**Title:** Spontaneous intraperitoneal bleeding secondary to warfarin, presenting as an acute appendicitis: A case report with the review of literature.

**Authors:**

Jayesh Sagar\(^1\*\) MBBS, MS, DNB, MRCS  
Vikas Kumar\(^2\) MBBS, MS  
Bethani Sagar\(^3\) BSc, BASM  
D K Shah\(^4\) MBBS, MS

**Hospital:** Royal Free Hospital, London

**Affiliation:** 1. Royal Free Hospital, London  2. Princess Alexandra Hospital, Harlow  3. Stoke Mandeville Hospital, Aylesbury  4. S.S.G.Hospital, Baroda, India

**Correspondence Address:**  
J Sagar  
1, Ivy Walk  
Rickmansworth Road  
Northwood  
Middlesex. HA6 2QQ  
Tel: (+44) 07800531204  
E-mail: jsagar_2001@yahoo.com
Title
Spontaneous intraperitoneal bleeding secondary to warfarin, presenting as an acute appendicitis: A case report with the review of literature.

Key Words
Intraperitoneal bleeding – Warfarin – Appendicitis.

Abstract
Warfarin is a coumarin anticoagulant, used widely for therapeutic and prophylactic anticoagulation. Though it is considered as a life saving medicine, it is associated with the significant adverse effects including intra-peritoneal bleeding, which have been very well documented in literature. However, presentation of warfarin induced intraperitoneal bleeding as an acute appendicitis has not been reported in English literature. We report this rare, spontaneous intra-peritoneal bleeding secondary to warfarin, mimicking the signs and symptoms of an acute appendicitis for the first time.
Introduction

Warfarin is a coumarin anticoagulant, widely used for the therapeutic and prophylactic anticoagulation. Although it is considered as a life saving medicine, it is associated with the several significant adverse effects. Intra-peritoneal bleeding is one of the complications, usually following trivial trauma. There are only very few reported cases of the spontaneous haemoperitoneum in English literature without any evident cause (1,2). Spontaneous onset of the intra-peritoneal bleeding due to warfarin is also exceptional. We report a case of the spontaneous intra-peritoneal bleeding secondary to warfarin therapy, mimicking the signs and symptoms of an acute appendicitis in a 41-year old Caucasian female, for the first time in English literature. We strongly recommend the consideration of this rare complication in the differential diagnosis of all the cases of acute abdomen in patients who are on warfarin therapy regardless of INR levels. We also suggest the use of the radiological investigations in such cases to achieve diagnosis to avoid unnecessary surgical intervention.

Case History

A 41 year-old Caucasian female patient was referred to us by general practitioner (G.P.) with 2 days history of the migratory abdominal pain. The pain started in the periumbilical region, which later on localised to right iliac fossa. Initially, the pain was constant and dull, but became sharp and exaggerated with body movements. She was also complaining of four episodes of vomiting and nausea with the loss of appetite. She occasionally felt pain in her right shoulder. There was no history of even trivial trauma. She had 3 episodes of pulmonary embolism following hysterectomy and she had been on warfarin for prophylaxis since then. She was also taking tylex,
pantoprazole, tramadol, senna, migraleve, zimovane and fentanyl citrate lozenges as her regular medications. She had 35-pack year history of smoking. On examination, she was afebrile (temperature of 37.8°C noticed by G.P. 6 hours before presentation to us) but tachycardic with pulse of 134/minute. There was no bruising or haematoma in the abdominal wall. The abdomen was distended with marked in the right lower quadrant. There were guarding and rebound tenderness in the right iliac fossa. The rectal examination revealed tenderness in right pelvic wall. The urine dipstick was positive for ketones and trace of protein. The blood investigations showed haemoglobin of 10.8 gm/dl with reduced haematocrit of 32%, WBC of $11.8 \times 10^9$ and INR of 2.2. The biochemistry did not reveal any abnormality. The clinical diagnosis of acute appendicitis was made. She was scoring 8 according to Alvarado scoring system. The decision for appendicectomy was made and the consent was given for the emergency appendicectomy. Through the Lanz incision, 200 ml of haemorrhagic fluid was aspirated from the peritoneal cavity. The appendix and mesoappendix were looking normal. The appendectomy was performed. During operation several blood clots were present so the incision was converted to the formal transverse infra umbilical laparotomy incision. On exploration, large 10x15 cm size blood clot was evacuated from the pelvis. Thorough search for the active bleeding was made but there was no active bleeding site. The final diagnosis of the spontaneous intra-peritoneal bleeding secondary to warfarin was made. The abdomen was closed with low suction drain, which drained about 200 ml of the serosanguinous fluid over next 2 days. The warfarin was stopped after the operation. The patient recovered well without any complications and discharged back to the community with follow up arranged. At 2 weeks, patient was doing well without any complaints and complications.
Discussion

