

# Renal Vein Thrombosis as a Presenting Sign in a Boy with Lupus Nephritis-Case Report

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## Abstract

Renal vein thrombosis (RVT) is a rare phenomenon that involves the renal veins or their tributaries. Beyond the neonatal age, it can be associated with several conditions such as coagulopathy, nephrotic syndrome, and autoimmune diseases, which include antiphospholipid syndrome and systemic lupus erythematosus (SLE). We describe a case of an 11-year-old boy presenting with abdominal pain and diagnosed with renal vein thrombosis as a presenting manifestation of membranous lupus nephritis. RVT as a presenting sign of SLE has been reported only in few cases and, to our knowledge, never in a male pediatric patient. Thrombotic complications responded to intense immunosuppression combined with an anticoagulation treatment regimen, but nephrosis persisted. High degree of suspicion is required for prompt diagnosis of this rare and clinically challenging condition.

**Index terms**— renal vein thrombosis, systemic lupus erythematosus, membranous lupus nephritis, pediatric case report, rheumatology.

Acute onset abdominal pain with hematuria is one of the most challenging presentations in pediatric practice. The differential diagnosis includes nephrolithiasis, pyelonephritis, trauma, and, rarely, renal vein thrombosis (RVT) [1]. The term renal vein thrombosis is used to describe the thrombus in the major renal veins or their tributaries. This condition may present either with acute symptoms or go unnoticed until complications develop such as pulmonary embolism or worsening renal function. The most common pediatric form of RVT is neonatal, usually following severe dehydration or prolonged hypotension. It is a rare entity characterized clinically by the triad of gross hematuria, flank mass, and thrombocytopenia [2]. A Abstract-Renal vein thrombosis (RVT) is a rare phenomenon that involves the renal veins or their tributaries. Beyond the neonatal age, it can be associated with several conditions such as coagulopathy, nephrotic syndrome, and autoimmune diseases, which include antiphospholipid syndrome and systemic lupus erythematosus (SLE).

We describe a case of an 11-year-old boy presenting with abdominal pain and diagnosed with renal vein thrombosis as a presenting manifestation of membranous lupus nephritis. RVT as a presenting sign of SLE has been reported only in few cases and, to our knowledge, never in a male pediatric patient. Thrombotic complications responded to intense immunosuppression combined with an anticoagulation treatment regimen, but nephrosis persisted. High degree of suspicion is required for prompt diagnosis of this rare and clinically challenging condition.

RVT in older children and adults can be associated with several conditions such as coagulopathy, trauma, infection, autoimmune diseases, including SLE, but most commonly with nephrotic syndrome with an incidence of 21.4% found in a large meta-analysis [3][4].

Membranous nephropathy (MN) is an immune-complex-mediated entity and is a common cause of nephrotic syndrome in adults but occurs less frequently in children (1%-2%) [5]. MN is most often a primary disease but could develop secondary to infections such as hepatitis B, exposure to medications, or systemic lupus erythematosus (SLE) which is defined as class V lupus nephritis.

### 3 KEYWORDS: RENAL VEIN THROMBOSIS, SYSTEMIC LUPUS ERYTHEMATOSUS, MEMBRANOUS LUPUS NEPHRITIS, PEDIATRIC CASE REPORT, RHEUMATOLOGY.

SLE is a multisystem autoimmune disease characterized by a broad spectrum of clinical manifestations and a multitude of laboratory abnormalities. Up to 10-20% of SLE patients present in childhood. Worldwide prevalence of pediatric SLE rates ranges from 3.3 to 8.8 per 100,000 children and adolescents, depending upon their ethnic distribution 6 .

Lupus nephritis is one of the cardinal manifestations of SLE, occurring more often in children than in adults. Renal involvement is present in up to two-thirds of pediatric SLE patients 7 including direct glomerular injury or thrombotic vascular involvement, such as RVT. Patients with SLE may not always present with multi-organ clinical manifestations and serologic findings simultaneously.

We describe here a case of an 11-year-old boy with SLE that initially presented with RVT.

