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Benign gynaecological pathology causing vascular presentations: Three cases of women with peripheral thromboses

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Abstract

Introduction

Benign or malignant gynaecological disease can compress iliac vessels leading to deep vein thrombosis (DVT) or acute arterial ischemia. Women have a higher incidence of thrombosis in comparison to males, with a higher prevalence of pro-thrombotic factors such as pregnancy, use of combined oral contraceptives, and gynaecological pathologies.

Cases

Case 1 is a 45-year old Caucasian woman who presented with a left sided DVT, menorrhagia and anaemia secondary to a multi-fibroid uterus. Case 2 was a 38 year old Caucasian female who presented with a left sided DVT secondary to a singular large uterine fibroid (21cm diameter). Case 3 was a Caucasian female who presented with acute arterial ischemia and contralateral DVT due to compressive effect from a exceptionally large benign ovarian pathology.

Results

This case series highlights the need to consider vascular complications in young female patients as sequelae of possible pelvic pathology.

Conclusion

Investigation for pelvic gynaecological disease should be considered in assessment of women with lower limb thrombotic vascular pathology, especially in the absence of typical vascular risk factors.

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Introduction

Various conditions can cause compression of pelvic veins resulting in ilio-femoral deep vein thrombosis (DVT) including: gynaecological and abdominal pathologies, multiparous pregnancies and iliac vein compression syndrome, otherwise known as May-Thurner Syndrome[1]. Pregnancy, combined oral contraceptive use, fibroids and malignancy are all independently associated with an increased risk of developing DVT[2]. This is a case series of three women who presented with provoked peripheral vessel thrombosis in the setting of an underlying gynaecological pathology.

Methods

We present a retrospective report of three patients known to have vascular complications secondary to pelvic pathology. A retrospective examination of the healthcare records of the three patients was made. All patients provided written consent to have their healthcare records, data and imaging used for the purposes of research and publication.

Case 1

In our first case a 45-year-old para-one Caucasian woman presented with unilateral left leg oedema and calf tenderness. A venous duplex demonstrated thrombus in the left femoral vein and the patient was discharged on 5mg BD apixaban. A loading dose of apixaban 10mg BD for one week was not prescribed. Past medical history was significant for a provoked left leg DVT in the setting of pregnancy 16 years previously at 40+11 weeks gestation. There were no other personal or familial risk factors for venous thromboembolism (VTE) identified. Unfortunately, the patient re-presented two weeks later with worsening leg pain and swelling despite compliance with apixaban 5mg BD. A repeat duplex showed propagation of the thrombus whilst on direct-oral anticoagulation (DOAC) therapy; with the thrombus now extending into the iliac vein (Figure 1A). On further review of investigations, a microcytic anaemia was identified with subsequent haematinics confirming an iron deficiency anaemia. On further questioning the patient complained of symptomatic anaemia, chronic fatigue and menorrhagia ongoing for approximately 5 years. An ultrasound (US) pelvis was requested to identify a potential cause of the menorrhagia along with a CT venogram to check for an underlying May-Thurner Syndrome. Radiology investigations revealed a large diffusely fibroid uterus, measuring 12x10cm, the largest single fibroid measuring 3.8 x 4.7 x 4.4cm (Figure 1C). On CT venography the fibroid uterus was causing compression of the left external iliac vein (Figure 1B).

She was treated acutely with an unfractionated heparin infusion, and thereafter with therapeutic Rivaroxaban. Iron infusions were administered and the patient was discharged on oral iron supplementation along with norethisterone for symptomatic menorrhagia

pending definitive surgical intervention. The administration of a progestogen, in the context of a pre-existing DVT[3-5], was discussed with the Haematology Service and on the balance of risks associated with symptomatic anaemia was given without complication. The patient underwent an urgent transabdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO) which addressed both the menorrhagia and the provoking and compressive cause of her DVT. The patient continued on therapeutic anticoagulation for a provoked DVT until 3 months post-operatively. She had complete clinical resolution of her symptoms.