Warfarin is a life saving drug, extensively used in treatment and prophylaxis for the deep vein thrombosis, pulmonary embolism, valvular heart disease, atrial fibrillation, recurrent systemic emboli, recurrent myocardial infarction, prosthetic heart valves and prosthetic implants (3,4). However, it is associated with the serious adverse effects such as the haematuria, soft tissue bleeding and haematoma, intra cerebral bleed, skin necrosis, purple toe syndrome and abdominal bleed. Theoretically, the bleeding can occur in any part of the body following anticoagulation therapy. Bleeding in gastrointestinal tract is by far the most common complication of warfarin. Bleeding may occur intra-, extra- or retroperitoneally (5,6), but the intramural bowel haematoma is the most common cause of the abdominal pain in the patients who are on anticoagulantion therapy (6,7,8). It is crucial to differentiate between the intra-peritoneal bleeding and the intramural haematoma as most of the intramural bowel haematomas respond to non operative treatment (9,10). Here, we report the rare complication of warfarin therapy - spontaneous intraperitoneal bleeding, mimicking an acute appendicitis. According to our knowledge, such clinical presentation has not been reported in English literature.

Two most important determinants of the warfarin induced bleeding is the intensity of therapy and the maximal time in therapeutic range (3). Bleeding is a major complication in early phase of warfarin therapy according to most studies (3,11). Bleeding is more likely to occur in patients with the more intense therapeutic range (INR between 2.5 and 3.5) than in the less intense therapeutic range of warfarin (INR between 2 and 3) (11,12). Another interesting point about this case is the presentation
of this severe clinical condition in the less intense therapeutic range of warfarin (INR 2.2).

The polypharmacia effects of the patient’s medications may explain the possible reason of the spontaneous intra-peritoneal bleeding. The long term use of paracetamol and pantoprazole as well as long term smoking (4) may play role in enhancing the anticoagulant action of warfarin, but we must admit that INR was in a therapeutic range at time of presentation.

This also raises a question about the present management of acute appendicitis in UK, as we have not yet accepted the CT scan as a mandatory investigation for the diagnosis of appendicitis. Although the Alvarado scoring system has been a useful means for the management of an acute appendicitis, we think, the CT scan and/or ultrasound in this case might have confirmed the diagnosis and patient would have been avoided the surgery and been observed with the reversal of anticoagulation (13). Though the CT scan may not be possible due to the medical reasons or the fear of over utilization, we recommend the use of the radiological imaging in such cases. The other interesting point in this case is the history of occasional pain in right shoulder at time of presentation. This may be due to the blood under the diaphragm causing irritation of the phrenic nerve, leading to referred pain in the shoulder (well known as Kehr’s sign) but this became evident retrospectively only.

This case provides a learning lesson to the young junior surgeons as well as to other specialists such as general practioners and physicians to consider this rare but significant complication of warfarin in the differential diagnosis of all the cases of acute abdomen/abdominal pain in patients who are on warfarin therapy, even if INR is in the low therapeutic range. We also strongly recommend the use of the radiological
investigations such as CT scan or ultrasound in these cases to achieve diagnosis and to avoid unnecessary surgery.

References


