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THE MYSTERY BEHIND THROMBOEMBOLISM IN A PATIENT WITH NEPHROTIC SYNDROME

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Abstract

Hypercoaguable state with nephrotic syndrome is a well-known clinical entity. Tendency of hypercoagulability is directly linked to low serum protein and albumin concentrations. The possible reasons of hypercoagulability are explained as renal losses of anti thrombin III, factor VIII and plasminogen. The presentation may have various spectrums depending on the organ system involved. The current scientific literature suggests that patients with nephrotic syndrome and pulmonary embolism may benefit from life long anticoagulation.

Keywords:
PE with underlying Nephrotic syndrome, Treatment of PE with nephrotic syndrome, pulmonary embolism, Nephrotic syndrome and thromboembolic disease.

Introduction

Thromboembolic events in both arterial and venous circulation with nephrotic syndrome are well documented. In patients with thromboembolic disease, hypoalbuminemia is a clue in tandem with spot urine albumin for nephrotic syndrome and needs to be confirmed with 24hours urine protein. Definitive diagnosis is achieved by kidney biopsy after ruling out other causes of thrombophilia and hypercoagulability.

We hereby report a case of 21 years old male patient who was diagnosed to have bilateral pulmonary embolism. Apart from features of massive pulmonary embolism there was also evidence of severe hypoalbuminemia. Further investigations revealed dyslipidemia and hypercholesterolemia hinting towards renal loss of proteins and diagnosis of Nephrotic syndrome was suspected which was later confirmed by 24 hours urine protein. Thrombophilia and vasculitic markers were negative. He was managed with systemic thrombolysis followed by anticoagulation therapy, steroids, and statins.

Case report

A 21 years old, normotensive, non-diabetic gentleman presented to emergency room with complaints of increased breathlessness on rest, hemoptysis and facial swelling for 5-6 days. He had no complaints of chest pain, palpitation or fever in the recent past. He was a non-smoker with no history of bronchial asthma, DVT, pulmonary embolism or any thromboembolic events (stroke, MI, amaurosis fugax, limb ischemia) in any other systems in the past. He had no history of any trauma, surgery, prior hospitalization or prolonged immobilization in the past. General examination of the patient revealed a conscious, oriented and afebrile patient with tachycardia (116/min), B.P (110/80 mmHg), tachypnea (26/min) and hypoxia (oxygen saturation on room air 90%). Chest examination revealed bilateral decreased air entry, bilateral basal crepts and left sided pleural rub. Other systemic examination was unremarkable. Initial blood investigations revealed deranged leukocyte count (N-86, L-6, M-16), TLC – 19.6, deranged kidney function test – Protein total – 3.7, Albumin – 1.32, Globulin 2.38, SGOT 15.1, SGPT-11, ALP – 78.5. Blood Gas analysis - pH: 7.49, pCO2: 36mmHg, pO2: 55mmHg,Lac:0. 9mmol/L, Hct: 39%, HCO3-: 27.4mmol/L, BE (B): -10.5mmol/l, BE ecf: 4.1mmol/L. Lipid profile revealed TG-474mg/dl, LDL 370mg/dl, HDL-53mg/dl, and Cholesterol-1120mg/dl. Blood serology revealed C3=203mg/dl, C4=30.9mg/dl, lupus anticoagulant. cANCA, pANCA, anti DsDNA, anti nuclear antibody (ANA), anti beta 2 gp1 antibody, PLA2R antibody, proteins C, protein S, factor V Leiden mutation were negative. Urine routine and micro examination revealed albuminuria (++++), with 6-8 pus /HPF pus cells and occasional RBCs. Urine for micro albuminuria was 50mg/l and 24Hrs urine protein was 11.8g/24hr.ECG (Fig: 2) revealed sinus tachycardia with classical S1, Q3, and T3 pattern. 2D Echo

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revealed mild TR (PASP=45mmHg) with mild dilated RA/RV/MPA, presence of right ventricular systolic dysfunction and hypokinetic RV wall, rest of the report were within normal limit.

