Case Report

Need of the Hour: Warfarin-induced Massive Intraperitoneal Bleed

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Abstract

Warfarin is an oral anticoagulant which is a natural coumarin derivative used for the treatment of various diseases such as thromboembolic disorders, prosthetic heart valves, and atrial fibrillation. Bleeding tendencies have been the most commonly reported adverse effects of warfarin, limiting its use and requiring the need for regular monitoring. Despite many warfarin management strategies being taken for the prevention, bleeding still continues to be a problem to be dealt with. The authors report a case of spontaneous intraperitoneal bleeding due to warfarin use in a 54-year-old female patient.

Keywords: Anticoagulant, bleeding, conservative management, spontaneous

Introduction

Warfarin sodium is the commonly used highly efficacious oral anticoagulant. It is the coumarin derivative widely used for pulmonary embolism and thrombotic disorders such as deep-vein thrombosis, prosthetic heart valves, and chronic atrial fibrillation for both therapeutic and prophylactic measures.[1] Warfarin inhibits intrinsic and extrinsic pathways of vitamin K-dependent coagulation cascade and procoagulant proteins.[2] The main difficulty related with the usage of warfarin is the disparity in pharmacological response in individuals. This necessitates dose adjustments of warfarin for the equilibrium of anticoagulation and bleeding risk that are predisposed by various factors such as the age, gender, illness, concomitant medication, body surface area, and genetic disparity.[3]

The major complication of anticoagulant therapy is bleeding. It was observed that rate of blood loss categorized as major (intracranial, retroperitoneal, hospitalization, or need for blood transfusion) is variable with a range of 0%–10% and the fatal bleeding incidence was 0% to 2.9%.[4] Discussed below is a case of warfarin-induced spontaneous intraperitoneal bleeding.

Case Report

A 54-year-old female came with complaints of pain abdomen for 3 days; she did not pass stools and urine for 1 day. She complained that pain started in flanks with fullness and tightness over the lower abdomen. Her history revealed that she was diagnosed as a case of chronic pulmonary thromboembolism after doing a plain and contrast computed tomography scan of thorax with pulmonary angiogram which showed that the upper lobar branch of left main pulmonary artery and its segmental branches were not visualized with complete occlusion, following which a likelihood diagnosis of chronic thrombosis was made. She was started on oral warfarin 7 mg once a day for 3 weeks. HAS-BLED scoring was done before starting warfarin, and the score was "zero," and her kidney function tests were found to be normal (creatinine clearance of 87 ml/min, estimated by Cockcroft–Gault equation).

During her present admission on examination, ecchymotic patches of around 15 cm × 12 cm were seen on the lower abdomen with tenderness [Figure 1]. Pallor was seen with decreased hemoglobin values (6.5 g/dl), increased prothrombin time (PT) (>120 s), and increased international normalized ratio (INR) (4.70). On abdominal computed tomography scan,

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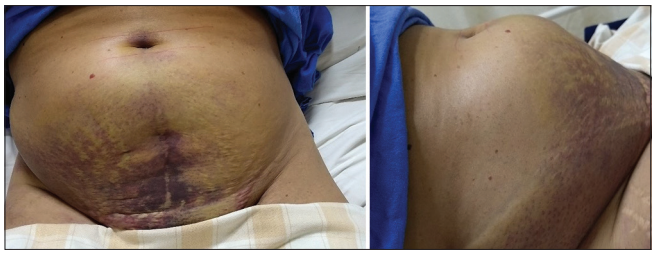

Figure 1: Ecchymotic patches over the lower abdomen

hematomas were seen in the right anterior abdominal wall and pelvic cavity [Figure 2]. Her concomitant medications included oral phenylephrine 10 mg twice daily, oral paracetamol 500 mg twice daily, and an expectorant syrup for the complaints of fever and rhinitis. She also mentioned that for 2 days; she was taking oral mefenamic acid 500 mg once daily for backache. As there was no alternate cause found for the bleeding, it was diagnosed to be a case of warfarin-induced spontaneous intraperitoneal bleed. Management was conservative, involving bed rest, analgesics, and subcutaneous vitamin K at a dose of 10 mg/ml daily for 1 week, and warfarin was withheld. She was also given blood transfusion (four units of fresh-frozen plasma and one pint packed red blood cells) to treat anemia. During the recovering period, her hemoglobin was 8.8 g/dl, PT 15.1 s and INR 1.43, and finally, her hemoglobin (10.6 g/dl), PT (11.6 s) and INR (1.09) values recovered to normal after 13 days of treatment. The causality of the adverse drug reaction was analyzed using Naranjo algorithm, which gave us a score of 7, denoting "probable" causality.[5]

