Recovery of renal function after bilateral renal vein thrombosis episode as complication of membranous glomerulopathy: case report

Recuperação da função renal após episódio de trombose de veia renal bilateral como complicação da glomerulopatia membranosa: relato de caso

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Abstract

Renal vein thrombosis (RVT) is a complication often associated with nephrotic syndrome. It occurs due to a state of hypercoagulability common in the diseases that attend to this syndromic diagnosis. It should be suspected whenever there is nephrotic syndrome associated with sudden flank pain, hematuria and worsening of proteinuria. Bilateral RVT also presents with frequently oliguric renal dysfunction. This case reports a 33-year-old patient hospitalized for a nephrotic syndrome, with etiologic investigation suggestive of primary membranous glomerulopathy, which evolved with bilateral RVT associated with deterioration of renal function and need for renal replacement therapy. He promptly performed angiography with thrombectomy and thrombolysis, evolving with recovery of renal function in two weeks.

Keywords: glomerulonephritis, membranous; proteinuria; venous thrombosis.

Resumo

A trombose de veia renal (TVR) é uma complicação muitas vezes associada à síndrome nefrótica. Ocorre devido a um estado de hipercoagulabilidade comum nas enfermidades que cursam com esse diagnóstico sindrômico. Deve ser suspeitada sempre que houver síndrome nefrótica associada à dor súbita em flanco, hematúria e piora da proteinúria. TVR bilateral cursa, ainda, com disfunção renal frequentemente oligúrica. Esse caso reporta um paciente de 33 anos internado por um quadro de síndrome nefrótica, com investigação etiológica sugestiva de glomerulopatia membranosa primária, que evoluiu com TVR bilateral associada à deterioração da função renal e necessidade de terapia substitutiva renal. Realizou, prontamente, angiografia com trombectomia e trombólise, evoluindo com recuperação da função renal em duas semanas.

Palavras-chave: glomerulonefrite membranosa; trombose venosa; proteinúria.

Case report

A 33-year-old male patient, previously healthy and without known comorbidities, was admitted to the Nephrology Service of the General Hospital of Fortaleza (HGF), complaining of gastric fullness, lower limb edema, unproductive cough and frothy urine for three months. He also reported dyspnea on average efforts progressing to great efforts 15 days from admission. He had a weight loss of 10 kg in this period.

Good general condition, eupneic, alert and oriented; small, palpable, mobile, fibroelastic lymph node with approximately one centimeter in the left posterior cervical chain. Heart auscultation without changes. Respiratory auscultation with universal vesicular murmur present, reduced in the left base. Flat abdomen, flaccid, painless to palpation, without visceromegaly, Traube free. Palpable peripheral pulses with lower limb edema (+/4+), absence of cyanosis and well perfused extremities.

Laboratory tests included albumin 2.5 mg/dl, and non-reactive FAN and ANTI-DNA, and negative cryoglobulinemia. Non-reactive serologies for HIV, hepatitis B, hepatitis C and syphilis. Complement within normal ranges, erythrocyte sedimentation rate 140 mg/dl and PCR 8.5 mg/dl. Protein electrophoresis with

absence of monoclonal peak. The remaining laboratory tests are described in Table 1.

Urinary tract ultrasonography (US) evidenced slightly increased kidneys (RD: 13.8 x 6.8 x 5.8cm Parenchyma 1.5cm - RE: 13 x 7.1 x 6.1cm - Parenchyma: 1,5cm) and increased cortical echogenicity, suggestive of parenchymal nephropathy with no stones. She undertook investigation of secondary causes of nephrotic syndrome that were all negative, and a renal biopsy was performed, which was suggestive of membranous glomerulopathy, according to the light microscopy illustrated in Figure 1.

