

Renal Vein Thrombosis and Membranous Nephropathy – Report of 2 Cases

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Abstract

Patients with nephrotic syndrome presents a high risk of arterial and venous thrombosis, mainly deep vein thrombosis and renal vein thrombosis (RVT). We describe two cases of patients with diagnosis of membranous nephropathy and RVT. The first patient was 32 years, male, and admitted with nephrotic syndrome. Laboratory tests showed urea 16mg/dL, creatinine 0.9mg/dL; proteinuria 17g/day. Abdominal ultrasound evidenced obstruction of right and left renal veins and left inferior vena cava. Renal biopsy was compatible with membranous nephropathy. The second patient, a 27 years old male was admitted with nephritic syndrome. Laboratory tests at admission showed urea 25mg/dL; creatinine 1.1mg/dL; 24h proteinuria 3.86g, abdominal ultrasound showed endoluminal obstruction of left renal vein and increased size left kidney. Renal biopsy showed membranous nephropathy. RVT is not common in patients with nephrotic syndrome, and it is more frequent in membranous nephropathy. Treatment includes intravenous anticoagulant followed by oral drugs. Prophylaxis in nephritic patients is controversial.

Keyword: Nephrotic syndrome, Thrombosis, Membranous glomerulonephritis, Blood coagulation

Introduction

Patients with nephrotic syndrome have a higher risk for venous and arterial thrombosis, mainly deep vein thrombosis (DVT) and renal vein thrombosis (RVT). The prevalence is estimated in 5% and 60%, mainly in patients with membranous nephropathy.¹⁻³

The prevalence of pulmonary embolism and DVT in patients with nephritic syndrome is based on case series. The prevalence of DVT in some cohorts was higher than the prevalence of RVT and in some series the prevalence of RVT was higher¹⁻¹⁶. The presence of asymptomatic pulmonary embolism and RVT were also described in nephrotic syndrome.^{8,9,17} The relative higher prevalence of RVT and its association with pulmonary embolism suggests that RVT was the origin of emboli in these patients with nephrotic syndrome.¹⁸⁻²⁰

RVT can be unilateral or bilateral; it can extend through inferior vena cava and can be associated with pulmonary embolism. The risk of thrombosis is proportional to the severity of nephritic syndrome, mainly with serum levels of albumin lower than 2g/dL and proteinuria higher than 10g/day.^{1,2} The majority of RVT cases are insidious and asymptomatic, without a clear association with proteinuria increase or renal function worsening. This paper describes two cases of membranous nephropathy complicated with RVT.

Case Reports

Case 1

A 32 years-old man was admitted with history of edema for three months, initially in lower limbs, that progressed to perineal region and abdomen, associated with oliguria. He also referred weight loss, associated with muscular pain and asthenia. At admission he had a good general appearance,



Fig-1: Ultrasound with doppler showing partial obstruction in right renal vein (A), left renal vein (B) and adjacent inferior vena cava (C).

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and the physical examination was unremarkable, unless for the presence of tender abdomen, with edema in abdominal wall and lower limbs. Laboratory tests at admission showed Hemoglobin 13.8g/dL; White blood count 8330/mm³; INR 0.86; Urea 16mg/dL; Creatinine 0.9mg/dL; K⁺ 3.9mEq/L; Na⁺ 144mEq/L; C3 129mg/dL; C4 48mg/dL; albumin 2g/dL; proteinuria de 24h 15g/day; negative antinuclear antibodies (ANA). Viral serologies were negative. An abdominal ultrasound with Doppler showed increased size kidneys, with increased echogenicity, obstruction of right renal vein, left renal vein and adjacent portion of inferior vena cava, compatible with renal vein thrombosis (Figure 1).

