Interesting Case

Renal vein thrombosis as a presenting symptom of multiple genetic pro-coagulant defects

Talya Wolak¹, Boris Rogachev¹, David Tovbin¹, Yancu Hertzanu², Moshe Zlotnik¹ and Gilles Lugassy³

¹Department of Nephrology and ²Department of Radiology and Nuclear Medicine, Soroka Medical Center, Ben Gurion University of the Negev and ³Hematology Institute, Barzilai Medical Center, Ben Gurion University of the Negev, Beer-Sheva, Israel

Keywords: hypercoagulation; renal vein thrombosis

Introduction

Renal vein thrombosis (RVT) may present as an acute or chronic event, the latter being more common, and patients are usually asymptomatic. Acute RVT is more frequent in younger patients and is characterized by a sudden onset of severe flank pain associated with marked costovertebral angle tenderness and macroscopic haematuria.

RVT is a known complication of the nephrotic syndrome. Other causes of acute RVT include membranous nephropathy and amyloidosis, trauma, oral contraceptive drugs, dehydration (mostly in infants) and steroid administration [1].

Case

A previously healthy 27-year-old female was admitted to the nephrology department suffering from severe pain in the left flank. The pain had begun 3 weeks previously during a vacation in India and 24 h after fasting. She was diagnosed as suffering from renal colic and was treated only with analgesia, with no improvement. Until the present episode, her past medical history had been unremarkable and the only medication she had taken to date was oral contraceptives.

On physical examination, she appeared to be in good clinical condition: blood pressure 107/80 mmHg, pulse 60 beats/min, body temperature 36.6°C. Skin, lungs and heart were normal. There was marked tenderness in the left flank. No lymphadenopathy was detected and the neurological examination was unremarkable. Urine appeared grossly normal. On microscopic examination there were 30 red blood cells in the field.

Laboratory tests on admission were haemoglobin 13.0 g/dl, white blood cells 5.71 × 10⁹/l, platelets 272 × 10⁹/l, glucose 71 mg/dl, urea 25 mg/dl, creatinine 1.09 mg/dl, potassium 4.8 mEq/l, sodium 142 mEq/l, albumin 3.5 g/dl, globulin 3.5 g/dl and urine protein 140 mg/24h. Prothrombin time (PT), international normalized ration (INR) and activated partial thromboplastin time were normal.

Spiral computed tomography (CT) of the abdomen was performed (Figure 1), revealing a normal right kidney and an enlarged left kidney, with a delay in the nephrographic effect in the left kidney and with a filling defect in the left renal vein. Dynamic renal scan demonstrated good function and perfusion of the right kidney (70%), and abnormal perfusion and decreased function of the left kidney (30%).

Anticoagulant treatment was initiated with heparin and warfarin. A repeat CT scan 1 week later showed improvement of the blood flow in the left renal vein system. The patient’s condition improved considerably and she was subsequently discharged after the INR rose above 2.

The patient was instructed to discontinue oral contraceptives and to continue with the warfarin. A repeat CT scan 1 week later showed improvement of the blood flow in the left renal vein system. The patient’s condition improved considerably and she was subsequently discharged after the INR rose above 2.

The patient was instructed to discontinue oral contraceptives and to continue with the warfarin. Although a renal scan conducted 3 months later showed improvement in the perfusion of the left kidney, it constituted only 38% of total renal function. The laboratory data a few months later were normal: haemoglobin 13.2 g/dl, white blood cells 6.5 × 10⁹/l, platelets 206 × 10⁹/l, urea 14.3 mg/dl, creatinine 0.8 mg/dl, potassium 3.8 mEq/l, albumin 3.9 g/dl, globulin 4.0 g/dl and sodium 142 mEq/l. Investigation for hypercoagulation diseases was conducted and the results were antithrombin III antibody (Ab) 104%.
methylenetetrahydrofolate reductase (MTHFR) gene deficiency – homozygote, PT mutation 20210 – heterozygote, factor V Leiden – heterozygote, factor VIII 190 (%), homocysteine 11.5 qMole/l, anticardiolipin Ab GPL (IgG phospholipid) 0.93 U/ml (normal), rheumatoid factor – negative, antinuclear Ab – negative, C3 – 115 mg% (normal) and C4 – 43 mg% (normal).

