AN INTERESTING CASE OF PULMONARY HYPERTENSION

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Abstract:
A 24 years old female patient presented with progressively increasing breathlessness over a period of 3 months and bleeding per rectum for past 3 days. She also had swelling of legs—both sides, symmetrical, painless, extending up to knees. No history of chest pain, palpitation, syncope, cough, orthopnea. No history of hematemesis, jaundice, any other bleeding manifestations. No history of abdominal pain, abdominal distension, oliguria. No history of any comorbid illness like diabetes, hypertensive, PT, asthmatic, epileptic, long term drug intake. She is a non-vegetarian, non-alcoholic, has regular menstrual periods, unmarried. No other family members suffering from similar illness. She lives in Chennai, has finished her undergraduate in B Sc computer science. She went to a private hospital 2 months back for breathlessness. Echo done there was suggestive of severe pulmonary hypertension?primary idiopathic type & started on T.sildenafil 50mg BD. She discontinued the drug after few days.

On examination, she was well built, afebrile, no pallor, not icteric, dyspneic at rest. She had no cyanosis/clubbing or significant lymphadenopathy. Bilateral pitting pedal edema.

Key word: Pulmonary hypertension, Pulmonary thromboembolism, DVT, SLE, APLS

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present which was non-tender. No bleeding gums, purpuric spots. Fundus examination normal. She had tachycardia, tachypnea, Spo2-92%, elevated jugular venous pressure. Cardiac examination revealed palpable P2, parasternal heave, with no thrill. P2 loud in pulmonary area, no murmur. Lungs were clear. We started evaluating her as PULMONARY HYPERTENSION? CAUSE WITH FEATURES OF RIGHT HEART FAILURE & HEMATOCHERIAA Basic investigations revealed raised ESR-70 mm/hr and platelets-60,000 cells/mm3, Hb-11 gms%. Bleeding time was prolonged, PT-12 sec (control-12 secs), aPTT-50 secs (control-28 secs) which did not correct with mixing & incubation. Her renal function tests & liver function tests were within normal limits. Urine analysis revealed albumin-2+, sugar-nil, no deposits. Chest X-ray showed cardiomegaly, enlarged main pulmonary arteries, right atrial enlargement.

**CHEST XRAY-PA VIEW**

ECG-100/min, sinus rhythm, right axis deviation, RVH+, S1Q3T3 pattern, T inversion V1-4, LIII

USG-abdomen & pelvis-normal study

ECHO-RA, RV dilated, moderate TR, severe PHT, normal LV function, EF-55%, intact IAS, IVSP

Pulmonary function tests-mild restrictive pattern. After initial investigations, severe pulmonary hypertension/cor pulmonale was confirmed, but cause was not identified. We suspected PULMONARY EMBOLISM and proceeded with further investigations. Meanwhile thrombocytopenia and coagulopathy was corrected with platelets & fresh frozen plasma transfusion. D-dimer was elevated.

HIV ELISA-negative, HBsAg & anti-HCV negative.

Thyroid function tests-normal. 24 hrs urine protein-750 mg/day. ANA & anti-dsDNA-positive, serum C3, C4 reduced. Anti-cardiolipin Antibody-IgG, IgM positive

Lupus anticoagulant LA1-121 sec, LA2-56 sec, ratio LA1/LA2-2.16 (>2 positive) Serum LDH-621 U/L, serum homocysteine-normal, FDP-normal

BONE MARROW study megakaryocytes increased, erythropoiesis normal

CECT-chest-cardiomegaly CT-pulmonary angiogram Eccentric filling defect in the right lower lobe segmental pulmonary artery suggestive of ?recanalised embolus/residual thrombus with features suggestive of secondary
Lowerlimb venous doppler-thrombus noted in both common femoral, superficial femoral & popliteal veins (Lt>Rt). After hematochezia stopped with increase in platelet count, she was started on heparin initially and then on acitrom with monitoring of PT/INR. She was also started on steroids-prednisolone 1mg/kg. She felt symptomatically better, dyspnea improved, platelet count was stabilized over one lac and was discharged with advice to continue steroids & acitrom with monitoring of PT/INR once in 15 days and to come for regular follow up. She had elevated ACL antibody titre & positive lupus anticoagulant even after 12 wks which confirmed antiphospholipid antibody syndrome.

Final diagnosis of the case was CHRONIC PULMONARY THROMBOEMBOLISM WITH SECONDARY PULMONARY HYPERTENSION/SYSTEMIC LUPUS ERYTHEMATOSUS WITH SECONDARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME/DVT BOTH LOWER LIMBS

DISCUSSION:

Pulmonary hypertension- defined as an abnormal elevation in pulmonary artery pressure as a result of left heart failure, pulmonary parenchymal or vascular disease, thromboembolism, or a combination of these factors. Whether the pulmonary hypertension arises from cardiac, pulmonary, or intrinsic vascular disease, it generally is a feature of advanced disease.

