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Warfarin induced Ovarian Haematoma Mimicking Torsion Ovarian Tumour

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ABSTRACT

Warfarin toxicity presenting as acute abdomen in a woman with chronic anticoagulation is rare. A 29 year old woman with Rheumatic heart disease with history of mitral Valve replacement who was on anticoagulation with warfarin presented with pain abdomen of 2 weeks duration and she was clinically diagnosed as torsion ovarian cyst. On USG abdomen there was a complex adnexal mass of 6x8 cms with Doppler flow. Her International Normalised Ratio was more than 10 and hence a diagnosis of Ovarian haematoma was entertained and she was managed medically with dose titration of anticoagulants and her pain abdomen subsided and she was discharged home after normalising her International normalised ratio and laparotomy was thus avoided.

1 Background

The clinical features of a torsion ovarian tumour include pain abdomen, vomiting in the presence of an adnexal mass. But in a woman with anticoagulation the cause of these features can be due to toxicity of anticoagulants mimicking ectopic pregnancy or Ovarian tumour. Toxicity can be acute or chronic and results in significant morbid events and sometimes mortality. Intraperitoneal haemorrhage from ovary has been reported in few occasions in women on warfarin therapy necessitating laparotomy [1,2[. Laparotomy can be avoided for adnexal mass when warfarin toxicity is diagnosed .

CASE:

A 29 year old para1 LCB 8 years ago, attended our emergency services on 5.8.2019 with a referral differential diagnosis of left ovarian chocolate cyst torsion / fibroid with degeneration along USG report. She complained of pain lower abdomen of 2 weeks duration and there was no vomiting or fainting attacks.

Her menstrual history was normal. Cycles were regular with a flow lasting for 5 days and occurring once in 28 days and her LMP was 1.8.2019. There was no dysmenorrhea or menorrhagia.

Her past history revealed that she was a known case of RHD severe MS, severe MR mild TR since childhood, underwent mitral valve replacement in 2015 and on anticoagulation with warfarin since then. In 2016 she underwent bilateral embolectomy and thrombolysis for struck prosthetic valve. In 2017, Thrombectomy for stuck prosthetic valve was done and she was on 2.5 mg and 5 mg of warfarin initially and later increased to 10 mg since July 2018 and her INR was maintained between 1.2 to 1.8 till July 2019.

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She was on tab.Asprin 75 mg once daily, tab Digoxin 0.25 mg , Lasix 40 mg once daily and Tab. Kaypen 125 mg twice daily and syrup Kcl apart from anticoagulants. There is no history of increased dose intake of Warfarin. There is no history of Diabetes mellitus , hypertension or hypothyroidism.

Her general condition was good with a pulse rate of 94/min, BP of 110/60 mm Hg and there was mild palor. There was a midline vertical scar of length 10 cm on chest Her Respiratory system was normal. Cardiovascular system was normal except for a click sound. Per abdominal examination revealed minimal tenderness in suprapubic region and right iliac fossa and there was no mass or free fluid. Per speculum examination revealed fresh bleeding through Os and bimanual examination showed a retroverted uterus of 10 weeks size with tenderness in anterior fornix. Per rectal examination uterus was felt retroverted and there was no other mass..

TAS in the Emergency department revealed normal sized uterus with a heterogeneous mass of 4.7 x 7.2 cm anterior to uterus with minimal free fluid in pelvis. TVS revealed normal right ovary and left ovary not separately visualised from the mass. A clinical diagnosis of torsion of left ovarian cyst was made.

Consultant review USG on 6.8. 2019 showed retroverted uterus of normal size, left sided heterogenous mass 6.5 x 6.8 cms (Fig -1) . Doppler flow at the periphery of the mass was present. A diagnosis of Ovarian haematoma was made and adviced to do PT and INR and conservative treatment was planned. Her INR was more than 10 and she was started on tranexamic acid and received FFP 25 ml.kg body weight given 8th hourly . Her Warfarin was stopped and Heparin was started when INR was 1.2 and then warfarin was restarted, gradually increased 7.5 mg daily (Table -1) With in a week her symptoms resolved completely and her INR normalised to 2 and she was discharged and adviced to follow up in Cardiology.Repeat USG showed Left Ovarian mass of 3 cms x 2.5 cms.

