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Case Report

Successful thrombolytic therapy for complicating large right atrial thrombus

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Abstract - *Thrombus embolization in the right side of the heart is an unusual disease process with high morbidity and mortality and its successful management poses a challenge. A 41-year-old male, 2 weeks after bilateral ankle fracture and immobilization, developed bilateral deep venous thrombosis. A large right atrial thrombus causing right ventricular dysfunction and pulmonary embolism was responsible for his acute dysponea. He was haemodynamically stable. He was treated with thrombolytics and anticoagulants. The literature search for the use of thrombolytic agents in patients with right heart thrombus complicating pulmonary thromboembolism, revealed limited reports. Our patient responded well to early tissue Plasminogen activator (t-PA) therapy and follow up with anticoagulation without any bleeding or systemic complication.*

Keywords: Pulmonary embolism, right heart thrombus, deep vein thrombosis, thrombolysis

Pulmonary thromboembolism (PTE) is a known complication of deep vein thrombosis, where an additional thromboembolus present in right heart further increases morbidity and possibly mortality as well. Haemodynamically unstable PTE is defined as massive embolism with hypotension, where thrombolytics have been found to show significant mortality benefit. In patients without hypotension, the accepted treatment is anticoagulant alone. There is lack of consensus on treatment of patients with right heart thromboemboli complicating PTE without hypotension. Again for patients with massive PTE without hypotension but with right ventricular dysfunction (RVD) exact guidelines regarding use of thrombolytics do not exist. We report a patient with large right atrial thrombus complicating PTE without hypotension but with RVD and successful thrombolysis using tissue plasminogen activator (t-PA) in management with rapid restoration of right ventricular dysfunction and complete recovery.

Case Report

A 41 year old man came to the Accident and Emergency (A & E) department with sudden onset of breathlessness, of one-day duration. He denied any history of chest pain, sweating or cough. The patient had suffered bilateral ankle fractures two weeks ago and was given Plaster of Paris (POP) cast in both lower extremities below the knee joints. He had no associated medical history for diabetes mellitus, hypertension, hypercholesterolemia, smoking or coronary artery disease. There was no past or family history of venous thrombosis. He had no drug allergies and current medications were non-steroidal anti-inflammatory drugs (NSAIDs) on as and when required basis only.

On initial evaluation in A & E, the patient was very orthopnoeic at rest, alert but anxious. Pulse rate was 132/min regular, respiratory rate 28/min, blood pressure 120/90 mmHg, with pulse oxymeter readings of Sa_{02} 98% on room air. He was afebrile and there was no cyanosis. His pedal oedema or calf tenderness could not be assessed due to POP. The chest was clear to auscultation and cardiac examination revealed tachycardia without any added sounds or murmurs. The rest of the systemic examination was unremarkable. Laboratory evaluation showed normal haemoglobin and WBC count with normal blood chemistry. Arterial blood gas measurements showed a pH of 7.48, PO_2 79 mm, PCO_2 28 mm and bicarbonate 21 mmol/L on oxygen flow rate of 4 L/min via facemask. The alveolar arterial gradient was 36 mm Hg. X-ray chest revealed prominent left pulmonary artery and sudden tapering of right pulmonary artery with obliteration of right cardiophrenic angle. Electrocardiogram (ECG) showed sinus tachycardia with S1, Q3, T3 pattern i.e. S wave in lead I, Q wave and T inversion in lead III along with incomplete right bundle branch block (RBBB). Plasma D-dimer assay was 8000 ug/L. The patient was shifted to the Intensive Care Unit. A weight based intravenous (I.V.) unfractioned heparin was started with supplemental oxygen 4-6 L/min. via facemask. The peripheral venous Doppler sonography of the lower extremities showed bilateral deep venous thrombosis. Bedside echocardiogram revealed moderate enlargement of right cardiac chambers with hypokinetic right ventricle along with a large thrombus in the right atrium prolapsing into the right ventricle *(Fig. 1)*.

