the abdomen and pelvis did not demonstrate any evidence of acute pathology. Given the unremarkable workup, she was discharged home with planned primary care follow-up and ongoing conservative management.

Four days after discharge she presented to the emergency department once again, this time with multiple episodes of near-syncope and a single witnessed syncopal episode. Her symptoms were associated with epigastric abdominal pain, decreased appetite, and daily non-bloody, non-bilious emetic episodes that developed shortly after her recent discharge. In triage, her vitals were within normal limits except for hypotension (85/63 mmHg, nadiring to 73/49 mmHg), for which she was provided with one liter of normal saline. Laboratory diagnostics were notable for a marked normocytic anemia (6.3 g/dL). CT of the abdomen and pelvis with contrast demonstrated splenomegaly, active extravasation into the anterior superior capsule with a large subcapsular and perisplenic hematoma, and a large hemoperitoneum, consistent with grade IV splenic rupture (Fig. 1). Given her adherence to apixaban she was transfused with 2 units of packed red blood cells and managed for DOAC-related bleeding with 4-Factor Prothrombin Complex Concentrate. Interventional radiology (IR) was consulted and performed a superior pole splenic artery embolization (Fig. 2). Post-procedure she remained

hemodynamically stable; however, her course was complicated of recurrent mild tachycardia, hypotension, and a post transfusion hemoglobin drop (6.3 g/dL from 7.2 g/dL). Repeat CT with contrast was performed and demonstrated stable findings. She returned to Interventional Radiology for coil embolization of the proximal splenic artery. She required 2 units of packed red blood cells after which her hemoglobin remained stable at 8.4 g/dL with no further episodes of bleeding and was subsequently discharged. Her splenic function was spared, and she did not receive any vaccinations upon discharge.

Of note, the patient was taking apixaban in the context of a provoked DVT sustained three years prior. After discussion with her primary care physician to confirm to provoked nature of her DVT, anticoagulation was discontinued at the time of discharge.

3. Discussion

Atraumatic splenic rupture is a rare but potentially fatal complication of direct oral anticoagulant (DOAC) use with a mortality rate of up to 13%.⁶ It has been hypothesized that anticoagulant use alters splenic hemostasis, thereby predisposing to micro-trauma and reactive macrophage infiltration, with resultant splenic rupture.^{8,9} Diagnostic delay, specifically in the setting of non-specific complaints,^{5,8–10} and an oftentimes unremarkable physical examination has been noted to be one of the main contributors to mortality.⁷ Atraumatic splenic rupture accounts for 3.2% of splenic ruptures as reported in one study, with approximately one-third of cases associated with anticoagulant use.^{5,6} CT remains the imaging modality of choice for diagnosis, providing not only an overall grade of splenic injury, with important implications for management decisions, but also evidence of active bleeding.⁴

Management of atraumatic splenic rupture in the context of DOAC use focuses initially on stabilization of hemodynamics and DOAC reversal, if necessary. Currently published literature advocates for reversal in the setting of anticoagulant mediated atraumatic splenic rupture, however careful consideration to the timing of the last anticoagulant dose as well as cost and local availability of the reversal agents should be taken into consideration.⁹ While Andexanet Alfa is considered the standard reversal agent for apixaban and rivaroxaban, its use is often limited by availability and cost. The patient in this report received Four Factor Prothrombin Complex Concentrate (4F-PCC; K-centra), which contains non-activated vitamin K-dependent factors (F2, F7, F9, and F10) with the ultimate goal of supplementing native, yet



Fig. 1. Enlarged spleen with active hematoma and extravasation visible as indicated by the darker areas within the spleen (red arrow). The extravasated blood can also be appreciated around the liver, seen as the dark crescent shape on the lateral border of the liver (yellow arrow).