After 1 week of admission, he was submitted to another complete abdomen US, due to an ill-defined abdominal pain, which showed signs suggestive of thrombosis of the right renal vein. After that, full anticoagulation with continuous infusion of heparin was initiated; on the following day, the patient developed anuria for more than 12 hours, nausea, two emetic episodes, two febrile episodes (37.8°C and 38.1°C) and worsening of nitrogenous slags (creatinine 5.6 and urea 60), with suspicion of bilateral renal vein thrombosis. The patient was submitted to renal angiography (arteriography and phlebography), which confirmed the hypothesis of bilateral renal vein thrombosis (Figure 2). Bilateral thrombectomy and thrombolysis were performed on the left and the patient was maintained in anticoagulation (initially with heparin and subsequently with warfarin).

The patient remained on hemodialysis for two weeks, evolving with progressive improvement in diuresis and renal function. He was discharged with renal function recovery, creatinine of 1.66 mg/dl. First outpatient visit after discharge the patient had creatinine of 0.77mg/dl.

Discussion

Renal vein thrombosis (RVT) was described by Rayer in 1840 and its association with nephrotic syndrome (NS) was first reported in 1939 by Doroe, Schlesinger and Savitz.[1]

Initially, there were conflicting reports about the cause and effect relationship of the RVT in the NS, but in the last years RVT was better described as a consequence of NS.[2]

RVT is seen more frequently in membranous glomerulopathies and membranoproliferative than in other types, such as minimal lesion and FSGS.[3]

Advanced age, membranous nephropathy, severe proteinuria and hypoalbuminemia are recognized as increased risk factors for the development of thromboembolism.[4]

The RVT pathogenic mechanism in the NS is not fully understood, but it is established that the NS is associated with a state of hypercoagulability, and it is further reinforced by urinary loss and, consequently, reduced serum antithrombin level III.[5]

The clinical condition results from the balance between acute occlusion, extension of thrombosis and development of collateral circulation. The acute presentation of renal vein thrombosis is infrequent and is mainly characterized by acute flank pain and hematuria. The laboratory findings that may suggest RVT are proteinuria (significant increase after event), increase in serum creatinine, hematuria, glycosuria, pyuria, hyperchloremic acidosis.[6,7] In most cases, the patients are asymptomatic, making the RVT underdiagnosed.[8]

Early diagnosis is essential because it is a reversible condition. The gold standard diagnostic test is renal phlebography, but USG with renal vein Doppler and contrast abdominal CT have been fast and safe noninvasive measurements for the direct visualization of the thrombus.[9,10]

The recommended treatment is full anticoagulation, which should be started immediately. The current recommendation is to begin with heparinization and after combining warfarin, and the total time for anticoagulation for a first episode of venous thromboembolism is at least 3-6 months, and until the cause of NS has been resolved or is in remission.[11,12]

In relation to the new oral anticoagulants (direct factor Xa inhibitors and direct thrombin inhibitor), warfarin anticoagulation is already recommended as an option in the treatment of general deep venous thromboembolism and pulmonary embolism.[13,14] The great limitation in the use of these medications is the impossibility of using them in patients with creatinine clearance lower than 15ml/min.[15]

Thrombolysis has not been fully studied in NS-associated thromboembolism. Most of the evidence for its use has been derived from reports and series of cases that are generally of limited value. Therefore, most experts recommend thrombolytic therapy for severe bilateral RVT or massive pulmonary embolism.[16]

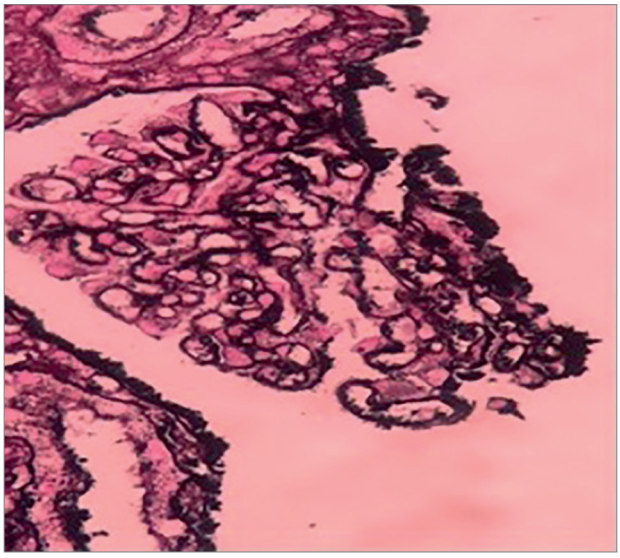
The reported case illustrates an acute presentation of left-sided RVT, with probably chronic right RVT,