Figure 1

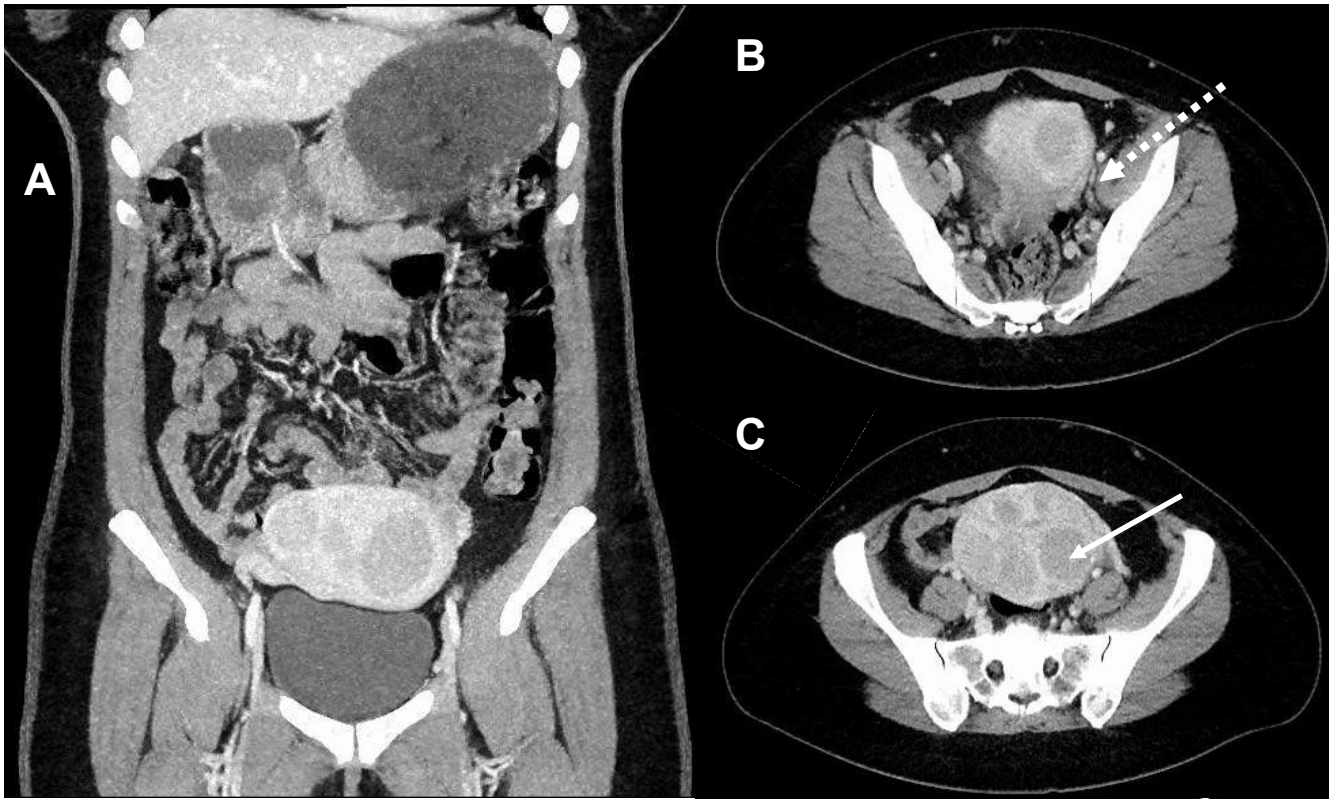

Figure 1. A) Coronal CT fibroid uterus, with diffuse fibroids throughout the fundus *B)* Axial CT, the external iliac vein on the left is compressed by the fibroid uterus, though it is still patent (dashed arrow), *C)* Axial CT showing fibroid uterus diameter (12cm) and highlights the largest of fibroid (white solid arrow), which measured 3.8x4.7x4.4cm

Case 2

The second case is a 38-year-old Caucasian female who presented with urosepsis and left lower limb swelling. Initial treatment consisted of intravenous co-amoxiclav and fluids. Despite antibiotics the patient developed progressive back pain and left lower limb pain. Her

past medical history was notable for menorrhagia and an 8cm fibroid in the fundus of her uterus, discovered 3 years previously when she underwent fertility investigations. The patient had previously used the combined oral contraceptive pill with no thrombotic complications.