## 1 II.

## 2 Case Presentation

Upon admission, his blood pressure was elevated -139/101 mmHg, with the rest of his vital signs normal for age. His physical examination revealed abdominal tenderness on the left upper quadrant, and was otherwise unremarkable, with no palpable masses or edema. Laboratory tests showed normal hemoglobin, neutrophilia with an absolute neutrophil count of  $9.6 \times 10^3/\mu\text{l}$ , with low platelets count of  $85 \times 10^3/\mu\text{l}$ . Renal A previously healthy 11-year-old boy presented to the ER with a history of 3 days of left flank pain and vomiting. He had no fever, dysuria, or any urinary complaints.

## 3 Keywords: renal vein thrombosis, systemic lupus erythematosus, membranous lupus nephritis, pediatric case report, rheumatology.

function tests were within normal range with a serum creatinine of 0.71 mg/dl (Estimated GFR 114 ml/min/1.73m<sup>2</sup>). He had hypoalbuminemia of 2.7 (3.4-5) g/dL. Coagulation studies revealed normal PT/PTT with elevated fibrinogen-682 mg/dl (200-500) and elevated D-Dimer; $>10000$  ng/ml (0-500).

Urinalysis showed microscopic hematuria with few casts on microscopy, trace leukocytes and nephrotic range proteinuria with total protein to creatinine ratio (T/C) of 14000 mg/gr (normal  $<200$ ).

Urgent computed tomographic (CT) scan revealed increased left renal vein density suspicious for RVT (Fig. 1A). CT angiography demonstrated thrombosis of renal vein extending to the inferior vena cava (Fig. 1B) and a massive infarct of the left kidney.

On repeated focused anamnesis, the boy had a history of a migratory bilateral knee pain and a facial rash with photosensitivity that quickly resolved several months before admission. Family history reveals maternal aunt with a history of recurrent miscarriages. There was no other family history suggestive of coagulopathy or autoimmunity.

Immunological workup revealed mild hypocomplementemia; C3 of 79mg/dL, and C4 of 9mg/dL (respective normal range: 90-180 and 10-40 mg/dL). Antinuclear antibody (Ab) titer $>1:160$ , antidouble-stranded DNA Ab was positive both in ELISA study (Ab titer  $>300$ , normal range 0-6 IU/ml) and upon immunofluorescent staining using Crithidialuciliae technique, anti-Sm and anti-RNP antibodies as well as direct Coombs test were also positive.

At that time, the patient fulfilled the validated pediatric diagnostic criteria of SLE 8 . Immunosuppressive therapy was initiated in the form of pulse methyl prednisolone therapy (3 doses of 750 mg methylprednisolone, which is 15 mg/kg/dose, followed by 50 mg/day PO Prednisone). Hydroxychloroquine and mycophenolate mofetil (550 mg/m<sup>2</sup>/dose BID) treatment was initiated. He was also treated by SC Enoxaparin injection (1 mg/kg twice daily initially, then monitored using an anti-Xa assay targeting 0.5-1 unit/ml).

The thrombophilia studies have not rendered diagnostic information: serum lupus anticoagulant and anti-cardiolipin antibodies concentrations were only mildly elevated, and not consistent with the presumed diagnosis of APLA secondary to SLE. However, Lipoprotein A as well as IX, X, and XIII clotting factors indices were high. Protein C activity, protein S antigen, and Antithrombin III were normal.

After few days the patient developed edema of lower extremities concomitant with worsening proteinuria and decreasing serum albumin. Tacrolimus was added with targeted trough blood levels of 7-9 ng/ml, as well as ACE inhibitors.

Renal biopsy is generally indicated for SLE nephritis. However, it was deferred because the risk of both thrombotic and bleeding complications seemed to outweigh the benefits from pathological grading. Two months later, the thrombus in the left renal vein resolved on the following renal duplex study. DMSA renal scan revealed normally-appearing kidneys with left kidney functioning even mildly better compared to the right (53% vs 47%). At that time, we performed US-guided kidney biopsy. Pathological studies were compatible with membranous lupus nephritis (MLN) with focal interstitial fibrosis and tubular atrophy (Fig 2).

