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ORIGINAL ARTICLE

Extensive Thromboembolism in a Young Patient of Nephrotic Syndrome

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ABSTRACT

Nephrotic syndrome (NS) is a well-known cause of hypercoagulability of blood with an associated risk of thromboembolism. Thromboembolism is the result of persistent proteinuria and increased production of hypercoagulable factors by the liver. One of the lethal complications of nephrotic syndrome is pulmonary embolism. There are a wide variety of presentations of pulmonary embolism ranging from sinus tachycardia to cardiogenic shock and sudden death. In our case report a young patient with nephrotic syndrome presented with dyspnea and extensive thrombosis in the form of thrombosis of inferior vena cava, a clot in the right atrium (RA), and pulmonary embolism.

Keywords: Nephrotic syndrome, venous thromboembolism, pulmonary embolism, inferior vena

INTRODUCTION

Nephrotic syndrome is characterized by proteinuria, hyperlipidemia, hypoalbuminemia, and peripheral edema. It is frequently associated with hypercoagulability of blood [1]. Venous thrombosis leading to pulmonary embolism is one of the fatal complications of nephrotic syndrome. Pulmonary embolism is regarded as the third most common cause of cardiovascular disease [2]. Similarly, the prevalence of pulmonary embolism is not well documented in young patients. The pathophysiology behind the hypercoagulable state in nephrotic syndrome is the defect in glomeruli. This results in the loss of proteins particularly antithrombin and protein S

There is a shifting in balance towards increased production of procoagulant proteins by the liver so creating a prothrombotic state.

Case: Our patient is a 27-years-old male who presented with gradual onset of shortness of breath for 20 days with three episodes of hemoptysis. He was diagnosed with biopsy-proven membranous glomerulonephritis about 8 months back before his presentation in the emergency department. He was on a maintenance dose of prednisolone 5mg/d, furosemide 40mg/d, and lisinopril 5mg/d but he stopped these drugs about one month before. He had tachycardia (heart rate of 104/min), tachypnea (respiratory rate of 22/min), and decreased oxygen saturation (92%). He had no heart murmurs but bilateral pitting edema of the lower extremities. Complete blood

count, liver function tests, and renal function tests were normal. ESR was 67mm/1st hr. D-dimers 459ng/ml. Spot urine protein 2230mg/dl. Antithrombin levels are 60 % (range 75-125%). Echocardiography was performed that revealed dilated RV, Clot in RA as shown in, and IVC with moderate pulmonary hypertension. A clot in RA and IVC can be seen in Figures 1 . CT pulmonary angiogram demonstrated bilateral pulmonary embolism as shown in Figure 2. The patient was treated with intravenous heparin 80U/kg IV bolus followed by 18U/kg/hr. Later on, the patient was put on warfarin 5mg/d. There is gradual regression in the clot with improvement in symptoms.

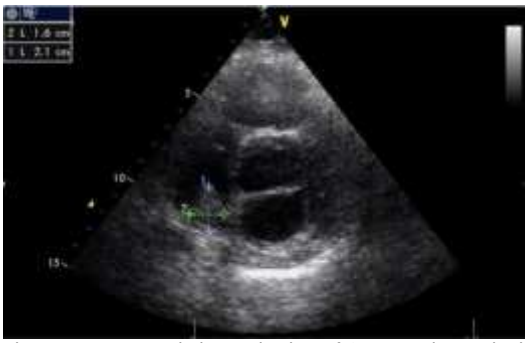

Figure 1: Parasternal short axis view of 2D TTE shows clot in right atrium measuring 16 21mm.

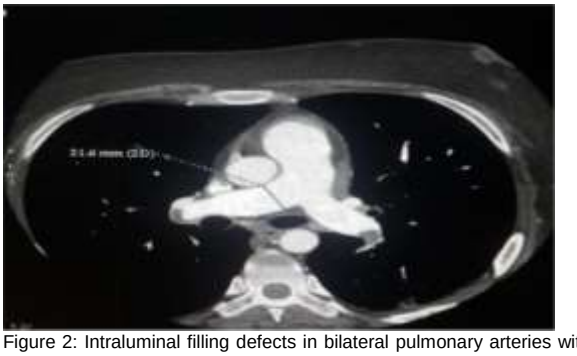

Figure 2: Intraluminal filling defects in bilateral pulmonary arteries with RPA 21.6mm.