The diagnosis of bilateral deep venous thrombus, large

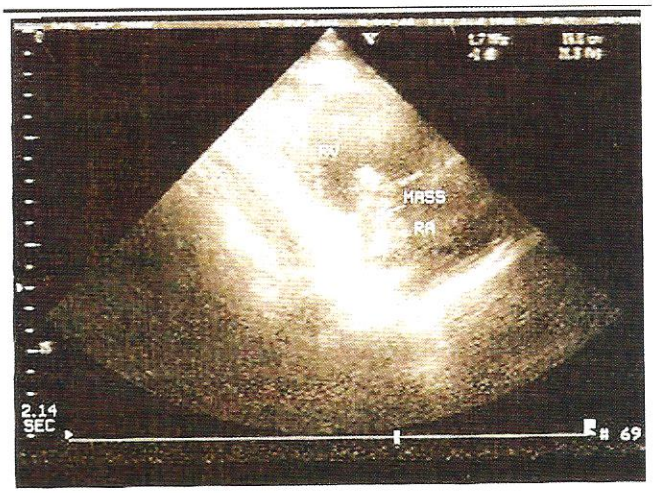

Fig. 1: Echocardiographic parasternal view showing right atrial thrombus prolapsing into right ventricle.

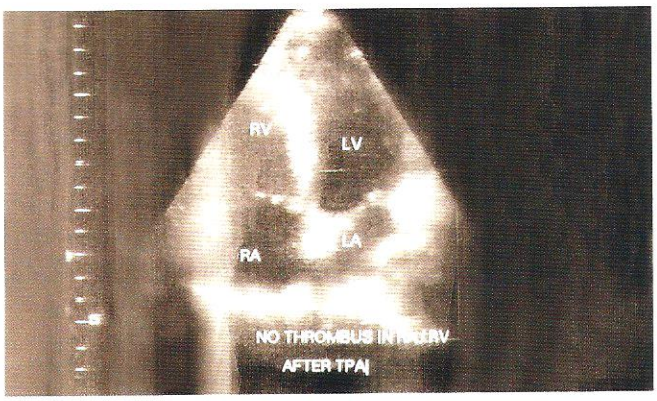

Fig. 2: Echocardiographic four chamber view with no right atrial or ventricular thrombus after tPA therapy.

right atrial thromboembolus, hemodynamically stable massive pulmonary embolism with RV dysfunction was made. In view of right ventricular dysfunction and no contra-indication of thrombolysis, the decision to give thrombolytic therapy was taken and 100 mg tissue Plasminogen activator (t-PA) was infused intravenously over 2 hours. This was followed by unfractioned heparin infusion keeping partial thromboplastin time (PTT) twice to the control value. Later he was switched on to oral anticoagulation therapy with warfarin.

Breathlessness decreased within 3 hours and subsequent ECG after 4 hours revealed normal sized right ventricle with no wall motion abnormality. There was no thrombus in right atrium or ventricle *(Fig. 2)*. Pulmonary perfusion and ventilation (VQ) nuclear scan done 2 days after thrombolysis, had mismatch perfusion and ventilation abnormality, consistent with high probability of pulmonary thromboembolism. It was involving lateral and antrobasal segments of lower lobe of right lung and superior segment of lingular lobe of left lung. The follow up anticoagulation with warfarin was maintained in therapeutic range i.e. international normalized ratio (INR) between 2-3 for 6 months. His clinical assessment one month after discharge showed no clinical or Echocardiographic evidence of right ventricular dysfunction or pulmonary hypertension.

His fractures showed significant recovery in 2 months then he was mobilized and gradually his weight bearing activities were allowed. He was rehabilitated back to his profession after 3 months.

Comment

Venous stasis because of prolonged immobilization promotes thrombosis. A prothrombotic state is also a risk factor for DVT, either on a hereditary or on an acquired basis. "Hypofibrinolysis" is decrease in endogenous tissue plasminogen activator (tPA) activity or an increase in the activity of plasminogen activator inhibitor 1 (PAI-1)[1], which predisposes to venous thrombosis. The use of intravenous unfractionated heparin to treat acute pulmonary embolism has proven its efficacy by promoting the body's own thrombolytic mechanism and regression in further thrombus formation. Heparin does not have a direct fibrinolytic effect on thrombin or fibrin of a formed thrombus. In patients with DVT and PTE fibrinolytic therapy has several theoretical advantages over anticoagulants *viz;* (a) more rapid and complete lysis of thrombi (b) preservation of native structure in the deep veins and (c) preservation of the postphlebitic syndrome.