Table 1. Investigations and Monitoring chart

Parameter	Value and Date						
	6.8.2019	7.8.2019	8.8.2019	9.8.2019	10.8.19	11.8.19	13.8.2019
Hb	11.3 gm%						
TLC	19,610						
DLC(N/L/M)	78/12/8						
Platelets	3.72 lakhs						
Urea	24 mg/dl						
Creatinine	0.76 mg /dl						
S. Total Bilirubin/Direct	1.16 mg%/0.13						
AST/ALT	42/8						
Total Protein	7.7 gm						
Albumin	4.3 gm						
PT/INR	113.1/10.61	19.5/1.3	17.2/1.22	18.7/1.3	17.6/1.25	19.7/1.5	19.8/2
Anticoagulation	stopped	stopped	Started	Dose titration			
Management	FFP	FFP	Heparin	Heparin+ Warfarin	H+W	H+W	Warfarin 7.5 mg

FFP- Fresh frozen Plasma; H- unfractionated Heparin ;W-Warfarin

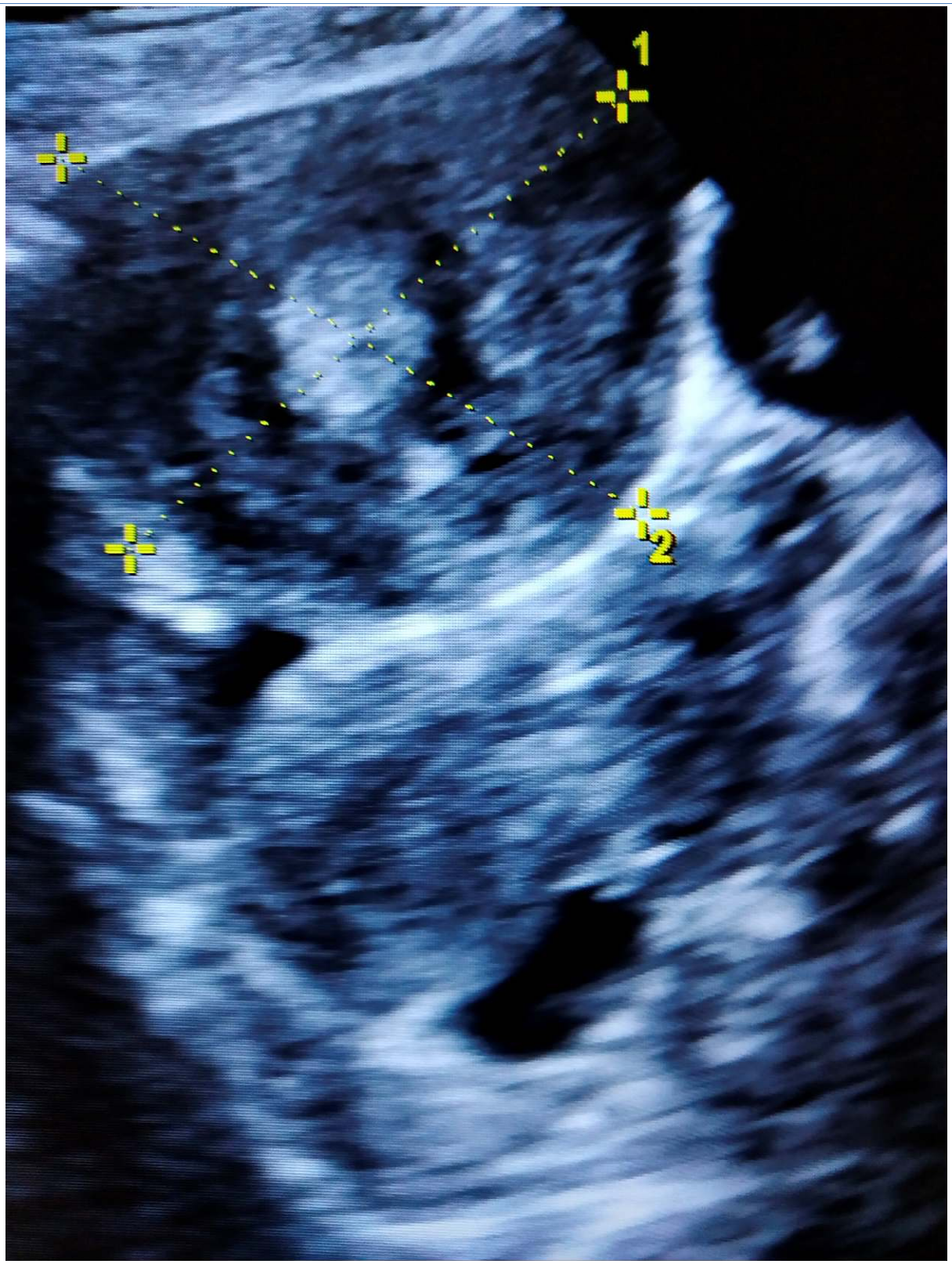


Figure 1: Retroverted uterus of normal size

2 Discussion

Anticoagulants are indicated lifelong in certain clinical situations like venous thromboembolism Pulmonary thromboembolism with high risk of recurrence and in heart disease with atrial fibrillation for therapy or for prevention. Artificial valve replacement is one such clinical scenario where lifelong anticoagulation is mandatory and warfarin is the main drug of choice. It is necessary to maintain the anticoagulation in the therapeutic range of 2 to 3 which is measured by International Normalised ratio (INR). INR over 3 indicates over coagulation and risk of spontaneous haemorrhage increases and a low INR <1.5 predisposes to thrombosis [3]. Warfarin toxicity is defined as INR of > 3.5 for those who are on warfarin for heart valve replacement and more than 3 for other conditions and Warfarin coagulopathy is reported to be present at an INR of >1.4 [4[.

Warfarin is a Vitamin K antagonist acts by inhibiting 2,3 Vitamin K epoxide reductase resulting in deficiency of its active form which in turn causes coagulation factors II,VII,IX,Protein C and Protein S inactive.2 It is absorbed rapidly from intestine and has an half life of 29-45 hours with a maximum serum concentration at 90 minutes. The side effects may not be immediate and there is no cut off level of INR described in literature at which haemorrhage starts [3]. The most common complication of anticoagulation is haemorrhage in to soft tissues and organs. Haemorrhage occurred when INR was with in normal range in 14.5% and in 36.4% when it was >5 [5]. The clinical findings vary depending on the site and extent of haemorrhage and the most common symptom was abdominal pain. The most common site of haematomas was rectus sheath and Ovarian haematomas were reported in only 1.8% [6].

