WARFARIN TOXICITY PRESENTING AS RUPTURED OVARIAN TUMOUR WITH HEMOPERITONEUM: A CASE REPORT

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Abstract
Warfarin, a coumarin derivative, is commonly used in prevention and treatment of thromboembolic events in various clinical situations. Although, a safe drug, its toxicity may result into intraperitoneal bleeding. Warfarin induced intraperitoneal bleeding is dose dependent and may have fatal outcome. A case is reported here, who presented with massive intraperitoneal haemorrhage secondary to warfarin toxicity. She had undergone mitral valve replacement six months before the episode. Clinical and imaging suggested a pelvic mass mimicking ruptured ovarian tumour. Her prothrombin time INR was 1.1 at the time of admission. Emergency laparotomy revealed a large organised blood clot in the pouch of Douglas extending to adnexal region, mimicking ruptured ovarian tumour. Warfarin was withdrawn for few days. Patient was transfused with fresh frozen plasma and fresh whole blood. Post operative recovery was uneventful. Warfarin in low dose was restarted for thromboembolic prophylaxis.

Keywords: Warfarin toxicity, Hemoperitoneum, Thrombo-prophylaxis, Ruptured ovarian tumour

1. Introduction
Warfarin is a coumarin derivative which is used widely in prevention and treatment of thromboembolic events. Although it is considered a safe emergency medicine, its overdose results into toxicity, in the form of bleeding from various body sites. Spontaneous hemoperitoneum is one such complication, in which haemorrhage can occur in the peritoneal cavity or in the retroperitoneal space. Warfarin toxicity is dose dependent. Patient with hemoperitoneum usually present with acute abdomen and report either in casualty department or are shifted to intensive care unit. We report this case of warfarin induced massive intraperitoneal haemorrhage, who presented with clinical and radiological features suggestive of ruptured ovarian tumour.

2. Case Report
A 28 year old young woman, on warfarin prophylaxis for mitral valve replacement, presented to casualty department with features suggestive of acute abdomen, distension of abdomen and haemorrhagic shock. She had undergone vaginal hysterectomy six years back for prolapse of uterus and had undergone mitral valve replacement four months back. Since then, she was taking oral warfarin 1 mg daily along with tab Verapamil (120 mg), tab fruselac and tab digoxin 0.25mg daily. On physical examination, she was conscious but anxious, lying still on bed, with cold clammy extremities. Her blood pressure was normal. Her pulse rate was 120/min, low volume. She had gross pallor. There was no bruising or haematomas on abdomen or at any other site. The abdomen was distended, tender with guarding and rigidity all over the abdomen. There was evidence of free fluid on percussion. Paracentesis revealed frank blood in the peritoneal cavity. Pelvic and per-rectal examination showed the presence of ten centimetres size soft to firm, tender mass occupying Pouch of Douglas. Pelvic and abdominal ultrasound revealed presence of hemoperitoneum and pelvic mass of 10 cms x 8 cms, posterior to urinary bladder, occupying Pouch of Douglas. Her investigations revealed Haemoglobin level of 4.2 grams, normal aPTT and INR. Her prothrombin time was more than 2 minutes. Her platelet count and blood biochemistry did not reveal any abnormality. The clinical diagnosis of hemoperitoneum possibly due to ruptured ovarian tumour was made. She was posted for emergency laparotomy. Preoperative, she was transfused with 2 units of whole blood and 4 units of fresh frozen plasma. Laparotomy revealed...
large blood clots in the paracolic gutter and sub diaphragmatic area. There was a big organized blood clot of size 10 x 8 cms in pouch of Douglas. Clots were removed from the abdominal cavity. Inspite the whole abdominal cavity being explored for the evidence of any active bleeding site, we could not find any source of active bleeding. The abdomen was closed after keeping a low suction drain in pouch of Douglas and perihepatic region. Postoperatively, she was transfused with additional 2 units of fresh whole blood and 2 units of fresh frozen plasma. She had uneventful postoperative period. Warfarin was restarted in smaller dose, ten days after surgery. She was discharged on fifteenth postoperative day. She reported to outpatient department two weeks after discharge from hospital and was doing well.

