

CASE REPORT

Warfarin-induced spontaneous retroperitoneal hemorrhage from the renal vein: A rare case with an uncommon etiology

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ABSTRACT

The overall rate of major bleeding in patients with atrial fibrillation receiving warfarin therapy is approximately 4%. Among these 4% patients, spontaneous retroperitoneal hemorrhage (SRH) is a rare but potentially lethal complication with a nonspecific presentation that can lead to missed or delayed diagnosis. The current literature provides little direction for diagnosis and management of such cases. Anticoagulation-related SRH is associated with a high mortality rate (approximately 20%). Despite the vague presentation, prompt diagnosis is crucial to reverse the anticoagulation and prevent further bleeding. Contrast-enhanced computed tomography (CT) of the abdomen is the imaging modality of choice in suspected cases. Patients with SRH require aggressive treatment with blood transfusions, interventional radiological procedures, percutaneous drainage or surgical evacuation of the hematoma. We report a case of warfarin-induced SRH from the renal vein in a patient who presented to our emergency department with acute, nonspecific abdominal pain and shock. We diagnosed the patient with warfarin-induced SRH on the basis of clinical suspicion and characteristic CT findings. We initially treated the patient conservatively, followed by embolization of the right renal artery during the late course of hospital stay, and he was discharged with good recovery. SRH should be considered in the differential diagnosis of abdominal pain, hypotension, and/or decreased hemoglobin levels in patients receiving anticoagulation therapy, especially in those with preexisting end-stage renal disease.

Keywords: warfarin-induced spontaneous retroperitoneal hemorrhage, retroperitoneal hematoma, warfarin, renal hemorrhage, renal vein, emergency, anticoagulation

INTRODUCTION

The overall rate of major bleeding in patients with atrial fibrillation (AF) receiving warfarin therapy is approximately 4%.¹ Among these 4% patients, spontaneous retroperitoneal hemorrhage (SRH) is a rare but potentially lethal complication with a nonspecific presentation that can lead to missed or delayed diagnosis.^{2,3} SRH is defined as a hematoma unrelated to invasive procedures, surgery, trauma, or abdominal aortic aneurysm.² According to an observational cohort study done in the department of emergency medicine in Mayo Clinic from January 2000 to December 2007, approximately 66.3% of patients with SRH receive anticoagulants alone, 30.3% receive antiplatelet medications alone, 16.5% receive both, and 15.3% receive neither,² without any obvious precipitating factors. Most patients receive anticoagulation therapy for venous thromboembolism (deep vein thrombosis and/or pulmonary embolism) or heart conditions (prosthetic valves and/or AF). Patients receiving anticoagulation therapy usually have more severe hematomas with a higher frequency of severe anemia and shock.⁴ Other risk factors for major bleeding in patients receiving anticoagulants include anemia, severe renal disease, age ≥ 75 years, prior bleeding, and hypertension.⁵ Patients with end-stage renal disease (ESRD) are more prone to hemorrhagic complications,⁵⁻⁷ mainly due to platelet dysfunction, anemia, and low vitamin K levels.

The clinical presentation of SRH is nonspecific, and patients usually present with abdominal, groin, hip, or back pain. Around one-third of patients may also present with hypotension or shock.⁴ Patients with a hematoma involving the iliopsoas muscles may present with femoral nerve palsy or a stroke mimic.^{2,4}

Massive bleeding into the retroperitoneum is a true emergency because it may cause intravascular volume depletion, with or without increasing the intraabdominal pressure, compromising perfusion to other vital organs.⁸⁻¹⁰ This requires prompt recognition to reverse the effect of anticoagulants and stop the bleeders. Only a few case reports have been published on the fatality of SRH.^{11,12} We report a case of warfarin-induced SRH from the renal vein that we

initially managed conservatively, followed by embolization of the right renal artery later during hospital stay, with good recovery.