Initial evaluation of our patient for pulmonary hypertension lead to the diagnosis of chronic thromboembolism which is usually due to inappropriately treated acute pulmonary embolism. However, some patients have impaired fibrinolytic resolution of the thromboembolism, which leads to organization and incomplete recanalization and chronic obstruction of the pulmonary vascular bed. In many patients, the initial pulmonary thromboembolism was undetected or untreated. Many of these patients have underlying thrombophilic disorders, such as the lupus anticoagulant - anticardiolipin antibody syndrome, prothrombin gene mutation, or Factor V Leiden mutation.

A perfusion lung scan or contrast-enhanced spiral CT scan usually reveals multiple thromboemboli. However, pulmonary angiography is necessary to determine the precise location and proximal extent of the thromboemboli, and hence the potential for operability. Pulmonary thromboendarterectomy is an established surgical treatment in patients whose thrombi are accessible to surgical removal. Lifelong anticoagulation using warfarin is mandatory. Thrombolytic therapy is rarely of help in patients with chronic thromboembolic pulmonary hypertension and may expose these patients to the increased risk of bleeding without potential benefit.

Systemic lupus erythematosus (SLE) is usually a multiorgan, multisystem autoimmune disease which predominantly occurs in women, with a gender ratio of 9:1. Onset is usually after puberty, typically in the 20s and
Common presentations are photosensitive rashes, polyarthritis, or nephritis, but still can present in varied manner. Characterized by autoantibody formation (specific autoantibodies include anti-dsDNA and anti-Sm) and often low complement levels (C3, C4). Our patient was a young female who presented with thrombocytopenia, prolonged aPTT, proteinuria, DVT and chronic pulmonary thromboembolism with positive autoantibodies and lupus anticoagulant. Thrombocytopenia in SLE is often associated with antiphospholipid syndrome and the sequelae of thromboembolic disease is of greatest concern than the bleeding propensity due to thrombocytopenia. There is occasionally need for splenectomy in situations of prolonged, unresponsive, severe thrombocytopenia. 

Antiphospholipid syndrome (APS) was described in full in the 1980s, after various previous reports of specific antibodies in people with systemic lupus erythematosus and thrombosis. The syndrome is sometimes referred to as "Hughes syndrome", after the rheumatologist Dr. Graham R.V. Hughes (St. Thomas’ Hospital, London, UK) who worked at the Louise Coote Lupus Unit at St Thomas’ Hospital in London and played a central role in the description of the condition.

About 50% of patients with systemic lupus erythematosus, have an antiphospholipid antibody, such as the lupus anticoagulant, antiphospholipid antibody, or anti-beta2 glycoprotein-1. Because phospholipids are integral parts of the control of coagulation, these antibodies can lead to a hypercoagulable state, antiphospholipid antibody syndrome. Antiphospholipid antibody syndrome (APS) is characterized by the presence of symptoms comprising of numerous arterial and venous thrombosis, recurrent miscarriages or preterm delivery and mild thrombocytopenia in the presence of anti-phospholipid antibodies (APL) including lupus anticoagulant (LA), antiphospholipid (ACL) or both. Anti-beta 2 glycoprotein I, antimitochondrial, antiendothelial, antiplatelet and anti-erythrocyte antibodies are also found.

APS patients can develop a broad spectrum of pulmonary disease. Pulmonary embolism and pulmonary artery hypertension are the most prevalent complications of this syndrome. Although, less prevalent complications such as pulmonary microvascular thrombosis, pulmonary capillaritis and alveolar hemorrhage have been reported as well. Recurrent pulmonary embolism can result in pulmonary artery hypertension and in severe cases, tricuspid valve insufficiency. Therefore, pulmonary embolism can be the first manifestation of anitphospholipid antibody syndrome. The outcome in patients with APS and pulmonary hypertension is usually fatal. The most dire presentation of APLAS is the catastrophic form, in which thrombosis is occurring in three or more organs over a short period of time. For thrombosis, lifelong anticoagulation with warfarin given & target INR 2.5-3.5 maintained. For recurrent fetal loss, aspirin and heparin, +/-steroids given. For catastrophic APLAS, high-dose steroids, anticoagulation, cyclophosphamide, plasmapheresis given. The reason for presenting this case is for the initial presentation of SLE as secondary pulmonary hypertension due to chronic pulmonary thromboembolism which might have arise from the asymptomatic DVT of legs or due to associated secondary antiphospholipid antibody syndrome.
CONCLUSION:
All secondary causes of pulmonary hypertension has to be excluded before categorising it as primary idiopathic type. Acute pulmonary thromboembolism is one of the curable causes for pulmonary hypertension. Pulmonary embolism may be the initial manifestation of APS especially in young adults. Pulmonary hypertension in SLE may be primary or secondary to pulmonary emboli which may be associated with APS. If there is thrombocytopenia in a SLE patient, always rule out associated APS. APS is a major source of morbidity in SLE & also contributes to mortality. Long term anticoagulation with careful monitoring of PT/INR & low dose aspirin help in preventing recurrence of thrombotic events and improving the survival in APS.

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