Diagnosis of haematomas in to soft tissues or luminal is challenging especially in the absence of haemoperitoneum and it is usually a diagnosis of exclusion. USG is the first modality in emergency setting in evaluating patients presenting with pain and distension of abdomen. A woman of reproductive age with mitral valve replacement on anticoagulants who was diagnosed as adnexal mass (Corpus luteal cyst rupture) with moderate haemoperitoneum was successfully managed conservatively with blood and blood products though her haemoglobin dropped to 4 gm% [7]. Laparotomy was resorted to in another woman of mitral valve replacement on anticoagulation who presented with massive haemoperitoneum with adnexal mass as her INR was 3.5 at the time of admission [1] . There are no specific features characteristic to haematomas on USG. They appear as hypoecheic heterogenous masses with surrounding increased echogenicity and calcifications may be present in organising haematomas making it difficult to differentiate from other benign or malignant masses [8]. In the present case heterogenous appearance of adnexal mass and presence of Doppler blood flow and the history of anticoagulation made us to come to a conclusion of Ovarian haematoma and to rule out torsion of adnexal mass. A large review which described the USG features of various Ovarian pathologies described spider-web-like appearance due to small haemorrhages with in the ovarian cyst and mentioned that blood clots can appear like solid components. The review also quoted that jelly like wobbling movement can be elicited by transvaginal examination on movement of the probe and the blood clot not to have blood flow on Doppler examination [9].

Other than USG and Doppler CT is reported to be helpful to arrive at accurate diagnosis.Contrast enhanced CT can detect sign of active haemorrhage as extravasation of contrast where as plain CT can miss it due isoattenuation of surrounding tissues. Inhomogenecity with isolated areas of hyperdensity is described as

a frequent and specific finding of anticoagulation on CT. CT angiography is essential to trace the source of bleeding[10[

Acute Warfarin toxicity can be life threatening if not recognised early and managed appropriately Massive ingestion of warfarin (>300mg). INR does not increase in dose dependent fashion and acute toxicity was reported in an attempt to suicide which was managed with Phytonandione [11] .Mortality was reported to have occurred in 12.7% [6].

Conservative approach is the choice of management by withholding the warfarin dose and infusing Fresh frozen plasma till INR normalises as in this case and other case reports and case series. Daily testing of INR is required for the first 5 days after initiation of therapy stability is to be expected by 3 to 5 days and the therapeutic dose to be maintained at an INR of 2.5 for valvular heart disease and a testing of 4 to 6 week interval would suffice to prevent toxicity [12].

3 Conclusion

In women on long term anticoagulation presenting with adnexal masses and pain abdomen toxicity of anticoagulation is to be ruled out before embarking on surgery . USG features are nonspecific but helpful to differ surgical management.

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