A venous duplex revealed an extensive left iliofemoral DVT. A CT venogram was performed to assess the full extent of the thrombosis and to check for an underlying May-Thurner Syndrome. This revealed a uterine mass, 20x11x21cm, compressing the distal inferior vena cava and the left common iliac vein (Figure 2). There was an extensive left common iliac and external iliac vein thrombus extending to the level of the left popliteal vein. A subsequent US pelvis revealed a 24x10x17cm well circumscribed, avascular isoechoic structure arising from the uterus with sonographic features most consistent with an enlargement of the single uterine fibroid. A CT pulmonary angiogram was negative for pulmonary embolus. The patient underwent catheter directed thrombolysis with tissue Plasminogen Activator (tPA), and thereafter an IV unfractionated heparin infusion (UFH). As the patient needed definitive surgery requiring interruption of anticoagulation within the first four weeks of an acute thrombosis a hematology consult was sought. They recommended placement of a temporary inferior vena cava (IVC) filter with cessation of IV UFH 4 hours perioperatively with a repeat APTT to ensure complete clearance of heparin. A uterine myomectomy was performed and 12 hours post-operatively therapeutic anticoagulation with LMWH was recommenced. The myomectomy did not breach the uterine cavity and there were no post-operative bleeding complications. The temporary IVC filter was removed whilst the patient was on therapeutic LMWH. Thereafter she was commenced on therapeutic apixaban for 6 months for her provoked DVT due to the extent of the initial thrombosis. At six months post-operatively the patient was reviewed, the DOAC was stopped, and was deemed safe to recommence efforts to conceive. She has since successfully delivered her second child by elective caesarean section.

Figure 2

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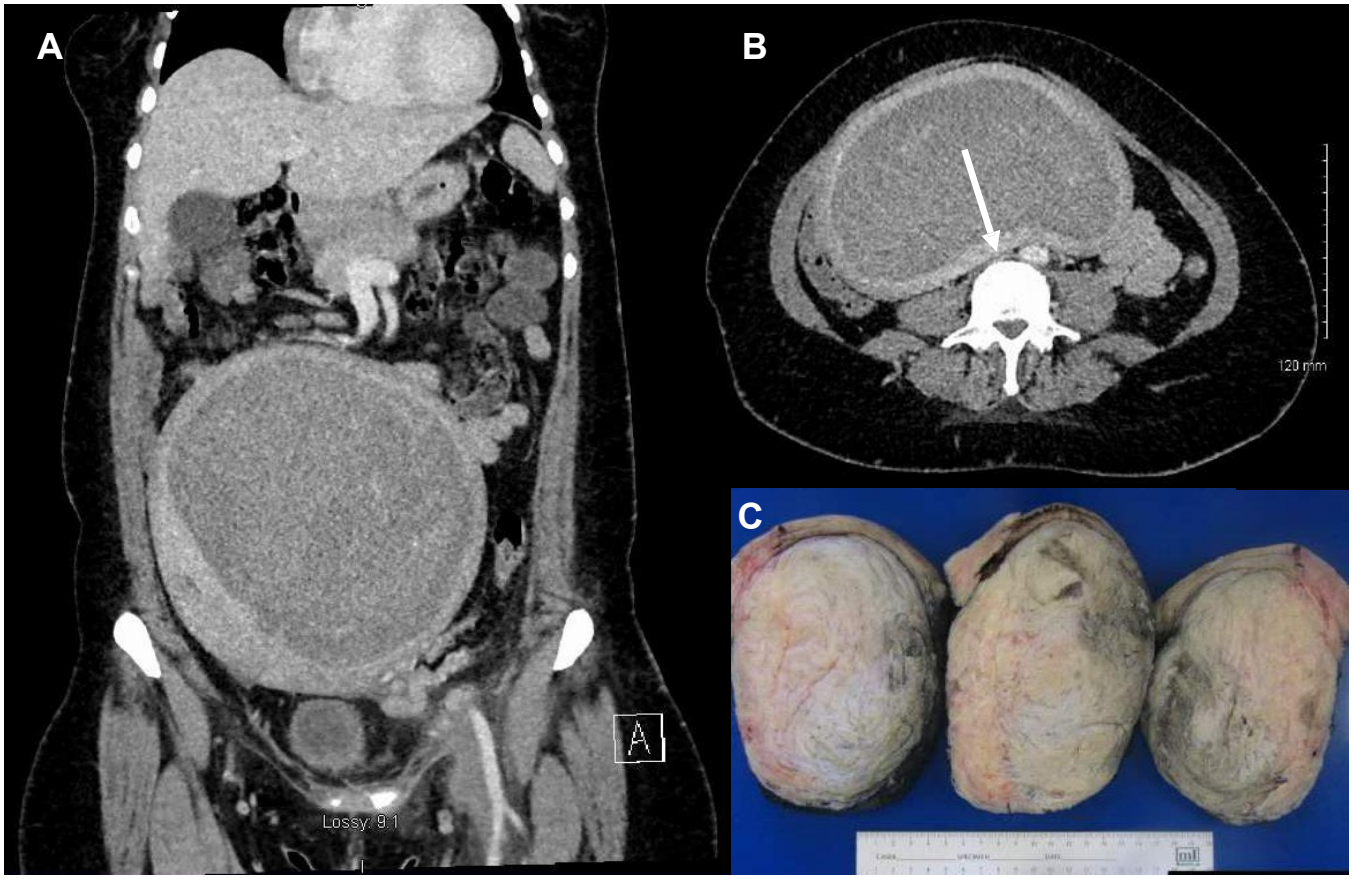