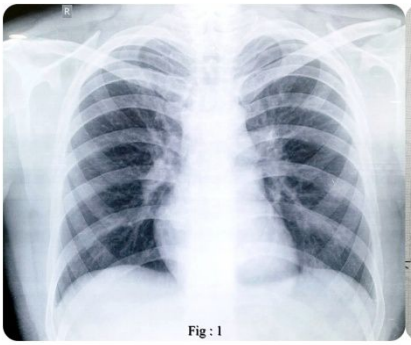


Fig : 1

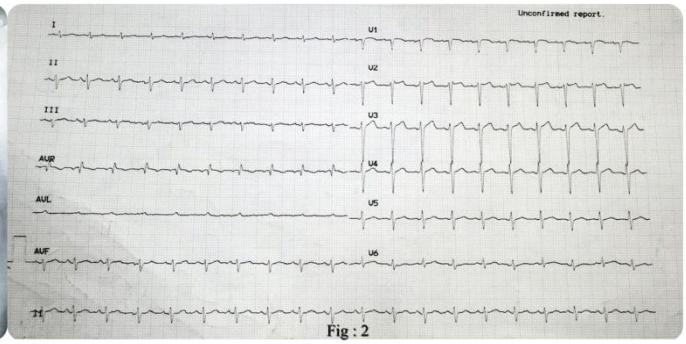
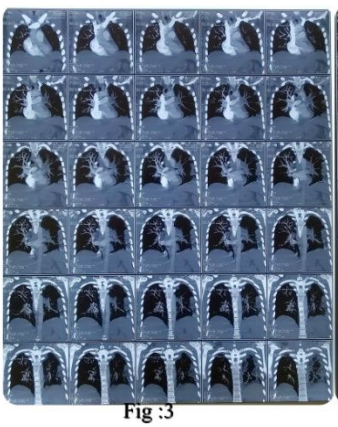


Fig : 2

CXR (Fig: 1) revealed Oligemic lung fields; ECG (Fig 2) revealed sinus tachycardia with ST-T changes in S1, Q3 and T3 pattern.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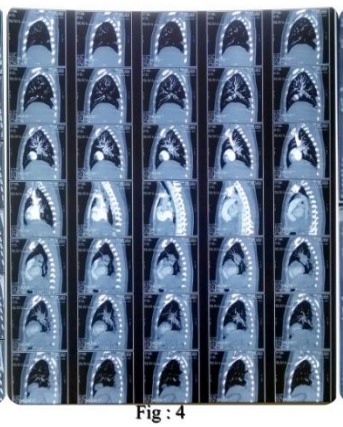
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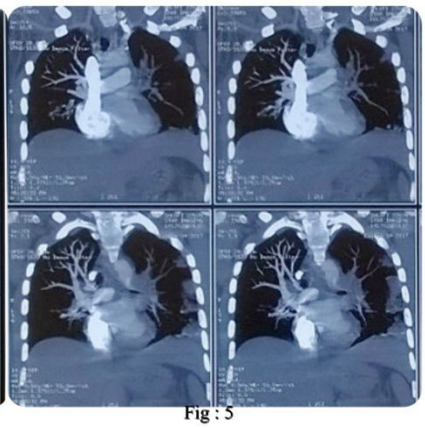
Fig : 5

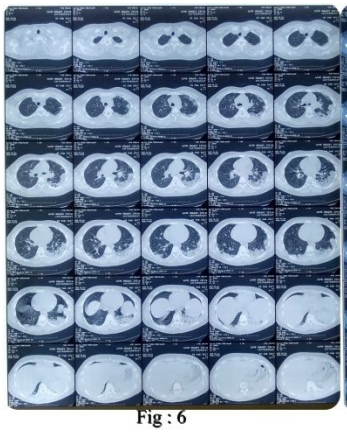
Fig : 6


Fig : 7

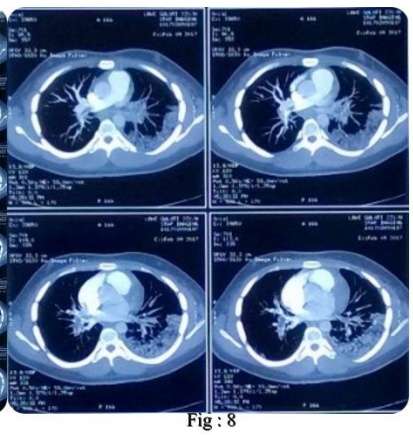
Fig : 8

(Fig: 3-8: CTPA revealed occlusion of left main pulmonary artery and descending branch of right main pulmonary artery. There were areas of peripheral consolidation seen in the left lung and right lung base, which were suggestive of massive infarction.)

