CASE REPORT

Pyrexia of unknown origin: inferior vena cava agenesis

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SUMMARY

A 26-year-old woman presented with a 5-day history of fever after returning from Bali. She denied sexual contact abroad. On examination, there was suprapubic tenderness and a widespread maculopapular rash. Malaria serology was negative and blood tests were normal except for an elevated C reactive protein. Treatment was initially with ceftriaxone, metronidazole and doxycycline, but her symptoms failed to improve. A CT pelvis suggested a possible tubo-ovarian abscess, a suspected inferior vena cava (IVC) anomaly and left internal iliac/femoral venous thrombosis. A gynaecology review demonstrated left tubo-ovarian tenderness and fullness. An MRI suggested pelvic inflammatory disease and thrombophlebitis affecting the pelvic veins; deep vein thrombosis (DVT) treatment was commenced. Further family history revealed thrombosis throughout multiple generations. Further imaging analysis demonstrated agenesis of the IVC with compensatory dilation of pelvic collaterals and an acute DVT of the deep pelvic venous system. The patient was discharged with direct oral anticoagulant therapy.

BACKGROUND

The presentation of fever in a young returning traveller may be a result of sexually transmitted disease. Clinical examination and initial imaging supported a diagnosis of pelvic inflammatory disease (PID). However, the subsequent failure of the patient to respond to treatment prompted more detailed pelvic imaging. This demonstrated a developmental abnormality in the inferior vena cava (IVC) with consequent hypertrophy of collaterals and a venous thrombosis. IVC abnormalities increase the risk of deep vein thrombosis (DVT) and are present in 0.3%–0.5% of the general population.[1] In those patients with a strong thrombotic family history, it is therefore important to consider structural vascular abnormalities and consequent thrombosis as a potential differential diagnosis in fever of unknown origin cases.

CASE PRESENTATION

A 26-year-old woman returned from Bali with a 5-day history of tiredness and back pain. It was noticed by family that she was shivering with a high temperature. No cough or dysuria was reported nor weight loss. At the time of presentation, she was menstruating, on the combined contraceptive pill/oral contraceptives and denied sexual contact while on holiday.

No medical history or regular medications were reported. The patient was up to date with her vaccinations and normally independent prior to travel.

On examination, the patient was feverish with right upper quadrant and suprapubic tenderness, with a maculopapular rash over the body—thought initially to be secondary to bed bugs that the patient had noticed in the last hostel she stayed in. The remainder of the clinical examination including cardiovascular and respiratory systems were normal and her calves were soft and non-tender.

INVESTIGATIONS

Bloods: C reactive protein 388, sodium 140 mmol/L, potassium 4.1 mmol/L, urea 2.8 mmol/L, creatinine 63 μmol/L, eGFR (estimated Glomerular Filtration Rate) >90 mL/min/1.73 m^2, albumin 32 g/L, ALP (alkaline phosphatase) 61 IU/L, ALT (alanine aminotransferase) 12 IU/L, bilirubin 6 μmol/L, INR (international normalised ratio) 1.1, white cell count 8.45×10^9/L, neutrophils 5.85×10^9/L, haemoglobin 126 g/L, platelets 291×10^9/L.

- Malaria screen negative.
- Dengue negative.

DIFFERENTIAL DIAGNOSIS

- PID.
- Pyelonephritis.
- Hepatitis.
- Dengue.

TREATMENT

The patient was started on ceftriaxone initially as appropriate broad-spectrum antibiotic cover for fever of unknown origin. Malaria and dengue screening tests were negative early in the course of investigation, and the clinical presentation and laboratory findings were not in keeping with these travel associated infections. Metronidazole and doxycycline were added for treatment of PID once imaging findings were reported.

Treatment dose low molecular weight heparin therapy was started on radiological diagnosis of pelvic DVT. This was switched to direct oral anticoagulant therapy following discussion with haematology.

