Bilateral renal vein thrombosis secondary to methylene tetrahydrofolate reductase mutation: a rare case

To the Editor,
Renal vein thrombosis (RVT) is a rare but serious complication that is associated with many systemic disorders [1]. Thromboembolic complications, especially RVT, are frequent in nephrotic syndrome and are very prevalent in membranous nephropathy [1]. Trauma, oral contraceptives, infection, inherited pro-coagulant defects, lupus anticoagulant, antiphospholipid syndrome and severe dehydration are the other most common causes of RVT in adults [1]. Herein, we describe bilateral RVT secondary to heterozygous methylene tetrahydrofolate reductase (MTHFR) mutation. During differential diagnosis, we wish to alert physicians that RVT may be a cause of flank pain and haematuria, even in subjects with no known risk factors for thrombosis. Because early diagnosis with appropriate treatment is associated with good prognosis, the present case highlights the importance of thrombophilic investigation in all patients with suspected RVT to avoid missing this rare but frequently curable condition.

To the best of our knowledge, this is the first reported case of RVT associated with MTHFR mutation in the adult population.

A 29-year-old woman was admitted to the hospital after complaining of sudden onset right flank pain. Her medical history was unremarkable and she was not using any drugs or oral contraceptives. She had one healthy 5-year-old child and no reported abortion or miscarriage. There was no family history of thrombosis. On admission, her vital signs and physical examination were normal except for right flank tenderness.

Admission laboratory analyses showed haemoglobin = 10.5 g/dL (12–16 g/dL), leucocyte = 12.3 × 10⁹/L, platelet = 515 × 10⁹/L, mean corpuscular volume (MCV) = 73.6 fl (80–96 fl) and C-reactive protein = 16 mg/L (0–10 mg/L). Her urinalysis showed microscopic haematuria. Her renal and liver function analyses were all normal. Chest and abdominal X-rays and electrocardiogram showed nothing remarkable. Abdominal ultrasonography (US) was suspicious for thrombosis of the right and left RV without any evidence of masses or hydronephrosis. Further investigation with Doppler US revealed absence of blood flow at the right RV, total continuous thrombosis from the right RV to the vena cava inferior (VCI) and a partial thrombosis at the left RV extending to the VCI. The patient was diagnosed with bilateral RVT. After these findings were confirmed with renal venography, manual thrombus aspiration was performed and optimal restoration of bilateral RV was obtained (Figure 1). Although a partial thrombus remained because of the difficulties and risks associated with mechanical total aspiration, a selective thrombolytic treatment was planned. Continuous streptokinase infusion was given through a catheter that was placed during venography. Anticoagulant therapy was continued with enoxaparin. On the following day, control angiography showed normal contrast transition and no thrombosis. At the third day, she was advised to continue anticoagulation with warfarin. An extensive workup to determine the underlying cause was performed. Her echocardiography and thoracoabdominal computed tomography (CT) findings were normal. She had no evidence of nephrotic syndrome or glomerulonephritis. Serum folate, vitamin B₁₂, complement, erythropoietin and homocysteine (Hcy) levels were all normal. Results for protein C and S deficiency, antinuclear antigen, anti-double-stranded DNA, lupus anticoagulant, anti-cardiolipin antibodies, antithrombin III and viral markers using blood that had been collected before anticoagulant therapy were all negative. Investigations into an underlying hereditary thrombophilia showed only heterozygous MTHFR-1298 gene mutation; a lifelong oral anticoagulant therapy with warfarin and aspirin was recommended. After 3 months, her control CT angiography showed no thrombosis in the RVs or VCI.

Diagnosis of RVT is difficult and physicians must have high suspicion of the disease to make early diagnosis, especially in young patients without any risk factors [2]. After confirmation of RVT, a full evaluation for underlying disorders should be undertaken to direct future therapy/precautions and to obtain prognostic indications for recur-

Fig. 1. Filling defects secondary to thrombosis in the right RV and VCI (white arrows) after contrast administration from vena cava superior.
Treatment for RVT has evolved from nephrectomy to thrombectomy and finally to thrombolytic therapy with anticoagulation, which is currently the standard treatment of choice [1].

Here, we present a young woman with bilateral RVT. Her case constituted the first clinical report of heterozygous MTHFR mutation with RVT, which was her only risk factor for the disease. MTHFR is a key enzyme for intracellular folate homeostasis and metabolism that catalyses the reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, the main circulating form of folate and the methyl donor for the vitamin B12-dependent remethylation of Hcy to methionine. Results from previous studies showed that the 677TT MTHFR genotype can be considered as an independent risk factor for both arterial and venous thrombosis and may itself increase the risk for thrombosis even in the absence of other thrombophilic risk factors [3,4]. Recently, a novel MTHFR polymorphism, 1298A3C, which changes glutamic acid into an alanine residue, was shown to be associated with decreased enzyme activity but did not result in decreased folate plasma levels or increased plasma Hcy concentrations in homozygous or heterozygous members of neural tube defect families [5]. Also, others have reported that MTHFR 1298CC and MTHFR 1298AC had no effect on the risk for vein thrombosis [6]. In contrast, we present the first adult case that shows a relation between RVT and MTHFR-1298.

Conflict of interest statement. None declared.

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don: 10.1093/ndtplus/sfq049

Advance Access publication 22 April 2010

A growing transplanted kidney

Sir,

Renal sinus lipomatosis (RSL) is a rare disease, described by replacement of parenchyma by sinus and/or perirenal fat. We report here an exceptional case of RSL on kidney graft after corticosteroid treatment was stopped, leading to functional graft transplantectomy.

A 74-year-old man received a first renal allograft in 2004. He was maintained on tacrolimus and mycophenolate mofetil with no rejection. Corticosteroid was stopped at the sixth month. The lowest serum creatinine level was 100 μmol/L. On February 2007, renal ultrasonography, performed for acute renal failure, showed dilatation of renal cavities. Contrast-enhanced computed tomography (CT) showed an enlarged kidney (14.3 cm) with an increased amount of fatty-like tissue in renal sinus and perirenal area (Figure 1). For 6 months, he experienced several obstructive renal failures and infections, leading to permanent nephrostomy. Biopsy of the sinus mass revealed an extensive fatty tissue with fibrosis. Finally, because of bilateral pulmonary embolism secondary to vena cava compression, persistent obstruction and continuous graft enlargement without conclusive histology, and despite good renal function, he underwent transplantectomy. Histological examination showed RSL (immunophenotypical labelling and biomolecular investigations negative for sarcoma) and atrophic chronic pyelonephritis graft.

RSL is essentially described on native kidneys [1,2]. Possible risk factors for RSL include ageing, obesity and pathologic states that cause renal inflammation such as intense corticotherapy and/or early rejection for transplants. Often, chronic or repeat urinary tract infections have been found, and one hypothesis is that RSL may be secondary to periodic leakages of urine into the peripelvic tissues [2]. RSL can also be part of replacement of destroyed or atrophic renal tissue [3]. It has also been suggested that high-dose steroid treatment by itself, Cushing’s syndrome or obesity may have contributed to the development of fibrolipomatosis [4]. Intriguingly, a very few cases of RSL have been reported in the renal transplant population [5]. This case is intriguing for several reasons: The time between transplantation and the first symptoms was quite long (3 years). The recipient of the contralateral kidney did not develop any RSL. The patient experienced his first urinary tract infection at the same time as the first acute obstructive renal failure. No history of earlier acute rejection episodes has been found. He did not have a long-term steroid treatment and was not obese. Finally, our case is also...