After 3 months, the patient's immunological studies improved significantly with complement returning to the normal level and a significant decrease of anti-double-stranded DNA Ab titer, which remained only mildly elevated -32 UI/ml on last analysis. However, severe nephrotic syndrome persisted with significant weight gain

and marked edema and hypoalbuminemia with serum albumin as low as 1.5 gr/dl. He was treated by intermittent IV albumin infusions on top of combined immunosuppression and supportive therapy, including diuretics, with mild improvement. After seven months of therapy, the patient received two doses of IV Rituximab 1000 mg/dose, and MMF was discontinued without significant change in his condition.

Anticoagulation was discontinued after three months of therapeutic and three more months of prophylactic therapy.

After one year of treatment, the boy maintains normal renal function but still has nephrotic range proteinuria with a last T/C of 3600 mg/gr and serum albumin of 2.7 mg/dl.

## 4 III.

## 5 Discussion

We describe here the case of a 11-year-old boy with SLE and membranous SLE nephritis which presented as RVT. Clinically suspected and biopsyproven membranous lupus nephritis was probably the main pathophysiological factor for this unusual presentation.

SLE manifests with a variety of clinical and laboratory features, which may differ according to age and gender. Pediatric SLE, while often presents similarly to adult-onset disease, may also present with more unusual or more severe features 9 .

Thrombotic complications of SLE significantly affect morbidity and mortality. The presence of antiphospholipid antibodies detected in up to half of SLE patients, both adults, and children, has long been recognized as the main risk factor for the development of thrombotic complications of the disease. However, SLE patients without SLE have a two-fold higher risk of thrombosis as well 10 . The pathogenesis mechanism of the latter phenomenon is unclear 10 . Among the thrombotic complications, deep vein thrombosis as well as cerebral vein thrombosis and arterial events are most common. RVT is a relatively rare phenomenon described in less than 1 to 3.6% of SLE patients in a few small studies 11 and usually occurs in SLE patients with thrombophlebitis and nephrotic syndrome. Thrombotic episodes, including RVT, are more common in both primary MN and MLN. They are found to occur in 3% to 23% of patients with MLN and are probably influenced by the proportion of patients with persistent nephrosis 12 . Proteinuria and severe hypoalbuminemia are the main risk factors for thrombosis in both primary and secondary MN, which we assume was the major risk factor in our patient who was negative for antiphospholipid antibodies.

To the best of our knowledge, we described here the first case of SLE presenting as an isolated RVT in an antiphospholipid antibody-negative boy.

We suggest to consider RVT in differential diagnosis of all patients presenting with abdominal or flank pain. If diagnosed, prompt evaluation for possible underlying conditions, including nephrotic syndrome and SLE is indicated in male and female patients.

Delayed treatment raises the risk of renal and thrombotic complications, while prompt diagnosis may lead to a better outcome in patients with this challenging condition.

## 6 Conflicts of interest:

The authors declare no conflict of interest.

RVT as a presenting symptom of SLE was described in a few case reports in adults [12][13] . The data regarding pediatric patients is extremely scarce, with only two cases described to-date, when RVT preceded the development of clinical and serological features of SLE: in 11 and 9-year-old girls, respectively [14][15] . <sup>1</sup>

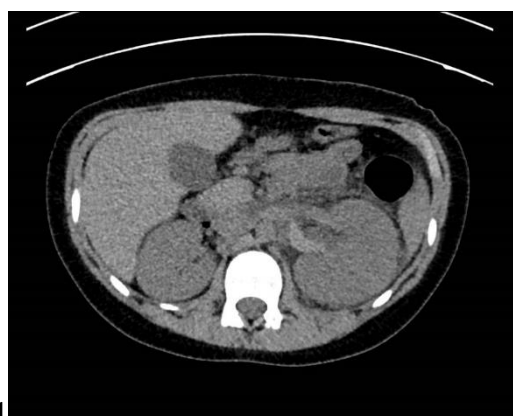


Figure 1: Figure 1 :

<sup>1</sup>Renal Vein Thrombosis as a Presenting Sign in a Boy with Lupus Nephritis-Case Report