OUTCOME AND FOLLOW-UP

The patient's persistent symptoms prompted a CT abdomen/pelvis for investigation for a possible psoas abscess. This demonstrated a complex soft-tissue density in the left side of the pelvis/tubo-ovarian region—possibly a tubal ovarian abscess and

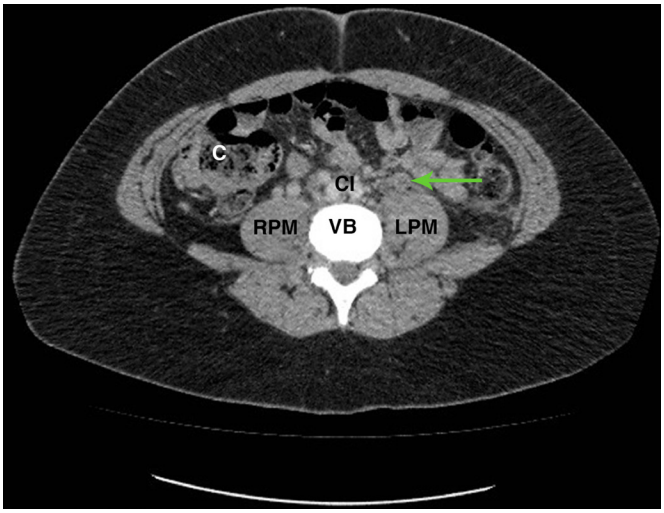

Figure 1 Axial CT slice at the level of L4 with arrow demonstrating thrombosis in the left ovarian vein anterior to the left psoas muscle. C, ascending colon; CI, bifurcation of aorta to common iliac arteries; LPM, left psoas major; RPM, right psoas major; VB, vertebral body.

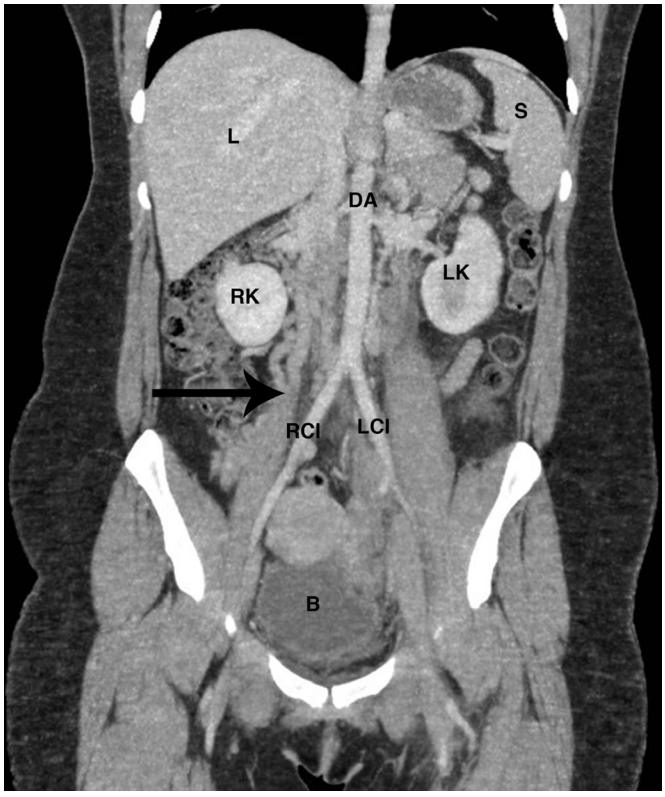

Figure 2 Coronal CT slice with arrow demonstrating the expected location of an inferior vena cava; in this patient replaced with distended collateral veins. B, bladder; DA, descending aorta; L, liver; LCI, left common iliac artery; LK, left kidney; RCI, right common iliac artery; RK, right kidney; S, spleen.

associated lymphadenopathy—and mild hydronephrosis. There was a left internal iliac/femoral venous thrombosis. Incidental note was made of a poorly visualised IVC with multiple smaller veins in the retroperitoneum suggestive of an IVC anomaly.

