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IgA nephropathy presenting with pulmonary thromboembolism and renal artery infarct

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ABSTRACT

Background: Venous and arterial thromboembolism are frequently seen in nephrotic syndrome. They generally occur during periods of sustained proteinuria in patients who are not responding to treatment and more commonly seen in minimal change disease and membranous nephropathy.

Case Presentation: A 28-year-old male presented to cardiology department of our hospital with worsening breathlessness for 1 week. We found pulmonary embolism and an infarct in the lower pole of the right kidney by CT pulmonary angiogram.

He had no previous history or features of nephrotic syndrome. Urine analysis showed numerous red blood cells, 3+ proteinuria and granular casts. Urine protein creatinine ratio was 5.2 g/g of creatinine. Serum creatinine was 2.61 mg/dL. Renal biopsy was suggestive of IgA nephropathy and patient was started on steroids and warfarin and responded to treatment.

Conclusions: Patients with nephrotic syndrome can rarely present initially with venous and arterial thromboembolism. Rarely even IgA nephropathy can present with such thromboembolic episodes.

Implication for health policy/practice/research/medical education:

Arterial and venous thrombosis commonly occurs after a prolonged period of nephrotic syndrome and hypoalbuminemia. In some rare cases, the initial presentation can itself just be arterial/venous thrombosis. Hence we should search for nephrotic syndrome in patients with thrombotic episodes. Though it is more commonly seen in minimal change disease, it can also be seen in IgA nephropathy.

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1. Background

Thromboembolic manifestations are not uncommon in glomerular diseases with nephrotic range proteinuria. Several factors are involved in the pathogenesis of hypercoagulable state in these patients; namely thrombocytosis, decreased levels of antithrombin III, plasminogen and free protein S, increased amounts of factor V, VIII and fibrinogen, increased platelet activation and hemoconcentration among other causes. Frequency of venous thromboembolism has varied from 2% in children to 42% in adults in various studies (1,2). A

relative risk of 1 to 5.5 of having arterial thromboembolic events has also been described in these patients mainly related to cardiovascular events (3). Among the various causes of nephrotic syndrome, association of membranous nephropathy and minimal change disease with thromboembolic events are well established while other glomerular diseases are not extensively reported (4,5). Here we report a case of IgA nephropathy who presented with pulmonary thromboembolism and renal artery thrombosis.

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2. Case Presentation

A 28-year old male presented to cardiology department of our hospital with worsening breathlessness for 1 week. He was evaluated for his persistent breathlessness. A CT pulmonary angiogram was conducted outside, which showed evidence of pulmonary embolism and an infarct in the lower pole of the right kidney (Figure 1). He was referred from the outside hospital to our cardiology department. The patient had no history of renal disease in the past.

On examination, the patient was tachypneic and needed oxygen at the rate of 4 L/min to maintain adequate saturation. His blood pressure was under control with minimal dose of calcium channel blocker. In view of the pulmonary thromboembolism, thrombolysis was initiated with Alteplase. Doppler studies were suggestive of deep vein thrombosis in the left mid superficial femoral vein and popliteal vein with areas of recanalization. He was evaluated for prothrombotic state, while protein C, protein S and homocysteine levels were normal. Antiphospholipid antibodies, factor V mutations and ANA were not detected. Urine analysis showed numerous red blood cells, 3+ proteinuria and granular casts. Urine protein creatinine ratio was 5.2 g/g of creatinine. Serum creatinine was 2.61 mg/dL. Serum albumin was 2.70 g/dL. Ultrasound of kidneys and renal Doppler were normal but dimercaptosuccinic acid (DMSA) was conducted. The results showed a large cold defect in right lower pole cortex and loss of cortical volume due to suspected renal artery infarct. Due to the presence of nephrotic range proteinuria, microhematuria, renal failure in a patient with arterial (renal artery) and venous thrombosis (Figures 2 and 3) (left femoropopliteal vein and pulmonary), a percutaneous renal biopsy was conducted. It was suggestive of IgA nephropathy by significant mesangial IgA deposits accompanied by mesangial hypercellularity, segmental endocapillary hypercellularity, segmental sclerosis (Figure 4A-B), crescents, moderate global glomerulosclerosis, chronic tubulointerstitial nephritis, nephrosclerosis and hypertensive vascular changes. The patient received 60 mg prednisolone/daily and warfarin. He was on follow up. On follow up patient symptomatically improved. Serum creatinine diminished to 1.7 mg/dL while serum albumin increased to 3.4 g/dL. Urine protein creatinine ratio decreased to 1.2 g/g. The patient is still on regular follow-up.

3. Discussion

Thromboembolism is one of the serious complications of nephrotic syndrome, both in children and in adults. Retrospective studies have shown that absolute risks of venous thromboembolic events and arterial thromboembolic events in patients with nephrotic



Figure 1. Computerized tomography image showing pulmonary thromboembolism.



Figure 2. Computerized tomography image showing renal artery infarct.