DISCUSSION

Pulmonary embolism has a short-term high mortality risk with a long-term risk of chronic thromboembolic pulmonary hypertension (CTEPH). Early diagnosis and treatment is the key to the management of pulmonary embolism. There are few reports of pulmonary embolism in young patients with nephrotic syndrome and it's very rare to see extensive thrombosis involving inferior vena cava and right atrium.

NS has primary and secondary causes. Primary causes include focal segmental glomerulosclerosis, membranous nephropathy, and minimal change disease [4]. While secondary causes of nephrotic syndrome include diabetes mellitus, amyloidosis, hepatitis B and C, nonsteroidal anti-inflammatory drugs, multiple myeloma, HIV [5]. High-risk thromboembolism in the form of arterial and venous thrombosis is associated with nephrotic syndrome. There is an imbalance between anticoagulant factors and procoagulant factors as there are decreased levels of antithrombin III and protein C, and increased levels of fibrinogen, factor V and factor VIII [3, 6] It has been suggested that the use of corticosteroids, immunosuppressants, and diuretics are involved in thromboembolism, whereas some studies have reported the antithrombotic effect of antiproteinuric therapies [7].

Histological diagnosis also has a role in determining the risk of thromboembolism in NS. Membranous nephropathy (MN) is more frequently associated with VTE (venous thromboembolism). In one of the studies, it is found that MN present in 48% of nephrotic patients with PE [8]. Another study by Hârza et al showed an increased prevalence of VTE in patients with MN as compared to focal segmental glomerulosclerosis and minimal change disease [9]. Other markers indicating increased susceptibility to thromboembolism are age >60years [8] high level of proteinuria, and albumin level <2.8 mg/dl.

In our case, the patient was young and active. But poor compliance with medication and biopsy-proven MN might have resulted in extensive thrombosis. Surprisingly he didn't develop renal thrombosis but the presence of thrombus in the right atrium and inferior vena suggest a high level of hypercoagulability. He

was hemodynamically stable so anticoagulation with heparin followed by warfarin remains the mainstay of treatment. Timely anticoagulation resulted in the dissolution of the clot and improvement in symptoms. If such a patient was not treated at the right time, this could result in massive pulmonary embolism and shock.

Management of patients in nephrotic syndrome complicated pulmonary thrombosis involves treating underlying cause by corticosteroids, immunosuppressive therapies, thrombolytic therapy, and anticoagulation. Typical treatment regimens consist of unfractionated or low-molecular-weight heparin with the transition to warfarin and some of the newer anticoagulants. INR should be maintained between 2-3. IVC filters in case of proximal deep venous thrombosis when anticoagulation is contraindicated. If the patient is hemodynamically unstable, thrombolytic therapy, percutaneous mechanical thrombectomy, or surgical thromboembolectomy may be instituted. Therapeutic anticoagulation for venous thromboembolism including asymptomatic renal vein thrombosis should be considered for at least 6 to 12 months in the absence of contraindications; however, expert consensus is to treat patients until they are no longer nephrotic and normal albuminemia has been restored [10].

In MN, prophylactic anticoagulation may be considered particularly when thrombosis risk is high in the absence of bleeding risks [10]. Regular follow-up, daily drug intake and maintenance of INR should be the target in a patient with nephrotic syndrome complicated by VTE.

CONCLUSION

Thromboembolism is well known complication of NS. Early recognition and treatment is the ultimate strategy to manage VTE and pulmonary embolism. CT pulmonary angiography is the definite test for diagnosing PE. Patient with nephrotic syndrome should be educated regarding the disease process and its predisposition to thromboembolism. Prophylactic anticoagulation may be given depending on bleeding and thrombotic risks.

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