Recurrent Venous Thromboembolism In A Patient With Nephrotic Syndrome On Rivaroxaban Therapy

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INTRODUCTION

Development of venous thromboembolisms (VTE) is a life-threatening complication of nephrotic syndrome. The prevalence is higher in adults (25%), than in children (3%) and usually affects renal veins, however thrombi in other vessels have been reported. The pathophysiology of hypercoagulable state in nephrotic syndrome mainly results from renal loss of hemostatic proteins, such as antithrombin and proteins S and C (1), however is thought to be multifactorial. Hypoalbuminemia plays an essential role in the pathogenesis as well. Albumins bind arachidonic acid making it unavailable to convert to thromboxane A2, a protein taking part in clot formation. With hypoalbuminemia, thromboxane A2 levels are increased, favoring a pro thrombotic state (1,2).

We present a case of recurrent pulmonary embolism (PE) with inferior vena cava (IVC) thrombus in a patient with profound hypoalbuminemia, who failed anticoagulation with rivaroxaban.

CASE PRESENTATION

22-year-old African-American female with past medical history as below presented to the ED with shortness of breath.

HOSPITAL COURSE

• VS: BP 136/89mmHg, HR 108/min, sat 99%, afebrile
• Pertinent labs: albumin <1.0g/dl, N troponin
• CT PE showed acute bilateral pulmonary emboli of moderate clot burden, without right heart strain.
• BOVA score= 0
• Diagnosed with recurrent PE and started on heparin drip
• Despite treatment, worsening symptoms
• Transthoracic echo showed an elongated mass in inferior vena cava, suspected of a clot, with normal ventricular function
• CT venogram of the abdomen confirmed the presence of a clot in the suprarenal IVC measuring 2.6 cm in length and 1.1 cm in width
• Patient underwent percutaneous mechanical suction thrombectomy using a T24 flotriever, resulting in successful thrombus removal and symptomatic improvement
• Transitioned from heparin drip to warfarin
• Remained symptom free during follow up 1 month later
• Scheduled for kidney biopsy in the outpatient setting

DISCUSSION

In the presented case, the patient had no history of kidney disease prior to delivery. Her severe proteinuria was found during 3rd trimester of pregnancy as a manifestation of preeclampsia. She missed her OBGYN and PCP follow up appointments so there was no assessment for proteinuria resolution. Patient’s first episode of PE 3 months later was thought to have been provoked, given postpartum period. Her hypoalbuminemia being <1.0 g/dl placed her at even higher thromboembolic risk. It has been shown in studies(3) that albumin level at diagnosis is the only independent predictor of VTE and increases the risk by 2.13-fold with each 1.0 g/dl reduction in serum albumin. Risk was determined to be the highest in patients whose albumin level was below 2.8 g/dl. This patient was initiated on Rivaroxaban as per standard treatment of PE and presented 1 month later with recurrent PE. DOACs have not been adequately studied in order to be approved for use in nephrotic syndrome, despite being an excellent choice for other groups of patients with PE. Most DOACs are renally cleared and protein bound in the range 92-95%, therefore their pharmacokinetics are influenced by reduced renal function and proteinuria(4). Moreover, because of increased activity of factors II, V, VII, VIII, X, XII, seen in nephrotic syndrome as a compensatory mechanism to hypoalbuminemia, rivaroxaban and apixaban being factor Xa inhibitors may not be effective with these increased levels(5). Conventional anticoagulation with vitamin K antagonists or heparin remains the standard therapy in the presence of thrombosis(6).

Figure 1. Timeline of past medical history prior to admission. Figure 2. Abdominal CT venogram. AP view on the left, sagittal view on the right. Green arrow indicating IVC thrombus.

KEY LEARNING POINTS

1. Nephrotic syndrome should be considered as a cause of recurrent VTEs in all young adults regardless of the presence of provoking factors.
2. Despite being a good therapeutic option for patients with PE, DOACs should be avoided in patients with thrombosis in the setting of nephrotic syndrome with profound hypoalbuminemia.
3. Warfarin and heparin are the preferred agents for treatment of pulmonary emboli in nephrotic patients.
4. IVC thrombosis is a rare but potentially dangerous complication of nephrotic syndrome and invasive treatment is recommended.

REFERENCES