Rapid improvement of right ventricular function and pulmonary perfusion, accomplished with thrombolytic therapy followed by heparin may lead to a lower mortality, lower recurrent PTE and lower chronic pulmonary thromboembolism in long run and possibly a lower mortality. Thrombolysis may,[1] prevent the downhill spiral of right sided heart failure by physical dissolution of anatomically obstructing pulmonary arterial thrombus,[2] prevent the continued release of serotonin and other neurohormonal factors that might otherwise lead to worsening pulmonary hypertension and[3] dissolve much of the source of the thrombus in the pelvic or deep leg veins, thereby decreasing the likelihood of recurrent large PTE. Patients should however be carefully screened for contra-indications to thrombolysis.

The risk of bleeding from thrombolysis should also be considered and patients must be selected keeping indications and contraindications in mind. For therapeutic decision, PTE can be categorized into three groups: (a) massive PTE with right ventricular dysfunction (RVD) and hypotension, (b) massive PTE with RVD but with-

out hypotension and (c) PTE without RVD. Massive PTE with cardiogenic shock has mortality almost approaching 100%. The most important determinant of mortality from PTE is shock due to right ventricular failure. The risk benefit ratio in this patient group clearly is in favor of thrombolysis. In massive PTE with RVD but no hypotension, the use of thrombolytic therapy has been shown to promote a more rapid clot lysis than heparin alone. Rapid recovery is observed in regional and global right ventricular dysfunction after thrombolytic therapy. The presence of right heart thrombus in addition to pulmonary thromboemboli carries with it an increased mortality rate compared to PTE alone but there are no established guidelines on the management. Our patient had presented with bilateral DVT with large right atrial thrombus and PTE with right ventricular dysfunction and no systemic hypotension. We found that thrombolysis with t-PA not only dissolved right atrial thrombus within hours but also improved RV dysfunction. Pooled data of similar 177 patients of right heart thromboembolism treated differently with anticoagulant therapy, surgical procedure, thrombolytic therapy or nothing - the mortality rate associated with no therapy was 100%, anticoagulation therapy 28.6%, surgical embolectomy 23.8% and that with thrombolytic therapy was 11.3% only.[10]

At Brigham and Women's hospital, five trials of PTE thrombolysis, including the largest trial 5 of tissue plasminogen activator (tPA 100 mg/2 hr) plus heparin versus heparin alone, were coordinated. Most importantly, no clinical episodes of PTE recurred among patients receiving tPA, but there were five (including two fatal) clinically suspected recurrent PTE within 14 days in heparin alone group (P = 0.06). Unlike patients with myocardial infarction, patients with PTE have a wide window for effective use of thrombolysis. Specifically, patients who receive thrombolysis up to 14 days after new symptoms or signs maintain an effective response.[6] Therefore patients suspected of having PTE should be considered as potentially eligible for thrombolysis if they have had any new symptoms or signs within the 2 weeks before presentation. Although t-PA 100mg/2 hr is the only contemporary FDA's approved dosing regimen for PE thrombolysis,[7] other regimens also appear promising, including 1,5,000 hundred thousands units of Streptokinase/2 hr 8 and double bolus Reteplase 9 (10 units bolus followed 30 minutes later by a second 10 unit bolus).

There is consensus on thrombolytic therapy in pulmonary embolism with right ventricular dysfunction and systemic hypotension, however management of patients with no systemic hypotension and thrombus in right heart, it is not so well established. It has been seen that patients treated with RA/RV thrombus with anticoagulants had high mortality.

Our patient's clinical course and long term improvement supports the use of thrombolytic therapy in patient with deep vein thrombosis with right heart thromboembolism even without haemodynamic compromise.

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