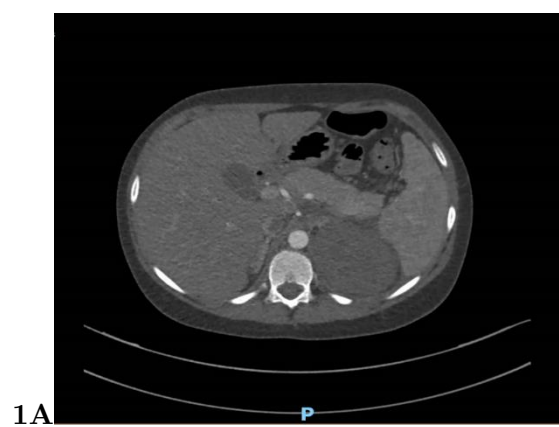


Figure 2: Fig. 1A :

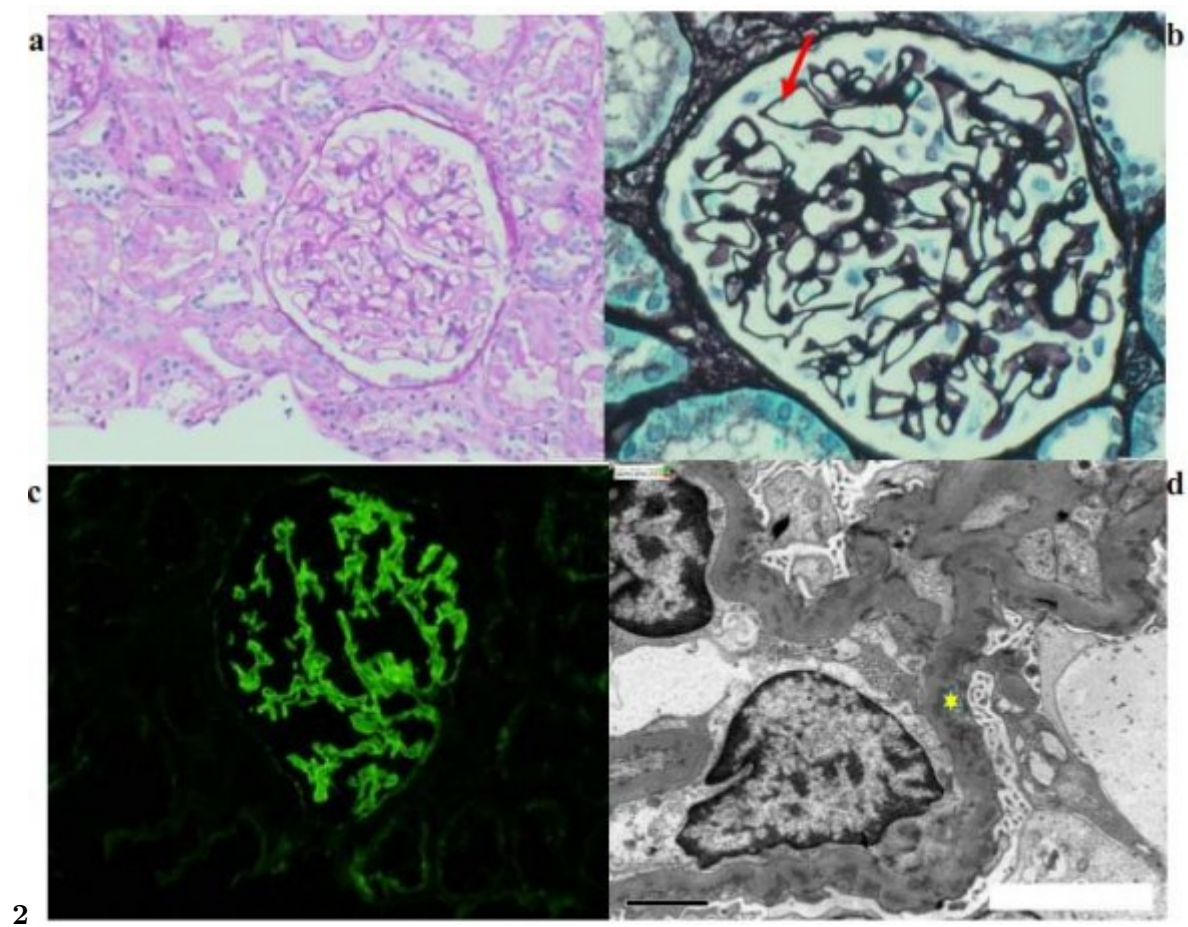


Figure 3: Figure 2 :

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