CASE PRESENTATION

A 67-year-old male patient presented to the emergency department with a history of abdominal pain for three days and fever for one day. The abdominal pain was of mild to moderate intensity and worsened in the right loin area a day before presentation. The pain was associated with hematuria without any history of trauma or abdominal procedure. The patient was a known case of ESRD and had been receiving continuous ambulatory peritoneal dialysis four times a day. He also reported slightly turbid peritoneal dialysis fluid and low outflow during the last three days. His chronic medical conditions included hypertension, congestive heart failure, and AF while receiving daily oral warfarin therapy. At the time of presentation, he had tachycardia (pulse rate, 150 bpm) and hypotension (blood pressure, 66/45 mmHg). His physical examination findings were unremarkable except for slight tenderness in the entire right side of the abdomen without any rebound tenderness or guarding. We performed a bedside ultrasound to detect an abdominal aortic aneurysm, but did not find any. At this time, we considered ruptured abdominal aortic aneurysm, septic shock secondary to bacterial peritonitis, mesenteric ischemia, appendicitis, perforated hollow viscus, or complicated renal colic such as pyelonephritis in the differential diagnoses. We inserted an intravenous (IV) line to collect blood samples and to administer medications. To manage the pain, we administered morphine 5 mg IV. We initiated adequate fluid resuscitation with 0.9% normal saline, aiming for a mean arterial blood pressure of ≥ 65 mmHg. Furthermore, we administered broad-spectrum IV antibiotics (piperacillin – tazobactam 2.25 g and vancomycin 1 g) to cover bacterial infection. Along with blood cell counts, we requested complete metabolic profile, coagulation profile, and blood cultures for investigation; furthermore, we sent peritoneal fluid for analysis. To identify other possible sources of infection, we performed a chest X-ray.

The initial blood tests revealed the following: white blood cell count, $13 \times 10^9/L$ (normal, $4 - 10 \times 10^9/L$); hemoglobin level, 11.7 g/dL (normal, 13 – 17 g/dL for men); venous blood gases (pH, 7.30; pCO₂, 50.7 mm Hg; and bicarbonate, 24 mmol/L); lactic acid

level, 6 mmol/L (normal, 0.5 – 1 mmol/L); and international normalized ratio (INR), 3.3 (the patient's AF target INR was 2.5). After initial fluid resuscitation via a peripheral line, his blood pressure remained below the targeted mean arterial pressure; therefore, we inserted an arterial line to closely monitor blood pressure and initiated treatment with low-dose vasopressors. We ordered a contrast-enhanced CT of the abdomen to detect an intraabdominal source of shock, as described earlier. It revealed a retroperitoneal hematoma 80 × 60 × 35 mm in size that was located posterior to the right kidney and was pushing the kidney anteriorly (Figure 1). Furthermore, we observed a hematoma 70 × 50 × 55 mm in size near the right upper-third of the kidney with calcific foci and perirenal fat stranding. We did not detect any active bleeding in the arterial phase (Figure 1); however, we noted extravasation and blush in late portal venous phase and delayed phase in the right kidney (Figure 2). Thus, we diagnosed the patient with SRH from the renal vein in the presence of warfarin therapy.

Considering the diagnosis of SRH and following a discussion with a cardiologist, we stopped warfarin and immediately administered two units of fresh frozen plasma (FFP) and 10 mg of vitamin K IV to reverse the anticoagulation. We cross-matched the blood and kept packed red blood cells on standby for transfusion in case of a further drop in hemoglobin



Figure 1. Abdominal contrast-enhanced computed tomography scan showing retroperitoneal hematoma on the right side (white asterisk) with no active bleeding in the arterial phase.

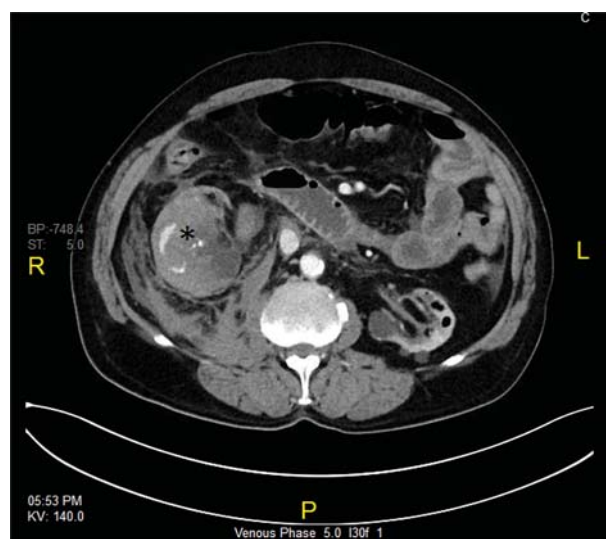


Figure 2. Abdominal contrast-enhanced computed tomography scan showing retroperitoneal hematoma on the right side with extravasation in the venous phase (black asterisk).

levels. Eventually, the patient's blood pressure stabilized, and we did not observe a significant drop in his hemoglobin levels on repeat measurements. We consulted a urologist, interventional radiologist, and vascular surgeon and made a collective decision to manage the case conservatively, as anticoagulation had been reversed, the patient was vitally stable, and there was no decline in his serial hemoglobin levels.

