Letter to the Editor

Nephrotic syndrome leading to recurrent pulmonary embolism: A report of two cases.

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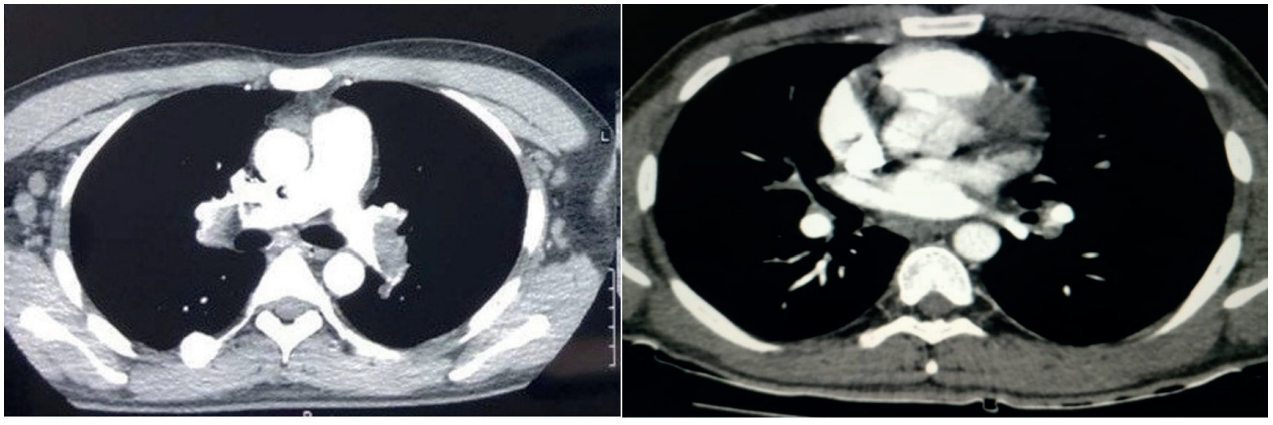
To the Editor,

A 34-year-old male, presented with breathlessness, cough and chest pain for 3 days. He was tachypneic, normotensive, with tachycardia and SpO2-89%. Doppler echocardiography (2D Echo) showed dilated right atrium and ventricle with pulmonary artery systolic pressure of 60 mm of Hg. NT-proBNP was 4326 pg/ml. Serum albumin was 1.92 gm/dl, rest of the laboratory parameters were normal. Computed Tomography Pulmonary angiography (CTPA) showed presence of thrombus in right and left main pulmonary arteries (Figure 1a).

As he had intermediate-high risk of early mortality, subcutaneous enoxaparin 1mg/kg was started with a plan to perform rescue thrombolysis in case of hemodynamic instability. Bilateral lower limb colour venous doppler was normal. After hospitalization, he developed bilateral pitting pedal edema and on evaluation a diagnosis of nephrotic syndrome was made. Renal biopsy was not performed as the patient was on anticoagulation. Enoxaparin was overlapped with dabigatran and after seven days of overlap, enoxaparin was stopped. Patient improved, his tachycardia and edema resolved and PaO2 improved. 2D-Echo after 14 days of anticoagulation revealed normal chamber dimensions with PASP of 40 mm of Hg. He was discharged on dabigatran, prednisolone and atorvastatin. He presented after a month with breathlessness and SpO2 was 90%. On 2D-Echo, PASP had increased to 55 mm of Hg. CTPA revealed partial resolution of thrombi in right and left pulmonary arteries but a new



1a 1b

Figure 1. a: CTPA mediastinal window showing bilateral pulmonary artery thrombus 1b: CTPA mediastinal window showing bilateral segmental pulmonary artery thrombus

thrombus was detected in left lobar pulmonary artery. Patient reported that he did not miss even a single dose of dabigatran. Dose of dabigatran was escalated to 220 mg BD from 150 mg BD.

After 14 days, his shortness of breath resolved, tachycardia had settled, and PaO2 improved.

A 23-year-old male presented with breathlessness for 2 days and swelling of both legs for 20 days. He had tachycardia, tachypnea, pedal edema and SpO2 was 91% on room air. 2D-Echo revealed normal chamber dimensions with PASP of 42 mm of Hg. CTPA revealed bilateral segmental pulmonary artery thrombus (Figure 1b).

Enoxaparin was started. Bilateral lower limb colour venous doppler was normal. He was diagnosed to have nephrotic syndrome. Patient was discharged on dabigatran, prednisolone, atorvastatin and diuretics.

After 14 days, patient presented with sudden worsening of breathlessness. 2D-Echo revealed dilated RA/RV with bowing of interventricular septum to the left. McConnell's sign was positive. Unfractionated heparin was administered intravenously in a bolus dose of 80U/kg followed by a maintenance dose of 18 U/kg/hour. CTPA revealed thrombus in right and left pulmonary arteries. As patient had high early mortality risk, he was thrombolysed with alteplase. However, patient expired after one hour due to obstructive shock.

Management of pulmonary embolism due to nephrotic syndrome is not different. After initial parental anticoagulation, patient can be shifted on oral anticoagulation. Anticoagulation is continued till the underlying disease has resolved or has gone into remission (1).

Both of our patients had recurrence of pulmonary embolism despite on adequate anticoagulation. Management of recurrent VTE despite on adequate anticoagulation and management of treatment failure with newer anticoagulants is not clearly defined. The strategies which can be tried if non-compliance has been excluded include switching to full dose LMWH, dose escalation, switching to another anticoagulant or addition of second anticoagulant. All the BISTRO-I, BISTRO-II, RENOVATE, REMODEL and RE-LY trials have shown a dose dependent decrease in VTE events with increase in dose of dabigatran (2). Thus, dose escalation of dabigatran to 220 mg BD may be considered in patients who develop recurrence of VTE on 150 mg BD of dabigatran. However, dose escalation has not been found to be effective with rivaroxaban (3). A meta-analysis of phase III trials by Kakkos et al showed that NOAC's are more effective than vitamin K antagonists in preventing VTE recurrence during the treatment of VTE (4). Also, several studies have shown that there is no difference in efficacy of various NOAC's in treatment of VTE (5). Thus, switching over from one NOAC to other or to warfarin in case of anticoagulation failure is not recommended. Schulman et al in a registry of 212 cancer patients who had recurrent VTE showed that additional VTE recurrence was less common when initial anticoagulant was replaced by LMWH (6). The evidence on use of dual anticoagulation for anticoagulation failure is limited only to case reports and hence more evidence from randomized controlled trials is needed (7, 8).

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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