A renal biopsy was performed. At optic microscopy it was observed global thickening of basal membrane and the presence of spikes. Direct immunofluorescence found deposits of IgG, C3d and kappa and lambda chains, compatible with diagnosis of membranous nephropathy. Treatment with cyclosporine 100mg twice a day was started. After 6 months the laboratory tests showed creatinine 0.9mg/dL, urea 11mg/dL and proteinuria of 4.87g/day. The hematology consultant suggested anticoagulation with warfarin 7.5mg/day during the first 3 months, followed by a decrease for 5mg/day during 9 months. Anticardiolipin test was negative.

Case 2

A 27 years-old man was admitted with complaints of left lumbar pain that irradiated to left paravertebral region, abdomen and left testis for four weeks. He also noted increase in testis size. After two weeks of the initial symptoms he presented dark urine and lower limbs edema. At physical examination he presented only flank pain at palpation and percussion and increased scrotal bursa. Laboratorial tests at admission showed Hemoglobin 12.9g/dL; White blood count 7230/mm³; platelets 294000/mm³; urea 25mg/dL; creatinine 1.1mg/dL; K⁺ 4.4mEq/L; Na⁺ 138mEq/L; C3 169mg/dL; C4 50mg/dL; negative lupus anticoagulant; albumin 2.5g/dL. Negative viral serologies. Proteinuria 3.86g/day. An abdominal ultrasound with doppler showed normal sized kidneys, with obstruction in left renal vein, compatible with thrombosis. The patient was investigated for coagulation disturbances by the Division of Hematology and was not found to have any disturbance. A renal biopsy was performed and the histological pattern was compatible with membranous nephropathy. Initial treatment consisted in cyclophosphamide 100mg, twice a day, prednisone 15mg/day and warfarin 10mg/day. He presented a favorable outcome, with complete remission of the manifestations.

Discussion

The incidence of thrombosis, both venous and arterial, is higher in patients with nephrotic syndrome than in the general population.²¹ The risk of thrombosis varies according to the type of glomerulopathy. It is higher in membranous nephropathy, followed by membranoproliferative glomerulonephritis and minimal change disease.^{22,23} This risk seem also to be associated with the severity of nephritic syndrome and can increase when albumin concentration falls below 2.0gm/dl^{21,22,24-27}. We showed two cases of renal vein thrombosis (RVT) secondary to membranous nephropathy, with complete remission after specific treatment.

The cause of hypercoagulable state in nephritic syndrome is not completely known. It is believed that antithrombin and plasminogen levels are decreased, due to urinary losses, associated with platelets activation and hyperfibrinogenemia.^{1,2}

RVT can be uni or bilateral and can extends to inferior vena cava. The course of RVT is more frequently chronic, but acute forms, as observed in the described cases, can occur.^{1,2}

RVT can manifest with symptoms of renal infarction: flank pain, microhematuria, increased levels of LDH, scrotal edema and increased size kidneys.²⁸ RVT can also be asymptomatic. In the first case, the patient did not present complaints directly associated with RVT, while the second presented characteristic lumbar pain.

The gold standard method for the diagnosis of RVT is renal venography, but less invasive procedures are more frequently used, as ultrasound with Doppler, magnetic resonance or angiotomography.^{25,29,30-34} We preferred to use ultrasound because of its easy accessibility and absence of risks of using contrast media, and we found positive results that confirmed the diagnosis of RVT.

Treatment of RVT consists in anticoagulation. In nephrotic syndrome there are two aspects of anticoagulation that must be left under consideration: anticoagulation to prevent thrombotic events and dissolution of thrombi with thrombolitics.^{1,2}

Patients with RVT should be treated as the cases of pulmonary embolism. Initially it can be done with heparin followed by warfarin.³⁵ Some patients with nephritic syndrome can be resistant to initial anticoagulation due to decreased levels of antithrombin. Oral anticoagulation is recommended for 6 to 12 weeks and can be prolonged if the patient remains with nephrotic syndrome.

In summary, RVT is not a common event in nephritic syndrome and it is more frequent in those with membranous nephropathy. Treatment consists in anticoagulation. Prophylaxis in high risk patients with nephritic syndrome is controversial, and further studies on this aspect are necessary.

Conflict of Interest: None

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