A screen for hypercoagulability was also recommended for first-degree relatives.

Discussion

We present a young woman with RVT, a severe thrombotic state, which constituted the first clinical manifestation of a combined hypercoagulation syndrome.

A high index of suspicion is needed to make a diagnosis of RVT. The diagnosis is especially difficult when the patient is young and without any known previous illness. The clinical presentation of RVT may mimic the symptoms of renal colic or acute pyelonephritis. One should keep in mind the possibility of RVT in cases with unresolved renal colic or pyelonephritis, especially in a patient with predisposing factors to hypercoagulability, such as oral contraceptives.

Our patient is a previously healthy 27-year-old woman who was taking oral contraceptives and had had an episode of dehydration 24 h before her symptoms began. Oral contraception is considered a relatively weak risk factor for venous thromboembolism. Bloemenkamp et al. recommended that venous thrombosis in the first period of oral contraceptive use might indicate the presence of an inherited clotting defect [2]. This underlying disorder in our patient presented as homozygous for the MTHFR gene deficiency, PT 20210 mutation heterozygote, factor V Leiden heterozygote and elevated factor VIII.

MTHFR gene deficiency is the most common form of genetic hyperhomocysteinaemia and results from production of a thermolabile variant of V-MTHFR with decreased activity. Homozygosity for this mutation enzyme is present in 9–17% of the population and heterozygosity can be detected in 30–41% of the general population [3]. Hyperhomocysteinaemia is known as an independent risk factor for atherosclerotic vascular disease [4]. It is also known to influence coagulation, increases platelet aggregation, activates factors V, X and XII, and inhibits antithrombin III and protein C.

Hereditary resistance to activated protein C is currently regarded as the most frequent cause of familial thrombosis. Most cases of resistance to activated protein C stem from missense mutation in the gene encoding factor V. This mutation, also known as factor V Leiden, has been found in 30–60% of cases of familial thrombophilia in patients of various ethnic origins [5]. The risk of thrombosis increases by 50–100% among homozygotes for factor V Leiden and by 5–10% among heterozygotes [6]. Many people who are heterozygous for this mutation may not have signs of thrombosis unless they have another genetic

Fig. 1. There is a delay in the nephrographic effect in the left kidney, with thrombus in the origin of the left renal vein.
defect or are exposed to additional precipitating factors [7]. Our patient, who is a heterozygote for factor V Leiden, had, in addition to genetic defects, exposure to oral contraceptives and was dehydrated.

Elevated plasma levels of factor VIII are associated with an increased risk for venous thrombosis. Among patients with venous thrombosis, the prevalence of an elevated plasma level of factor VIII is ~20% [8].

Another genetic polymorphism causing high risk for thrombosis is genetic variation in the 3'-untranslated region of the PT structural gene, involving a G to A substitution at nucleotide position 21210 (G20210A). Compared with normal homozygotes (G/G), heterozygous (G/A) carriers of this mutation have an almost 3-fold increased risk of venous thrombosis [9]. Arterial thrombosis was found in ≤5.7% of the cases [10]. The abnormality seems to be transmitted as an autosomal recessive trait.

In conclusion, we present a young woman who developed an acute episode of RVT, due to the combination of several risk factors for thrombosis, both genetic and environmental. Prompt diagnosis allowed early therapy of the thrombosis. An extensive aetiological investigation led to the finding of combined genetic thrombophilia, validating the clear indication for long-term anticoagulant therapy. This case illustrates the importance of a thrombophilic investigation in cases of thromboembolic disease, such as RVT. This is particularly important in atypical occurrences of thrombosis with symptoms that do not conform to the well-established risk factors for thromboembolic disease.

Conflict of interest statement. None declared.

References


Received for publication: 3.6.04
Accepted in revised form: 26.11.04