3. Discussion
Warfarin is a commonly used anticoagulant drug in treatment and prevention of thromboembolic conditions. More and more number of cases of warfarin toxicity are being reported in the literature. Physician prescribing this drug has to adjust the dose, in such a way that achieves effective thrombus prevention but also prevents the dose related toxicity. Warfarin toxicity is dose dependent. It exerts its action by inhibiting vitamin K dependent coagulation factors (II, VII, IX and X). It also inhibits the synthesis of natural anticoagulants in the blood, protein C and S. Due to difference in the half life of “coagulation factors” and “anticoagulants”, the coagulation system may be transiently biased towards clotting after starting warfarin. Hence one should start warfarin only after anticoagulating the patient with heparin, lest one may end up in thrombosis. The target International Normalized Ratio (INR) is maintained around 2-3. Spontaneous bleeding is one of the well reported and most common adverse effects of warfarin. Bleeding is usually subcutaneous or intramuscular. Management is generally to reduce the dose of warfarin. Various factors determine the bleeding complications of warfarin. These include old age, dose, duration of therapy, drug interaction and occult diseases. Many drugs interacts with warfarin, the common being NSAID. In fact the most common cause of bleeding secondary to warfarin is drug interaction. It has also been shown that warfarin when combined with anteplatelet drugs like clopidogrel have higher incidence of bleeding. Dedicated monitoring of the coagulation profile in patients taking long term warfarin is mandatory to prevent this complication. The major determinants of oral coagulant-induced bleeding are the intensity of the anticoagulant effect, underlying patient characteristics, and the length of therapy. There is good evidence that low-density oral anticoagulant therapy (targeted INR of 2.5; range, 2.0 to 3.0) is associated with a lower risk of bleeding than therapy targeted at a higher intensity. Lower intensity regimes (INR < 2) are associated with an even smaller increase in major bleeding. In terms of decision making for anticoagulant therapy, risk of bleeding cannot be considered alone, i.e. the potential decrease in thromboembolism must be balanced against the potential increased risk of bleeding. Initial Prothrombin Time (INR) is not an appropriate guide for treatment of bleeding complications of warfarin toxicity. Clinical manifestations were mere reliable and significant to treat for bleeding complications of warfarin toxicity (Warfarin toxicity in the emergency department). Present case had special features at presentation. She was on small dose (1 mg/day) of warfarin treatment and had normal INR values in the presence of severe intraperitoneal bleed. The CT abdomen in such cases can differentiate between ovarian tumour and a organised haematomas. On CT, the presence of a cellular-fluid level caused by the setting of cellular elements in the dependent portion of haematoma, so called haematocrit sign, is a highly sensitive (87%) and specific sign of coagulopathic haemorrhage. When contrast enhanced CT detects coagulopathy associated active extravasation, this is more frequently venous than arterial, usually not requiring surgery or embolization. Treatment in such situation is conservative, and based on withholding the anticoagulant medication. Present case provides lesson to specialist gynaecologist and radiologist, to keep the possibility of warfarin toxicity related.
organised pelvic haematoma that may mimic a pelvic tumour, even when the INR values are within normal safety range. Case report suggests that CT abdomen should preferably be done before any surgical interaction is planned in such cases. CT abdomen was not performed in this case, as patient could not afford the charges for this special investigation.

**Conclusion:**
Patients with toxicity to oral warfarin therapy may present with a clinical picture of acute abdomen due to haemoperitoneum. Proper clinical, haematological and radiological (USG & CT) evaluation is necessary for confirmation of diagnosis before any surgical intervention is planned. Warfarin related toxicity is treated by withholding the drug, transfusion of fresh frozen plasma and subsequent readjustment of the dose of warfarin. INR values are not reliable for assessment of warfarin toxicity.

**References:**