Pulmonary embolism as presenting feature of membranous nephropathy induced nephrotic syndrome

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Received - 21 March 2019 Initial Review - 05 April 2019 Accepted - 07 May 2019

ABSTRACT

Severe pulmonary embolism as first-time presentation of Nephrotic syndrome is rare but Nephrotic syndrome secondary to membranous nephropathy (MN) may impose a greater thrombotic risk for unclear reasons. Here, we report the case of a 36-year-old female patient presented with complaints of sudden onset of shortness of breath since 4-5 days and features of right-sided heart failure. There was no preceding history of any chronic disease or renal disease. She was diagnosed as having a bilateral severe pulmonary embolism. Extensive workup and renal biopsy were done which was suggestive of primary membranous nephropathy.

Keywords: *Heart failure, Nephropathy, Nephrotic syndrome, Pulmonary embolism.*

Thromboembolism is a well-known complication of Nephrotic syndrome. However, severe pulmonary embolism as first-time presentation of Nephrotic syndrome is rare. It is important to note that Nephrotic syndrome secondary to membranous nephropathy (MN) may impose a greater thrombotic risk for unclear reasons.The exact pathophysiologic mechanisms of venous thromboembolism in patients with Nephrotic syndrome have yet to be determined; however, alterations in the plasma levels of proteins involved in coagulation and fibrinolysis, enhanced platelet aggregation, low plasma albumin, hyperviscosity, and hyperlipidemia, are considered predisposing factors for venous thromboembolism.

A recent retrospective cohort study by Mahmoodi *et al* [1] found an annual incidence of symptomatic venous thromboembolism during the first 6 months of follow-up in 9.8% of 298 consecutive patients with Nephrotic syndrome. We describe here a female patient who presented with acute severe shortness of breath and features of right heart failure who on extensive workup was found to have bilateral severe pulmonary embolism due to membranous nephropathy.

CASE REPORT

A 36-year-old female patient admitted to the department with a complaint of sudden and severe onset of shortness of breath since 4-5 days which was progressive in nature. There was no history of orthopnea, paroxysmal nocturnal dyspnea, hemoptysis, syncope, chest pain, fever, and cough. A history of distension of abdomen since 15 days was present. There was no past history of tuberculosis, diabetes, and hypertension.

On examination, respiratory rate was 24/min, was not able to maintain saturation in room air, jugular venous pressure (JVP) was raised and dependent edema was present. Systemic examination was suggestive of bilateral pleural effusion and ascites.

A posterior-anterior (PA) view of chest X-ray was done which was suggestive of bilateral pleural effusion. On the basis of initial history, clinical examination and investigation, a provisional diagnosis of an acute pulmonary venous thromboembolism and the right ventricular myocardial infarction were kept.

Further investigations were done. Troponin-I was 615.4, D-dimer was raised (>2<4), electrocardiogram (ECG) suggestive of sinus tachycardia. Echocardiogram (ECHO) revealed severe tricuspid regurgitation (TR), severe pulmonary arterial hypertension (PAH), normal left ventricular systolic function, no regional wall motion abnormality and dilated left atrium and left ventricle. Arterial blood gas (ABG) was suggestive of respiratory alkalosis. Urine routine and microscopic examination suggestive of proteins 4+, 10-15 RBCs and 24hr urinary proteins were 8.9gm/24hrs. The ascitic fluid analysis was suggestive of low Serum Ascites Albumin Gradient (SAAG) ascites.

Biochemical investigations were suggestive of proteins 4.4gm/dl and albumin 1.5gm/dl. Blood urea nitrogen (BUN) was 8, serum creatinine was 0.76mg/dl, thyroid stimulating hormone (TSH) was 5.64, cholesterol was 389mg/dl, triglycerides was 270mg/dl, low-density lipoprotein (LDL) was 266mg/dl and high-density lipoprotein (HDL) was 66mg/dl. Hepatitis B antigen (HBsAg) and Hepatitis C were negative.