The gynaecology review following the CT abdomen/pelvis report noted the tenderness to the left iliac fossa and vague mass. White non-offensive discharge was found on vaginal examination, with no cervical excitation. Tenderness and fullness was found to the left tubo-ovarian area only.

A subsequent MRI pelvis showed anomalous venous structures within the abdomen and pelvis with likely thrombosis and inflammation of grossly dilated varices within the left side of the pelvis. The scan also demonstrated wall enhancement post contrast associated with moderate inflammatory change in the left side of the pelvis.

She was maintained on PID treatment. The patient's symptoms failed to resolve and she reported increased pain. A second gynaecology consultant reviewed the images and determined that the ongoing pain was likely due to inflammation secondary to thrombotic varices in the pelvis. Further review of previous imaging demonstrated agenesis of the IVC (AIVC) with compensatory dilation of pelvic collaterals and an acute DVT of the deep pelvic venous system (see figures 1 and 2). A more detailed family history revealed that her father had had three previous DVTs and other family members had multiple pulmonary embolisms.

The patient was increased to treatment dose (1.5 mg/kg) low molecular weight heparin. A filter in the larger collateral vein was discussed with haematology, but not recommended. She was discharged on rivaroxaban and followed up by haematology in thrombosis clinic.

A repeat MRI pelvis was carried out, which showed multiple bilateral pelvic varicosities. There was some resolution of the thrombosis, and she will continue under gynaecology follow-up.

DISCUSSION

IVC abnormalities are present in 0.3%–0.5% of the general population,[2] rising to 0.6%–2% in those with cardiac abnormalities. The incidence of AIVC in the general population is estimated to be 0.0005%–1%[3–6]; however, this may rise to as high as 9% in young patients presenting with thrombosis investigated with CT/MRI.[7]

DVT associated with IVC abnormalities are well described in the literature attributed to poor collateral venous drainage often resulting in proximal and bilateral DVTs.[7 8]

Our case highlights the potential for misdiagnosing pelvic DVT in this atypical population presenting with features such as pelvic pain and menorrhagia in young women.[9] In addition, while AIVC is usually asymptomatic and often diagnosed incidentally, first presentations are often with venous thrombosis though fever and rigours have been described as well as subsequent lower-limb oedema.[10]

Due to the increased risk of DVT in the collateral vessels,[3–5] previous case reports endorse screening of the IVC in young patients presenting with idiopathic DVT[11] with either ultrasound or CT venography, though MRI has also been described as an effective imaging technique for IVC abnormalities.[4 6 10 12] The network of collateral vessels in these patients can cause diagnostic issues in non-contrast CT scanning due to a tumour-like appearance.[13]

The authors are not aware of an increased risk to infections as a result of this congenital abnormality; however, there are case reports suggesting a higher risk of DVT if there is a concomitant infection, with one reporting pelvic thrombosis in a 14-year-old boy with *Mycoplasma pneumoniae* infection.[7]

Treatment generally involves the acute treatment of the thrombotic presentation with thrombolytics or heparinoids followed by longer-term preventative therapy including mechanical compression and lifelong anticoagulation.[7 10 14–17] Thrombolytic therapy for proximal DVTs has also been

delivered through a catheter-directed approach.[8] Additionally, multiple surgical techniques have been described.[18 19]

Stereotypical presentations can be misleading and it is important to review a diagnosis if the clinical course or response to treatment does not proceed as expected. In this case, imaging by a different modality was key to establishing the cause.

Learning points

- Congenital malformation of the inferior vena cava is a rare cause of pelvic and other deep vein thromboses and should be considered in young people with thromboses, particularly those with paediatric presentations.
- Review a diagnosis if the clinical course or response to treatment does not proceed as expected.

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