Figure 2. A) Coronal CT showing the extent of the uterine fibroid, *B)* Axial CT showing large single uterine fibroid compressing the inferior vena cava (white arrow), *C)* Clinical histopathology imaging following myomectomy

Case 3

The third subject is a 52-year-old para-two Caucasian woman, from the Irish travelling community, who had a three week delay in presentation to vascular services with critical limb ischemia. A venous duplex showed a thrombus from the proximal popliteal vein to the femoral vein. Her risk factors for arterial disease included a significant smoking history. The patient's past medical history was significant for an venous thromboembolism, which was an unprovoked DVT and a pulmonary embolism resulting in cardiac arrest 18 years previously. CT angiogram of the lower limb revealed acute arterial occlusions of the anterior tibial, tibio-peroneal trunk and posterior tibial arteries in the right lower limb, and DVTs were confirmed on the delayed images in the popliteal, femoral and external iliac veins. An incidental finding of a large septated multi-loculated pelvic mass in the abdomen was reported, most consistent with an ovarian mass roughly 25 x 15cm in diameter, and it was compressing the inferior vena cava and iliac veins (Figure 3A, 3B).

Management of the ischemic forefoot (Figure 4) was complicated by the late presentation, as the patient was outside the optimal window for embolectomy or thrombolysis. She was instead managed with immediate commencement of daily iloprost infusions and therapeutic tinzaparin. Similar to Case 2 the Haematology Team recommended temporary IVC filter placement to prevent pulmonary embolus whilst therapeutic anti-coagulation was held. The patient underwent a transabdominal hysterectomy and bilateral salpingo-oophorectomy under the care of the gynaecology team. The right ovarian cyst measured 28x23x16cm and weighed 5.85 kg (Figure 3C, 3D). On histological examination the features of the ovarian cyst favoured a benign necrotic mass that was most consistent with a mucinous cystadenoma. There was no evidence of malignancy.

One week later the patient underwent a transmetatarsal amputation for established gangrene secondary to hypoperfusion. Inter-operatively she was on therapeutic LMWH. However the wound failed to heal and the patient required a subsequent below-knee amputation. The IVC filter was removed post-operatively without complication. Since this surgery the wound has fully recovered and the patient is mobilizing with a prosthesis. She completed six months of therapeutic anti-coagulation with a DOAC, given her extensive thrombosis and previous history of pulmonary embolism.

