Abstract:
We describe a rare case of acute renal infarction with spontaneous arterial and venous thrombosis in 23-year old lady with no thrombotic risk factors apart from raised Factor VIII levels.

Keyword: Spontaneous renal infarction, Elevated Factor VIII levels

CASE SUMMARY:
A 23-year newly-wed homemaker from Kanyakumari with no known comorbidities presented to her primary physician with sudden onset non-radiating, left loin pain of a stabbing nature. The pain progressively increased over 8 hours, and was associated with 1 episode of vomiting. There was a history of passing “brown-coloured” urine once. She had low-grade fever which developed after 2 units of blood were transfused at a local nursing home, where she was noted to be pale and dehydrated. There was no oliguria / calculuria / burning micturition / trauma / pedal edema or foamy urine. She had no joint pain / dysphagia / digital ischemia / chest pain or breathlessness. She denied history of abortions / pregnancies / OCP use. She was started on antibiotics with a presumptive diagnosis of left acute pyelonephritis. Urine and blood cultures were sterile. Ultrasonography revealed an edematous left kidney. Renal Doppler showed an absence of blood flow in the left kidney, at which point she was referred to our centre for further evaluation.

She was asymptomatic when she presented to our hospital. The general physical & abdominal examination revealed no abnormality. Duplex Doppler showed a hypoechoic left kidney with no evidence of both arterial and venous colour flow. The right renal vein showed normal colour flow, spectral pattern and phasicity. (Fig.1)

CT Angiogram revealed a diffusely hypodense 10.5 cm-sized left kidney with loss of cortico-medullary differentiation and a thin peripheral rim of enhancement (Fig.2). The left renal artery was diffusely attenuated.
with a non-visualised distal segment at the hilum (Figs. 3&4). The proximal segment from the ostium to mid-segment did not show a thrombus, suggestive of a primary renal vein thrombosis with secondary arterial occlusion. The left renal vein was not opacified with contrast (Fig.5). There was no hydronephrosis. The right kidney measured 10.7 cm and was normal.

Her blood investigations revealed a serum creatinine of 0.8 mg%; Urine protein/urine creatinine ratio and urinalysis were normal. The urine culture grew contaminants. Her haemoglobin, total leukocyte count, ESR, blood sugars, fasting lipid profile and liver function tests were all within normal limits. There was mild thrombocytopenia with a manual platelet count of 90,000/cumm. The HIV test was negative. The levels of C3, C4, antidiolipin, IgG antibodies to B2-Glycoprotein I complex, homocysteine, fibrinogen, D-Dimer, PT, APTT, protein C, protein S, AT III, APCR and DRVTT for lupus anticoagulant were all normal. Ham’s test, sucrose lysis test, and sickle test were negative. The thrombotic workup was notable for the presence of a raised Factor VIII level. D-Dimer levels were also elevated, as expected in the presence of an ongoing thrombosis. A rheumatology consult was sought and it was opined that there was no evidence to suggest an underlying connective disorder. The case was reviewed with a hematologist, on whose advice she was started on tab. Warfarin and low molecular weight heparin therapy. The latter was stopped once the target INR of 2.5-3.0 was reached. As the risk of bleeding would increase significantly with the addition of an antiplatelet, it was decided not to start her on Aspirin / Clopidogrel for now. She was asymptomatic at discharge and has been advised life-long Warfarin therapy and close follow-up at regular intervals.

**DISCUSSION:**
This lady was referred to us for evaluation of of an infarcted left kidney with no obvious cause evident. The diagnosis of renal infarct was first confirmed by Doppler and angiography, which showed a renal vein thrombus and hypoattenuated left renal artery. Renal vein thrombosis (RVT), which is a well-described entity in neonates (1), is relatively rare in adults. Apart from infection, trauma and malignancies, RVT is most commonly associated with nephrotic syndrome (2). Other known causes (3) of renal vein thrombosis are tabulated below. Renal arterial thrombosis causing renal infarction has also been described, with a varying number of aetiologies ranging from prothrombotic states (4) to idiopathic causes (5).