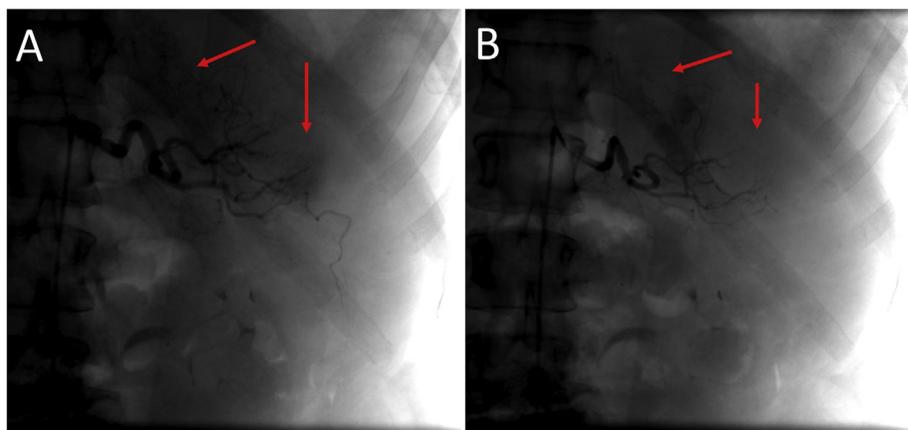


Fig. 2. Splenic artery angiography. (A) demonstrates active extravasation as seen by the subtly darker areas indicating contrast outside the blood vessels (red arrows), suggestive of ongoing hemorrhage. (B) demonstrates post-embolization sequences where these darker patches are no longer visible.

currently inhibited clotting factors.¹³ While 4F-PCC has not yet been extensively studied in patients on apixaban, early studies show that its use (25 units/kg) reversed the anticoagulant effects of patients on therapeutic doses of apixaban.¹⁴ For patients receiving reversal, close monitoring for recurrent thrombosis, even in the context of resumption of anticoagulation is required, given that the 30-day thrombosis rate appears to be between 4.8 and 10% depending on agent use, with a presumed underlying contribution of the patients underlying coagulable baseline state.¹³

Guidelines pertaining to surgical or catheter-directed management are limited, with no definitive consensus statements. Our patient initially received medical management with 4F-PCC and catheter-based management with selective superior pole arterial embolization. As noted, her course was complicated by a recurrent hemoglobin decline with associated relative hemodynamic instability for which she underwent more proximal arterial embolization. In general, our management was consistent

with the recommendation that hemodynamically stable patients can be sent for non-operative embolization while hemodynamically unstable patients should receive surgical intervention.¹⁵ Multiple case series have recommended surgery as the definitive treatment for atraumatic splenic rupture.^{5,6,11} One study found that up to 60% of patients undergoing embolization needed subsequent surgical intervention.¹⁰ Another large systematic review by Renzulli et al. found that 85.3% of atraumatic splenic rupture cases underwent surgical management with a marked improvement in mortality (7.4% vs. 14.7%) compared to non-operatively managed cases.⁶ Furthermore, 17% of those initially managed medically required secondary operative intervention with a mortality rate of 4.4%.⁶ This study not only highlighted the dichotomy between traumatic and atraumatic splenic rupture, but also advocated for surgical management of hemodynamically stable patients, highlighting baseline splenic dysfunction with functional asplenia.⁶ Nevertheless, it remains to be determined whether individuals with atraumatic

Table 1. Grade classification of splenic rupture and management for each grade.

Grade	Features	Management
I	Subscapular hematoma <10% of surface area Parenchymal laceration <1cm	If hemodynamically stable: conservative management and monitoring with repeat imaging in 1 week
II	Subscapular hematoma 10%-50% of surface area Intraparenchymal hematoma <5cm Parenchymal laceration 1-3cm	If hemodynamically unstable: Urgent surgical intervention (laparotomy)
III	Subscapular hematoma >50% of surface area Intraparenchymal hematoma >5cm Parenchymal laceration >3cm	
IV	Involvement of splenic vascular injury or active bleeding	Splenic angiography with embolization or surgical intervention
V	Completely shattered spleen Devascularization of the entire spleen	Urgent surgical intervention

splenic rupture in the context of anticoagulation are functionally asplenic. In contrast, Miller et al. favors non-operative management in hemodynamically stable patients, with the goal of splenic salvage given little evidence of splenic dysfunction before or after embolization.¹⁵ Splenic artery embolization is currently recommended for grade 4–5 injury by the American Association for the Surgery of Trauma Organ Injury Scale (see Table 1).¹⁵

4. Conclusion

Atraumatic splenic rupture is a serious but rare complication in patients taking DOACs. The diagnosis is often delayed in the setting of non-specific presenting symptoms. A comprehensive history and broad initial differential are imperative to aid in early diagnosis. Diagnostic imaging should be used to guide management. Careful consideration should be given to the duration of anticoagulation therapy, the timing of the last dose, and the need for ongoing anticoagulation to further limit the risk of atraumatic splenic rupture. Specific research pertaining to the pathophysiology of anticoagulation-related atraumatic splenic rupture is needed and best practices for management of this disease are warranted.

Conflict of interest

The authors report there are no competing interests to declare.

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