Table 1 Laboratory tests performed during hospitalization

Day	1	2*	3	4	5	6	7	8**	9***
Hb (g/dL)	11.7	8.3	7.2	7.0	7.4	8.5	8.0	-	-
Platelets (units/mm^3)	206.200	377.000	400.000	417.500	412.500	490.000	400.000	-	-
Ur (mg/dL)	34	54	38	45	45	64	62	10	28
Cr (mg/dL)	1.2	5.4	5.7	6.8	7.0	8.0	4.9	1.6	0.77
CT (mg/dL)	648	-	-	-	333	-	-	-	-
HDL (mg/dL)	38	-	-	-	34	-	-	-	-
LDL (mg/dL)	473	-	-	-	243	-	-	-	-
ASLO (UI/ml)	< 52.5	-	-	-	-	-	-	-	-
24h-urine proteinuria (g)	10.9	-	-	-	-	-	-	-	11.2
Urine summary	protein +++	-	-	-	-	-	-	-	protein ++

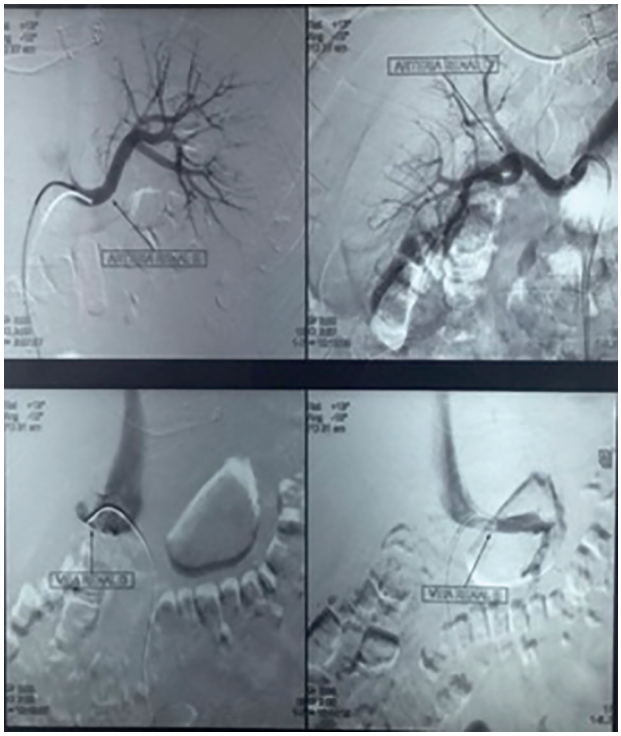
Hb - hemoglobin, PTA - prothrombin time of activity, Ur - urea, Cr - creatinine, CT - total cholesterol, HDL - high density lipoprotein, LDL - low density lipoprotein. * Initiated hemodialysis. ** Renal function at the time of the patient discharge. *** Renal function upon the patient's first outpatient return visit.

Figure 1. Light microscopy of the renal biopsy fragments - silver staining - evidencing thickening of glomerular basement membrane with spicules.



in a patient with NS. The patient did not present the classical clinical signs. Bilateral RVT was suspected due to anuria and sudden worsening of renal function. The venogram, gold standard, was performed to obtain the diagnosis, as well as the therapeutic intervention, with bilateral thrombectomy and thrombolysis located in the left renal vein. There was modest improvement in renal flow immediately and complete recovery of renal function after two weeks of the event.

Figura 2. Bilateral renal angiography (arterial and venous).



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