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In high suspicion of pulmonary embolism, he underwent CT angiogram (Fig 3- 8) which revealed almost complete occlusion of left main pulmonary artery and all its lobular and segmental branches with a large filling defect in the right main pulmonary artery of size 34 x 11mm - suggestive of an embolus. Most of the descending branch of right main pulmonary artery and segmental branch to apical –posterior segment of the right upper lobe showed filling defect which were also suggestive of embolus. There were areas of peripheral consolidation seen in the left lung and right lung base, which were suggestive of massive infarction. There was no evidence of thrombus in ultrasound venous color Doppler of IVC, bilateral renal veins and lower limb veins. Patient was started on systemic thrombolysis with Inj. Alteplase infusion - 10mg over 2 minutes and then 90mg over 2 hours. The patient tolerated the procedure well except for mild hemoptysis, which was managed conservatively. He was then started on parenteral anticoagulation (Inj. Heparin 500IU/hr.), which was adjusted according to APTT along with oral anticoagulation (T.Acitrome 2mg/3mg), IV antibiotics, Inj. Albumin 20%(100ml x 3 days), Statins (T.Atorvastatin 80mgHS), corticosteroid (T.Wysolone 60mg once daily), and Ipratropium bromide / Budenoside nebulization. The patient responded well to the treatment and was discharge in a stable condition.

Discussion

An individual with nephrotic syndrome carries an increased risk to have thromboembolic disease. Nephrotic syndrome is always characterized by proteinuria of ≥3.5 g/24 hours, albuminemia <3.0 g, peripheral edema, hyperlipidemia and lipiduria (1.2). On the other hand Thromboembolic diseases are serious life threatening conditions. Virchow's triad describes the three broad categories of factors that are thought to contribute to thrombosis which are listed as follows:

1. Hypercoaguable state
2. Endothelial damage
3. Hemodynamic changes (turbulence/stasis).

Risk of pulmonary embolism (PE) and DVT can be calculated with Well's score and PERC score. The commonest risk factors are prolonged immobilization, recent surgery, cancer, cardiac disease, autoimmune disease, prior history of DVT/PE or any hypercoaguable conditions such as Nephrotic syndrome and antiphospholipid antibody syndrome (2,3,4). Most features of nephrotic syndrome are directly related to the increased glomerular permeability such as proteinuria, hypoalbuminemia, and lipiduria. The hypercoaguable state seen in patients with primary nephrotic syndrome is believed to be secondary to glomerular pathology. Moreover hypoalbuminemia leads to increase in fibrinogen levels in patients with Nephrotic syndrome, which in turn increases hepatic fibrinogen synthesis and thereby enhancing platelet reactivity and red blood cell aggregation (2.5). Studies suggest, that inhibition of fibrinolysis is due to increase hepatic synthesis of clotting factors such as fibrinogen, factors V, VIII, Von-Will brand factor and plasminogen activator inhibitor which causes activation of the coagulation cascade and decreases the activity of the fibrinolytic system. Increased urinary losses of inhibitors of coagulation such as anti-thrombin III and plasminogen may also add to this (5).

As in our patient with breathlessness, mild hemoptysis and facial puffiness with no comorbidities, no inherent thrombophilia or history of endothelial damage (surgery, trauma) or stasis (prolonged immobilization) and lab investigations revealing mildly deranged kidney function, hypoalbuminemia, dyslipidemia, urine investigations revealing nephrotic range proteinuria narrowed our diagnosis to hypercoagulability due to nephrotic syndrome, being the cause of bilateral pulmonary artery embolism. Membranous nephropathy was considered as one on the differential but PLA2R antibody was negative. A renal biopsy would have been gold standard however patient and relative did not consent for the procedure. In view of the extent of the embolus as mentioned above he was managed with systemic Thrombolysis followed by anticoagulation therapy and other conservative measures.

Conclusion

Predictions of thromboembolic events are very important in patients with nephrotic syndrome. Histologic evidence of nephrotic syndrome is most important in assessing risk factors of any thromboembolic events (5). The diagnosis of membranous nephropathy is associated with an increased risk of venous thromboembolism (VTE). The risk is less with focal segmental glomerulosclerosis (FSGS) and IgANephropathy as compared to membranous

nephropathy (5). Studies defers about the duration of anticoagulation therapy required in such patients (5). However considering the risk to life involved in such cases we advocate life long anticoagulation if there are no other gross contraindications to the same.

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