Computed tomography (CT) angiography suggestive of acute thromboembolism of bilateral pulmonary arteries with bilateral pleural effusion (right side was more than left side)

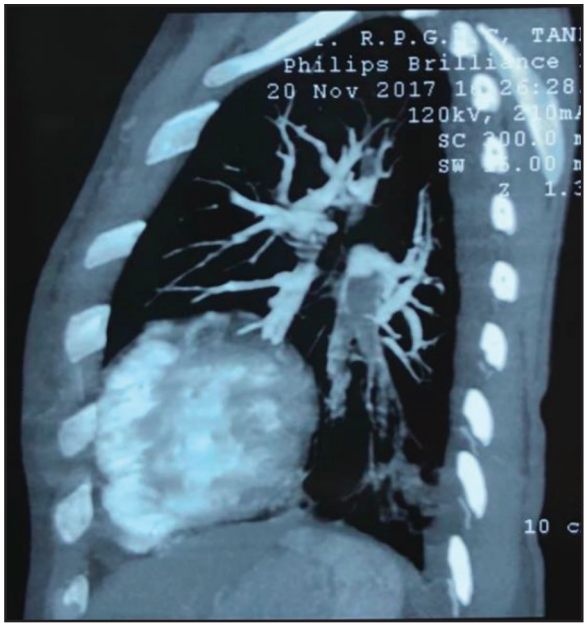

Figure 1: Computed tomography (CT) scan showing embolus in main pulmonary artery

(Fig. 1). Doppler study was suggestive of no renal and lower limb deep vein thrombosis. Ultrasound (USG) guided renal biopsy and histopathology tests were done in consultation with a nephrologist. Renal biopsy light microscopy was unremarkable, Immunofluorescence Ig G3 trace, IgG4 2+, C3 2+ along with capillary loops. On immunohistochemistry, PLA2R was positive and thrombospondin was negative.

Based on the above-mentioned investigations, a final diagnosis of acute pulmonary embolism secondary to PLA2R associated primary membranous nephropathy was made. The patient was put on angiotensin-converting enzyme (ACE) inhibitors/ Statins/ anticoagulants (tab warfarin with five days overlap of low molecular weight heparin), cyclophosphamide (months 2,4,6) and steroids (IV methylprednisolone followed by oral corticosteroids months 1,3,5). The patient is in close follow-up and is presently doing well.

DISCUSSION

Pulmonary embolism is a rare but potentially life-threatening complication of Nephrotic syndrome. Usually, in patients with Nephrotic syndrome there is an evidence of clotting factors such as fibrinogen, factors V and VIII, von-Willebrand factor, and plasminogen activator inhibitor 1.

A review of eight studies evaluating thromboembolic complications in Nephrotic syndrome found 81 (18%) of 458 patients with deep venous thromboembolism or pulmonary embolism [2]. The incidence varied from 8%, 5% to 36% in the literature. The renal venous thrombosis is the most frequently detected; it is asymptomatic in 90% of cases. We report a case of pulmonary embolism secondary to Nephrotic syndrome due to idiopathic membranous nephropathy. Our patient had two risk factors (serum albumin <1.5mg/dl and urine proteins >3gm/day).

The association of membranous nephropathy and renal vein thrombosis is more known than any other venous thrombosis, but it can occur in any site and with other causes of Nephrotic syndrome. In our case, pulmonary embolism was the first presenting feature of the Nephrotic syndrome. It was even reported by Hartland *et al*. [3], Peces *et al*. [4] and Ambler *et al*. [5]. No other site of thrombosis was detected in our patient. Pulmonary embolism may also complicate the course of known membranous glomerulonephritis, especially when the disease is still active.

Kutcher and Coll described 2 cases of known membranous glomerulonephritis complicated with renal veins thrombosis and pulmonary embolism [6]. We add to that the fact that membranous glomerulonephritis is inherently thrombogenic for understood reasons; the thromboembolic complications seem to be more frequent when the Nephrotic syndrome is due to membranous nephropathy than other causes [1].

CONCLUSION

Nephrotic syndrome is complicated by venous thromboembolism sufficiently frequently for the diagnosis to be considered in all patients with deep venous thromboembolism or pulmonary embolism. The message is simply don't forget to dip the urine and the serum albumin in such kind of patients.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Rana A, Sharma KN, Sharma T, Patial A. Pulmonary embolism as presenting feature of membranous nephropathy induced nephrotic syndrome. Indian J Case Reports. 2019;5(3):235-236.

Doi: 10.32677/IJCR.2019.v05.i03.012