CLINICAL VIGNETTE

Deep Venous Thrombosis and Hypercoagulable State as Presentation of Nephrotic Syndrome

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A 54-year-old white female was in good health until she presented to the emergency room with extreme hypoxia. Computerized tomographic angiography demonstrated bilateral prominent pulmonary emboli. She was admitted to the hospital for anticoagulation. Baseline prothrombin and partial thromboplastin were normal. Bilateral lower extremity doppler ultrasound showed no venous clot. Laboratories were remarkable for low serum protein (4.9 gm/dl) and albumin (0.9 gm/dl). Urinalysis demonstrated 3+ proteinuria. CT imaging of the abdomen and pelvis demonstrated a left renal vein thrombosis with extension into the inferior vena cava. She was felt to have nephrotic syndrome with hypercoagulable state with subsequent renal vein thrombosis. She was anticoagulated with enoxaparin and switched to warfarin with resolution of clot and pulmonary embolism over 3 months. The remainder of her thrombophilia work up was normal. Renal biopsy was not possible due to ongoing thrombosis and the risk of bleeding. Her nephrotic syndrome was treated with prednisone and cyclosporine with improvement in proteinuria.

A 59-year-old male with a history of minimal change disease of the kidney who was previously in good health except for minor proteinuria presented with rapid onset of anasarca and proteinuria. He also was found to have a left upper extremity deep venous thrombosis. His serum protein was 5.0 gm/dl and albumin 1.8 gm/dl. He was felt to have nephrotic syndrome. CT angiography of the chest demonstrated no evidence of pulmonary embolism. The remainder of his hypercoagulable work up was normal.

The patient was treated successfully with warfarin with resolution within 3 months. His nephrotic syndrome was treated successfully with prednisone and cyclophosphamide over the course of two years. He was felt to be in remission and warfarin was then discontinued.

Discussion

The patients described above presented with a well-known and common consequence of nephrotic syndrome.[1] In the first case, the exact nature of the renal disease was never determined given the inability to perform a renal biopsy. In the second case, the renal disease had already been established but did not present with complications until a later date when the proteinuria. worsened. The overall risk of venous thrombolism in this population with nephrotic syndrome varies but on average is 7.9 - 9.9 percent.[2] Most events occur within the first 3-6 months of the diagnosis.[3] It is important to note that pulmonary embolism can occur with or without concurrent deep venous thrombosis. Both cases represent this variability in presentation.

In the first case, the source of the pulmonary embolism was from renal vein thrombosis with obvious extension in to the inferior vena cava. Isolated pulmonary embolism has also been reported.[4] In fact, asymptomatic pulmonary embolism may be found in up to thirty percent of patients almost always associated with chronic renal vein thrombosis.[5] The prevalence of renal vein thrombosis varies but has been reported as high as 60% in some series.[1] It is usually found to be a chronic condition. While more common in patient with membranous glomerular nephropathy, it can occur in patient with any histology.[3]

While the histologic etiology of her nephrotic syndrome was never determined, one significant clinical predictor of renal vein thrombosis and her subsequent venous embolic complications is low serum albumin. The risk of thromboembolism in patients with a serum albumin less than 2.8 gm/dl had a 2.5 relative risk compare to those with albumin above 2.8.[6]

The second case also demonstrates the spontaneous onset of deep venous thrombosis with low serum albumin. He had rapid resolution of clot with the use of warfarin. The effectiveness of the newer factor X inhibitors is unknown.

The exact cause of hypercoagulable state in patient with nephrotic syndrome is unknown, but it is suggested that patients often have subclinical coagulation occurring as a result of decreased levels of antithrombin III and plasminogen.[4] Specifically, increased clotting in the renal vein, may be due to alterations in post glomerular circulation and hemoconcentration, promoting thrombosis.[1]

In both cases, therapeutic anticoagulation was initiated. In the first case, she remains on warfarin therapy until her nephrotic syndrome resolves. The first case demonstrates the need to remain on prophylactic anticoagulation until complete resolution of the underlying conditions.[4,7] In the second case, with full resolution of nephrotic syndrome, anticoagulation was discontinued. It is unclear whether prophylactic anticoagulation in the second case initially was warranted. There is a lack of randomized trials supporting prophylactic anticoagulation, and in his case, the absence of membranous

glomerulonephritis and/or other risk factors such as heart failure, morbid obesity or atrial fibrillation, the decision not to anticoagulate seemed appropriate.

In summary, these two cases represent the presentation of hypercoagulable state and deep venous thrombosis with underlying nephrotic syndrome. They were successfully treated with anticoagulation. Several considerations in this setting include careful evaluation of the level of proteinuria and albuminemia to help predict or prevent clot. Once clotting has been discovered, successful resolution of the nephrotic syndrome should be established before discontinuation of anticoagulants. Close collaboration between hematology and nephrology is necessary.

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