Figure 3

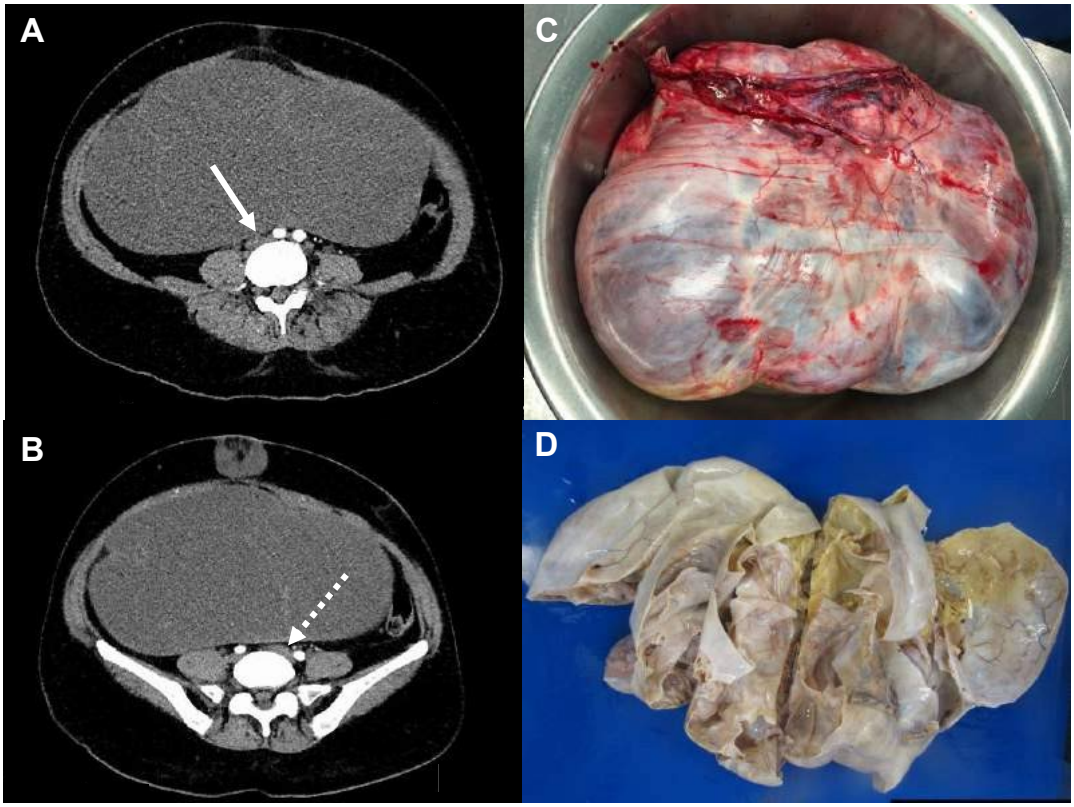

Figure 3. A) Axial CT showing large septated likely ovarian mass compressing the inferior vena

cava (solid arrow), *B)* Axial CT showing compression (dashed arrow) of the external iliac vein on the left by the ovarian mass against the lumbar spine, though it is still patent, *C)* Photographic imaging of the right ovarian cyst following removal, *D)* Clinical histopathological imaging of the ovarian mass.