We admitted the patient to the surgical intensive care unit (SICU) with a plan to repeat the contrast-enhanced CT of the abdomen after 12 hours to follow hematoma progression. Later, in SICU, the patient's hemoglobin levels dropped to 6.6 g/dL, for which he received blood transfusions, but the repeat CT scan did not show any hematoma progression. The patient was vitally stable, and exhibited stable hemoglobin levels (after the transfusions); thus it was decided to continue with conservative management.

During the patient's course in SICU, his abdominal pain recurred and blood pressure dropped on day 13 postadmission. A third contrast-enhanced CT of the abdomen with IV contrast was performed, which showed an increase in the size of the hematoma. Thus, embolization of the right renal artery was performed, following which the patient recovered well.

This case has been reported after obtaining the patient's informed consent and approval of the institutional review board of Hamad Medical Corporation.

DISCUSSION

This case describes a common emergency department presentation of shock with abdominal pain that we diagnosed as SRH from the renal vein, a rare complication of warfarin treatment. It highlights the importance of considering a wide range of differential diagnoses given the patient's medical history.

Although major bleeding is a well-known complication of warfarin therapy, SRH related to the renal vessels is a rare complication, and its diagnosis can be challenging when the presentation is nonspecific.

An INR of ≥ 3 in patients receiving warfarin therapy indicates an increased risk of major bleeding, especially in the elderly population.¹³ However, patients exhibiting a therapeutic range of INR are not immune to the possibility of SRH, as many patients with SRH may exhibit INR in the prescribed therapeutic range.⁴

Hematuria in patients receiving warfarin is more likely to be related to secondary factors such as an anatomic lesion, infection, or renal hemorrhage.¹⁴ Considering the nonspecific presentation of SRH, a high index of suspicion and timely use of appropriate imaging tests are important to avoid mortality or morbidity associated with a missed or delayed diagnosis. CT is an important diagnostic test in the emergency department, as it is a readily available, highly sensitive, noninvasive technique to obtain information about the site and extent of bleeding. The use of contrast media helps locate the active bleeder and determine the need for active intervention.

The management of warfarin-related bleeding depends on multiple factors such as the hemodynamic instability of the patient, the significance of bleeding, the supratherapeutic INR value, and the risk of a

thrombotic event associated with the reversal of anticoagulation. Therefore, a multispecialty approach is crucial for making appropriate decisions in a timely manner.

Invasive management approaches are reserved for cases where a conservative approach fails to help achieve timely control of the bleeding¹⁵ or where a hematoma in an anatomical region causes pressure effects.^{10,16,17} Conservative management of SRH secondary to the renal venous bleed is an acceptable initial approach, with other invasive options being radiological intervention, percutaneous drainage, or surgical evacuation of the hematoma.⁴ In patients with serious or life-threatening bleeding, apart from withholding warfarin and administering vitamin K, rapid reversal agents such as prothrombin complex concentrates (PCCs) or FFP should be administered.¹⁸ PCCs offer the following advantages over FFP: 1) they can be rapidly reconstituted with a small volume of infusion, 2) they can be delivered over a short period of time (20–30 minutes), 3) they have a faster onset of action, 4) and they do not require determining the patient's blood group.¹⁸ However, PCCs have a lower concentration of factor VII than FFP. Therefore, FFP can be used when PCCs are unavailable or in addition to PCCs to compensate for factor VII in selected cases.¹⁹

CONCLUSION

SRH should be considered in the differential diagnosis of abdominal pain, hypotension, and/or decreased hemoglobin levels in patients receiving anticoagulation therapy, especially in those with preexisting ESRD. Most patients can be treated conservatively, and timely embolization can be lifesaving in cases of active renal vessel bleeding.

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