**CAUSES OF RENAL VEIN THROMBOSIS:**
- **ENDOTHELIAL DAMAGE** Blunt trauma Trauma during venography Renal transplant Infiltration by tumour Acute rejection Vasculitis Spontaneous microtrauma to the endothelium e.g. in Homocystinuria
- **STASIS** Severe volume losses e.g. GI fluid loss, haemorrhage, dehydration Post transplant distortion / kink of renal vein Primary retroperitoneal processes with renal vein compression
- **HYPERCOAGULABILITY** Nephrotic Syndrome Membranous glomerulonephritis Membranoproliferative glomerulonephritis Focal segmental glomerulosclerosis Minimal change disease Sepsis:
  - Generalized/Localized Puerperium
  - Disseminated malignancy
  - Oral contraceptives
  - Intrinsic Hypercoagulability
Factor V Leiden (Resistance to activated protein C)  
Prothrombin gene mutation (G20210A)  
Deficiency of Protein S  
Deficiency of Protein C  
Deficiency of anti-thrombin  
POORLY UNDERSTOOD CAUSES  
Anti-phospholipid Syndrome  
Primary & Secondary e.g., SLE  
Behcet’s disease AIDS-associated nephropathy  

After establishing the presence of the infarct, we then proceeded to look for the aetiology in her. With no history of trauma available, infection as a possible cause was looked at. However, both her initial and subsequent urine and blood cultures were sterile. As the clinical symptoms in our patient mimicked acute pyelonephritis, she was erroneously treated elsewhere for this. In retrospect, her symptomatology was suggestive of a renal vein thrombosis, which was missed. In today’s era of antibiotics, renal vessel thrombosis precipitated by an acute pyelonephritis seems unlikely. Her physical findings did not point to vasculitis either; this was corroborated with negative vasculitic markers like lupus anticoagulant, PT and APTT. There were no features to suggest nephrotic syndrome. An underlying pro-coagulant disorder causing arterial thrombosis would have been consistent with this clinical picture; however, all the pro-coagulant parameters were negative, barring the elevated Factor VIII levels. Factor VIII is a clotting factor which is deficient in haemophilia. Elevated factor VIII levels have been implicated as an aetiological factor in both arterial (6) and venous (7) thrombotic events. The exact mechanism by which this occurs is yet to be elucidated. While the elevated factor VIII levels in our case could point to this as a possible cause (especially since all other known risk factors were negative), the aetiology was probably spontaneous. The management dilemma in our case involved treating the acute episode with established thrombus as well as ensuring the same process did not further recur and affect the solitary functioning remnant kidney. The question of the need for a nephrectomy of the thrombosed kidney also arose. There are only four indications mentioned in literature (3) for performing a nephrectomy in the event of renal vessel thrombosis—viz. acute life threatening hemorrhage from capsular rupture, renal allograft rupture, RCC with renal vein thrombosis, and long term sequelae of thrombosis like hypertension and infection.

The role of endovascular management of renal arterial thrombosis is not well-defined. The primary aim is to re-establish renal perfusion and preserve function. The options include pharmacomechanical Thrombectomy, intravascular fibrinolytic therapy and aspiration thrombectomy (8). Prolonged ischemic times and cortical atrophy are contraindications to the use of this approach. Studies have shown that the aetiology of the occlusion can make a difference to outcomes. Ouriel at al (8) found that thrombectomy was successful in restoring renal function in cases of thrombosis, but in embolic-traumatic cases embolectomy/reperfusion could not do so, despite initiation of therapy within 6 hours of the occlusion. Endovascular treatment plays a role in select cases of renal vein thrombosis also. Mechanical thrombectomy or chemical thrombolyisis using Streptokinase, Urokinase or recombinant TPA (tissue plasminogen activator) has been tried (9). These modalities have...
specific indications, enlisted below (3). IVC filters may need to be placed in those with a concomitant IVC thrombus or to prevent pulmonary embolism.

**INDICATIONS FOR THROMBECTOMY/THROMBOLYSIS IN RVT:**
- Treatment failure while on adequate anticoagulation
- Onset of complications e.g. pulmonary embolism
- Bilateral RVT
- Acute renal failure (Bilateral RVT/RVT in solitary kidney)
- Extension into inferior vena cava
- Contraindication to systemic anticoagulant therapy
- Renal transplant
- Severe, persistent flank pain
- By nature of its non-specific clinical presentation, the imaging and work-up required for renal vascular thrombosis is commonly missed. An algorithm to approach such cases is outlined below:

**SUMMARY**

Our case report highlights the need for awareness of this rare condition of renal infarction and what to do when confronted with such a case. The need for a thorough evaluation of all possible causes, with the use of a management algorithm, is suggested. Elevated factor VIII levels as a
possible cause must also be kept in mind when other aetiological factors have been ruled out. If indicated, prompt thrombolysis in the acute setting may prove valuable in salvaging renal function. Delayed presentation necessitates a nephrectomy only in select scenarios, while the rest mandatorily require anticoagulation therapy and close follow-up.

Fig. 1 Duplex Doppler ultrasound showing absence of a flow within a hypoechoic kidney
Fig. 2 Computerised tomography (CT) angiogram showing a hypodense left kidney with a thin cortical layer

Fig. 3 Diffusely attenuated left renal artery on the CT angiogram

Fig. 4 Reconstructed CT angiography image showing non-visualised left renal distal segmental arteries
REFERENCES:


