A Patient with Nephrotic Syndrome and Acute Flank Pain

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A 58-year-old man with nephrotic syndrome (8 g of protein per 24 hours and serum albumin 1.6 g/dl) due to biopsy-proven idiopathic membranous nephropathy (Figure 1A) diagnosed 3 weeks prior developed acute onset of right flank pain. Serum creatinine was 1.9 mg/dl (baseline, 0.9 mg/dl). Urinalysis demonstrated 1+ blood and 3+ protein, whereas urine microscopy revealed 30 isomorphic red blood cells per high power field. A computed-tomography angiogram of the abdomen (Figure 1B) was undertaken and it revealed an extensive right renal vein thrombus (RVT) (yellow arrow) extending into the inferior vena cava (white arrow) on venous phase imaging. The patient underwent percutaneous catheter thrombectomy and local thrombolytic therapy with recombinant tissue plasminogen activator followed by a heparin drip, which was transitioned to warfarin. The patient’s symptoms resolved over the next 48 hours and repeat imaging demonstrated resolution of renal venous and inferior vena cava thrombus.

RVT and other thrombotic complications (deep venous thrombosis, pulmonary embolization, cerebral venous thrombosis) may complicate severe nephrotic syndrome (proteinuria >3.5 g/dl and serum albumin <3 g/dl). Arterial thrombotic events are also increased with nephrotic syndrome. The prevalence of RVT with nephrotic syndrome ranges from 10% to 50%; however, this increases to 20%–60% in patients with membranous nephropathy (1). Risk for thrombosis is highest for membranous nephropathy as compared with other kidney lesions (2). A serum albumin <2.0 g/dl appears to be associated with increased risk for venous thrombosis and is a surrogate marker for hypercoagulability (2). Other hypercoagulable states as well as renal cell carcinoma can also present with RVT. In addition to acute flank pain as seen in this case, worsening proteinuria or declining kidney function in a patient with nephrotic syndrome may point to the development of RVT. A number of imaging modalities can diagnose RVT. Selective renal venography is the gold standard; however, noninvasive tests such as computed-tomography angiography with venous phase imaging and magnetic resonance venography are sufficiently sensitive and specific tests (3). Doppler ultrasonography has poor sensitivity and specificity.

Although it is not conclusively known, nephrotic syndrome appears to cause hypercoagulability through multiple mechanisms (1,4). There is decreased antithrombin III, plasminogen, and protein C/S due to loss

Figure 1. | A patient with nephrotic syndrome and acute flank pain. (A) Membranous nephropathy characterized by thickening of the capillary loops, due to subepithelial immune deposits, is observed under light microscopy (Masson trichrome stain). Original magnification, ×400. (B) Right renal vein thrombus (yellow arrow) extends into the inferior vena cava (white arrow) on venous phase imaging of a computed-tomography angiogram.
of these proteins in the urine. Hyperfibrinogenemia, high molecular weight fibrinogen moieties, increased platelet activation, and inhibition of plasminogen activation may also contribute to hypercoagulability. A physical factor that favors RVT in nephrotic syndrome includes concentration of blood in the postglomerular circulation, which enhances clot formation.

Treatment of RVT in a patient with nephrotic syndrome and AKI includes local thrombolytic therapy with or without percutaneous catheter thrombectomy (5). A combined approach is generally favored when there is a large clot burden, bilateral RVT, or a solitary kidney.

Teaching Points
- RVT and other thrombotic events may develop in patients with severe nephrotic syndrome. Loss of natural anticoagulants and synthesis of procoagulants underlie the formation of venous and arterial thrombus.
- Diagnosis of RVT can be made with selective renal venography (gold standard), whereas computed-tomography angiography with venous phase imaging and magnetic resonance venography represent excellent noninvasive alternatives.
- Treatment with local thrombolysis is recommended for patients with RVT complicated by AKI. Percutaneous catheter thrombectomy is recommended along with local thrombolysis in patients with a large clot burden, bilateral RVT, and single kidney. Therapy with warfarin is recommended while the patient remains nephrotic.

Disclosures
M. Perazella has nothing to disclose.

References