Discussion

Warfarin is being increasingly used prophylactically for various high-risk situations such as thromboembolic disorders (venous thromboembolism, deep-vein thrombosis, and pulmonary embolus) and prosthetic heart valves. The incidence of bleeding due to warfarin therapy is around 15%–20%per year and incidence of life-threatening or fatal bleeding associated with warfarin is around 1%–3% per year.[6]

Warfarin acts by inhibiting the C1 subunit of vitamin K epoxide reductase, which activates vitamin K-dependent coagulation factors (II, VII, IX, and X) and regulatory proteins (proteins C, S).[7] Assessment of anticoagulation by warfarin therapy is done by INR estimation to balance the risk of excessive bleeding. The therapeutic efficacy of warfarin therapy is reliant on maintaining the target INR range for the indication but is normally between 2.0 and 3.5.[6] Several bleeding complications are frequently associated with warfarin, including gastrointestinal and intracranial bleeding, rectus sheath, and retroperitoneal hematomas.[8]

In our case, PT and INR levels were markedly increased, indicating a bleeding state and also there were no comorbidities. The patient also mentioned of consuming mefenamic acid which could have caused a drug interaction with warfarin, leading to prolonged anticoagulant action. Nonsteroidal

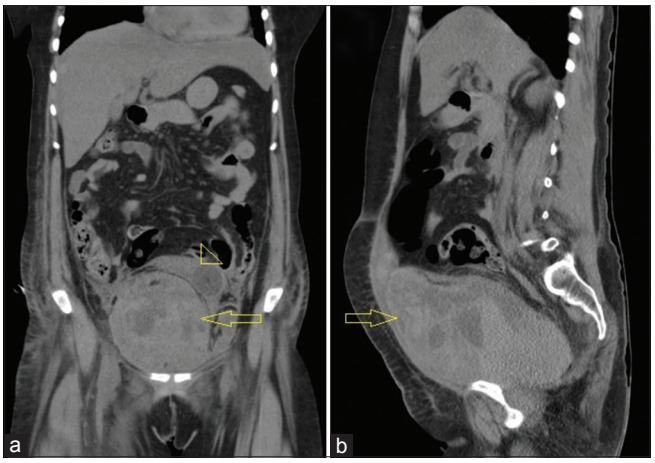

Figure 2: Computed tomography abdomen ([a]-coronal, [b]-sagittal view) showing a large hematoma (arrows), measuring 19.6 cm × 10.6 cm × 10.4 cm, extending from the right lower anterior abdominal wall into the pelvic cavity. In addition, note the lesion appears to displace the urinary bladder superiorly

anti-inflammatory drugs (NSAIDS) such as mefenamic acid are known to be the substrate of CYP2C9 which is also the enzyme-metabolizing warfarin.[9] Hence, warfarin metabolism is delayed, thereby increasing the anticoagulant activity. Intraperitoneal bleeding is a relatively unusual illness, which can be misdiagnosed such as acute abdomen. This can lead to unnecessary interventions such as operative procedures. Peritoneal fat present in the rectus sheath space has perforating branches of inferior epigastric artery that could rupture, leading to large hematomas in the rectus sheath and peritoneal cavity and also possibly spreading to the pelvic cavity.[10] Scoring of 7 based on Naranjo algorithm and probable reasons for this association are the temporal relationship, positive dechallenge, and all other likely causes for the spontaneous bleed are ruled out.[5] We did not restart the warfarin due to the risk of rebleeding. Ideal treatment in these situations is to start newer anticoagulants (e.g., dabigatran, rivaroxaban, and apixaban). These direct-acting oral anticoagulants are reported to confer a lower risk of bleeding than warfarin with no frequent PT and INR monitoring. However, our patient refused due to financial constraints.

Conclusion

Since warfarin has a narrow therapeutic window, initiation and management of warfarin therapy is often difficult. The goal of warfarin therapy should be maintained to administer the lowest effective dose for determining the target ranges of INR for the particular indication. It is also necessary for the clinicians to follow the guidelines for therapeutic success, managing the supratherapeutic INR levels and for the reversal of warfarin-induced hemorrhage. Unusual bleeding sites like the peritoneum have to be kept in mind before considering any operative or invasive procedures in the abdomen. Such conditions can be managed conservatively by reversing the hemorrhage using vitamin K and by the addition of blood

products. The need of the hour is that clinicians have to be cognizant of all drug interactions particularly the use of certain medications like NSAIDS before prescribing to the patients who are on anticoagulant therapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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