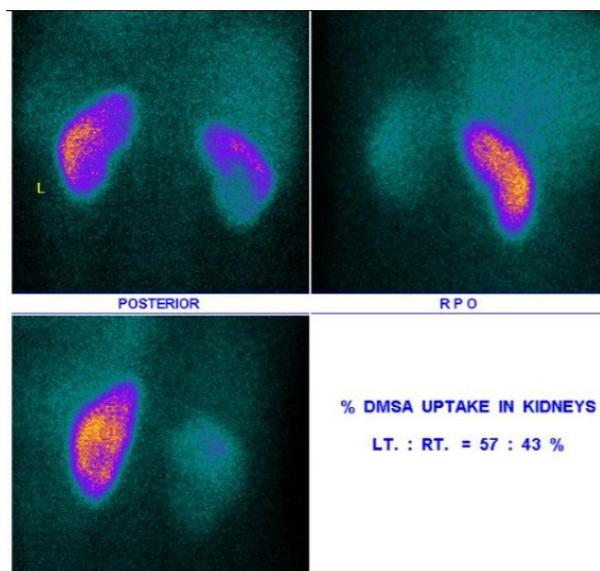


Figure 3. DMSA image of the kidneys.

syndromes were 1.02% per year and 1.48% per year respectively which were around 8 times higher than their incidences in age and gender matched population (6). There are numerous reasons for the increased thromboembolic events in patients with nephrotic syndrome. Nephrotic syndrome patients have a thrombotic milieu. This is due to various reasons which include thrombocytosis, low levels of antithrombin III, plasminogen and free protein S. Other reasons include increased amount of factor V,

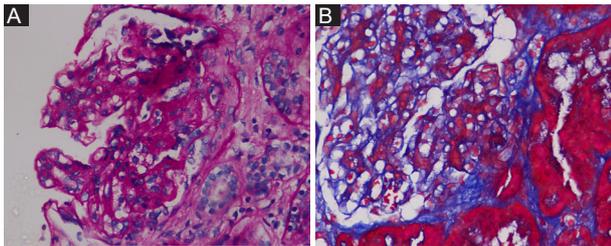


Figure 4. Glomerulus with mesangial hypercellularity and segmental sclerosis (A) PAS x400 (B) MT x400.

VIII and fibrinogen, increased platelet activation and hemoconcentration. Other factors which are thought to contribute include infections, plasma lipid abnormalities and hypovolemia. Increased proteinuria was found to be an important risk factor and it was also found to occur early in the course of the disease (5,7). The histological type was also shown to be important with membranous nephropathy commonly associated with venous thromboembolism and IgA nephropathy least (7).

Among the venous thromboembolism, some studies suggest that deep vein thrombosis of the extremities is the most common venous embolism (8,9), while other studies suggest pulmonary thromboembolism as the most common (10). There is wide variability in the incidence of renal vein thrombosis from 5% to 60% in various studies (5,10). The most common presentations of arterial thromboembolic events are myocardial infarctions, unstable angina, peripheral vascular disease and cerebral ischemic events (6,11). Arterial thrombosis is thought to be associated with degree of renal failure, age, previous atherosclerotic events and diabetes (6).

Reports of arterial thrombosis include mainly femoral, popliteal, brachial arteries along with coronary and cerebrovascular arteries (12,13). There are few case reports of renal infarctions associated with nephrotic syndrome but they are associated with either membranous nephropathy or minimal change, with no associated venous thromboembolism (14,15).

Patients with nephrotic syndromes usually develop thromboembolism during the course of the disease, when albumin decreases significantly. Rarely patients present with thromboembolism. In our review, we found few cases which were presented with deep vein thrombosis and pulmonary thromboembolism. However, they were either membranous nephropathy (16) or not biopsied (17). There were no reports of involvement of renal arteries, though reports of pulmonary artery thrombosis were found (17,18).

IgA nephropathy is one of the most common forms of glomerulonephritis in the world. Patient can present at any age but it is most commonly diagnosed in the second decade of life. Among the most important factors

for worsening renal failure in IgA patients is persistent proteinuria, with the greatest risk being in those with nephrotic range proteinuria (19,20).

There are very few reports on the incidence of thromboembolism in IgA nephropathy. A recent study showed a higher incidence of venous thromboembolism in membranous nephropathy and FSGS (7.85% versus 2.97%) when compared to IgA nephropathy (0.36%) (7). The incidence of arterial thromboembolic events in IgA nephropathy is even less clear. A study about the risk and predictors of arterial and venous thromboembolism in nephrotic syndrome found an annual incidence of 2.18 (12 out of 83 patients) in a group of patients who were declared as not specified group (out of which 17% were IgA nephropathy) (6). To the best of our knowledge, this is the only case of IgA nephropathy who presented with both venous and arterial thrombosis, pulmonary embolism and renal infarction.

4. Conclusions

Patients with nephrotic syndromes can rarely present initially with venous and arterial thromboembolism. Though venous thromboembolism is more common, arterial thrombosis can also be seen like renal artery in this patient. Among the nephrotic syndromes, though membranous nephropathy and FSGS present more commonly with thrombotic episodes, IgA nephropathy can also present with thrombosis.

Authors' contribution

MV, SS and AM managed the patient and prepared the manuscript. SN did the pathological diagnosis. RN and GK finalized the paper. All authors read and signed the final manuscript.

Conflicts of interest

There were no points of conflicts.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient has given his informed consent regarding the publication of this case report.

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