Figure 4

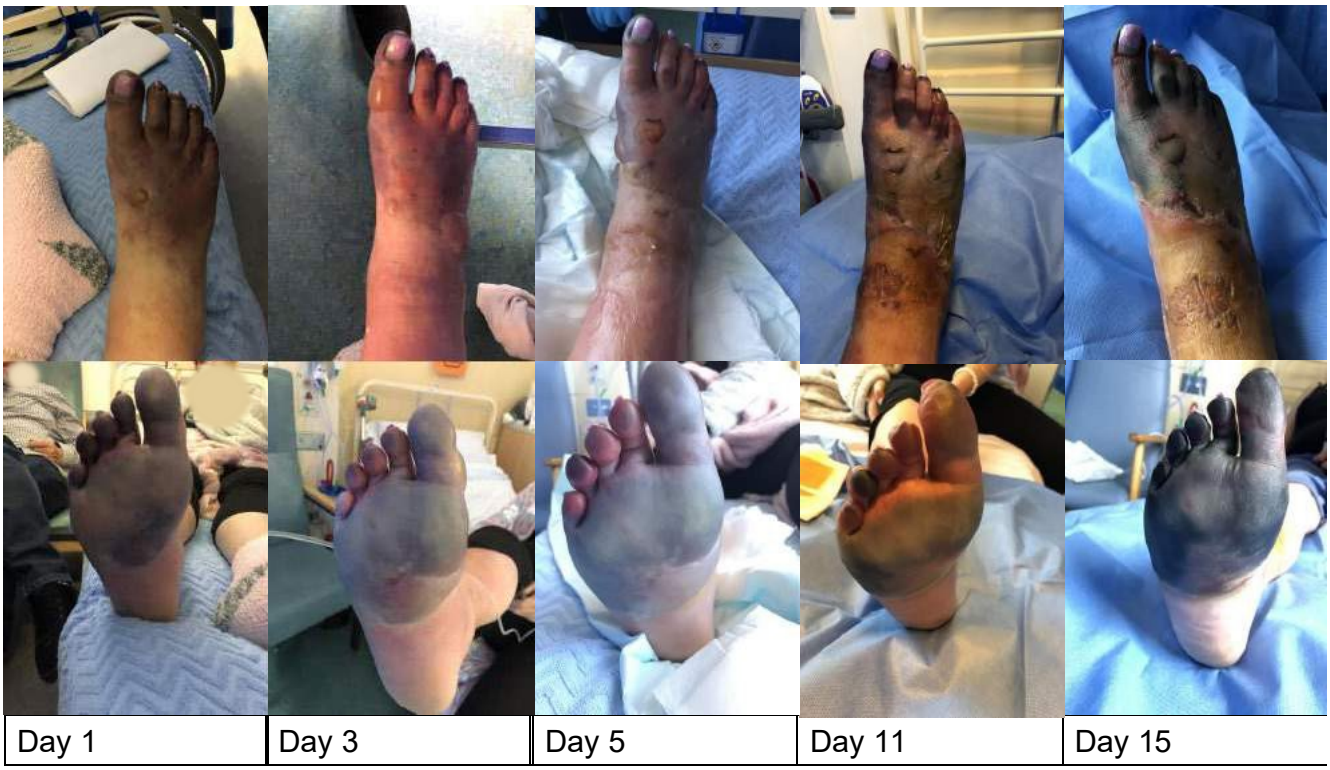

Figure 4. Case 3 Patient's right foot over the course of her iloprost treatment. Moderate improvement in perfusion to the skin was shown, but by day 14 of iloprost treatment the foot demarcates, the skin macerating with early signs of dry gangrene.

Discussion

We present three cases of women with gynaecological pathology causing venous thromboses. DVT/PE caused by fibroids is an established phenomenon[6,7], but one of a number of pathological processes needed to be considered in these women, who were all generally fit and well and two with no prior knowledge of their pelvic pathology. Cancer-associated thrombosis (CAT) is one reason for provoked DVT, and was considered in these cases, however, testing for CA-125, CEA and alpha-fetoprotein levels were negative in our cases and a benign provoking factor was identified. This made malignancy highly unlikely, but CAT should be considered in all patients presenting with diffuse or atypical thrombosis[8].

Underlying coagulation disorders can also be a cause for acute limb ischemia and DVT[9]. Our patients did not meet the criteria for thrombophilia testing, though anti-phospholipid antibody was completed and were also negative in all three cases, which was an important screen, in particular for the patient in Case 3.

Local protocol recommends empiric anti-coagulation for management of DVT and ischemic limb in line with current international guidelines[10,11]. Of note, the first case was initially discharged on maintenance dose of DOAC therapy, without a loading dose. Apixaban, when used therapeutically for a DVT, requires a loading dose of 10mg BD for one week, before dropping to therapeutic 5mg BD thereafter. Prescribing errors with DOACs are well described in the literature, with subtherapeutic being the most common[12]. Prescriber education regarding all DOACs, their indications and various dosages is paramount. Patient specific side effects such as DOAC-induced uterine bleeding in our patient cohort, also needs to be considered before the initiation of anti-coagulation, especially in the context of women with a known history of menorrhagia[13].

Active treatment for a DVT requires a minimum of three months of anticoagulation[11]. Selection of agent is based on local policy, national and international recommendations and individual patient factors. Thrombo-embolic events that are provoked by a reversible risk factor, have a low risk of recurrence and can usually be treated safely for three to six months of anti-coagulation[11] Compliance is key as interruption of anti-coagulation in early thrombosis treatment has a higher risk of DVT recurrence[14]. All three women received 3-6 months of anticoagulation for provoked VTE and were followed up by both Gynaecology and Haematology services.

We identified the need to ensure that appropriate dosing, especially loading doses, of therapeutic anticoagulation is provided when treating lower limb thrombosis. Once the provoking factor in the form of a gynaecological pathology was removed with surgical intervention the risk of recurrence was deemed exceptionally low. We also acknowledge that in circumstances were the interruption of anticoagulation for surgical intervention is indicated within the first month of an acute thrombosis consideration for an IVC filter placement should be given. It was important to note that IVC filters were promptly removed post-operatively in the respective cases, once it was deemed safe to re-anti-coagulate them, and that this timing should be managed and informed by specialist Haematology consultation.

In effect, the diagnosis of the underlying gynaecological pathology, and the prompt management of each of the causal pathologies, spared each of these women the diagnosis of an ‘unprovoked DVT’ and the long term anti-coagulation. Essential to the management of these patients was a multi-disciplinary approach. We conclude by highlighting that

gynaecological pathologies should be considered on the differential list, and that a short gynaecological history, an abdominal examination and a low threshold for abdominal ultrasound would be practical, affordable, and a non-invasive investigation to add to routine work-up of women presenting with lower limb thrombosis.

Conclusion

This is a case comparison of gynaecological pelvic pathologies that presented with vascular lower limb pathology, both DVT and acute limb ischemia. We highlight that gynaecological pathology is a syndrome that is not high on routine differential lists but is easily, and cheaply identified and non-invasively investigated, and most importantly often has a clear defined treatment with obvious benefits to the patients.

Declarations of Conflicts of Interest:
None declared.

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