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Case Series

Thrombus in transit – A case series on dilemma in management

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ABSTRACT

Thrombus in transit (TIT) is a rare but potentially fatal condition. Transthoracic echocardiography is the diagnostic modality of choice. The major complications of TIT are pulmonary embolism, right ventricular dysfunction, obstructive shock, and paradoxical embolism through patent foramen ovale. We hereby present a case series of four patients with TIT and the challenges faced while managing them.

Keywords: Thrombus in transit, Catheter directed thrombolysis, Tumor emboli in transit

INTRODUCTION

The case series can serve as a guideline for the management of Thrombus in transit (TIT) for which there are no clear and formal guidelines. Apart from systemic thrombolysis, mechanical thrombectomy and catheter directed thrombolysis (CDT) have a larger role to play in its management. The case series consists of following 4 cases of thrombus in transit:

CASE SERIES

Case 1

An 82-year-old lady with underlying coronary artery disease (CAD), hypertension, lymphedema, obstructive sleep apnea, and recent history of large duodenal ulcer bleeding 15 days back, came to our medical facility with chief complaints of breathing difficulty and hypotension. The patient was fluid resuscitated, given supplemental oxygen, inotropic support, and broad-spectrum antibiotics. ECG and chest X-ray done were within normal limits (WNL). Arterial blood gas (ABG) showed moderate hypoxemia with compensated Type 2 respiratory failure. Transthoracic echocardiography (TTE) showed a large mobile clot in the right atrium (RA) measuring 4.1 × 1.0 cm, severe tricuspid regurgitation (TR), PASP 78, dilated RA, right ventricle (RV) with RV systolic dysfunction, jerky septum, and left ventricular ejection fraction 50% [Figure 1]. Hence, it was diagnosed as TIT with massive pulmonary embolism (PE) with obstructive shock. The patient started on therapeutic anticoagulation with unfractionated heparin (UFH) with target APTT of 1.5–2 times of the upper limit of normal (ULN) with 6 hourly and hemoglobin monitoring. The patient is not an ideal candidate for systemic thrombolysis; hence, mechanical thrombectomy with CDT was planned. The bilateral lower limb venous Doppler done showed deep vein thrombosis (DVT) in the left proximal superficial femoral vein. Troponin I (0.71 ng/ml), NT-pro-BNP (30,000 pg/ml), and D dimer (6035 ng/ml) of the patient were raised. Mechanical thrombectomy done with Penumbra INDIGO CAT system and a multihole catheter left *in situ* for CDT with alteplase infusion at 1 mg/h. The UFH infusion was continued at 500 IU/h with 6 hourly CBC, PT, INR, and APTT monitoring. Patients' inotrope and oxygen requirements improved significantly with above interventions. TTE done after 24 h showed no RA clot, significant improvement in RV systolic function, and decrease in PASP from 78 to 58 mm Hg. Alteplase infusion was stopped after 24 h and patient was continued on UFH infusion. The dose of thrombolytic agent required in CDT (here 24 mg) is much less than for systemic thrombolysis (100 mg) with reduced risk of bleeding. After 48 h of intervention, there was >3 g fall in hemoglobin (from 10.4 g% to 7 g%) so UFH infusion was stopped. There was a right-sided thigh hematoma at the site of sheath insertion (USG size – 8.7 × 2.2 × 4.1 cm). She was transfused 2 units of packed RBCs to maintain hemoglobin ≥7 g%. Inferior vena cava (IVC) filter was placed at the time of removal of CDT catheter. Patient was holding hemoglobin with no increase in hematoma size. The computed tomography pulmonary angiography (CTPA) done to see thrombus burden revealed only segmental thrombus in the right pulmonary artery.

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Patient was then started on therapeutic anticoagulation with LMWH with regular hemoglobin monitoring which she tolerated well.

Case 2

A 45-year-old gentleman, with CAD, paroxysmal atrial fibrillation, chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD) on maintenance hemodialysis (MHD) through right internal jugular vein permacath, was admitted with chief complaints of shortness of breath and mild hypoxemia. ABG showed mild hypoxemia with compensated Type 2 respiratory failure. Chest X-ray showed hyperinflated lung fields. TTE showed RA clot of the size of 2.8 × 2.1 cm, global LV hypokinesia (EF 20%), and no signs of RV dyskinesia [Figure 2]. Doppler ultrasound of both lower and upper limb veins showed no DVT. TIT could be due to paroxysmal AF or permacath as a nidus for clot formation. The patient was treated with UFH infusion with APTT target 1.5–2 times ULN. UFH therapy was overlapped with warfarin for 5 days to target INR between 2 and 3.

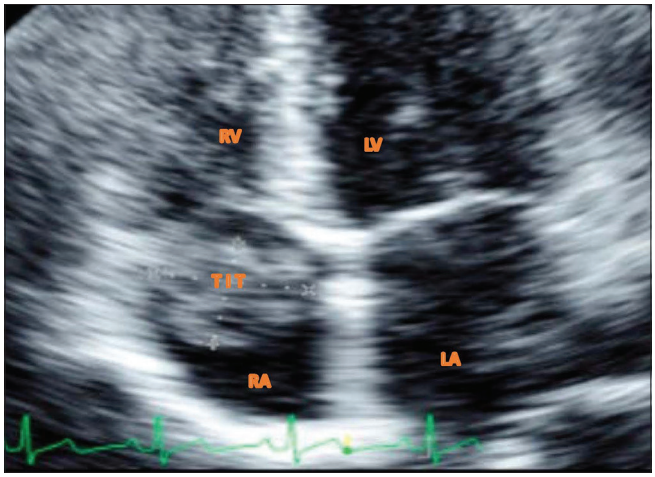

Figure 1: Right atrium thrombus in transit.

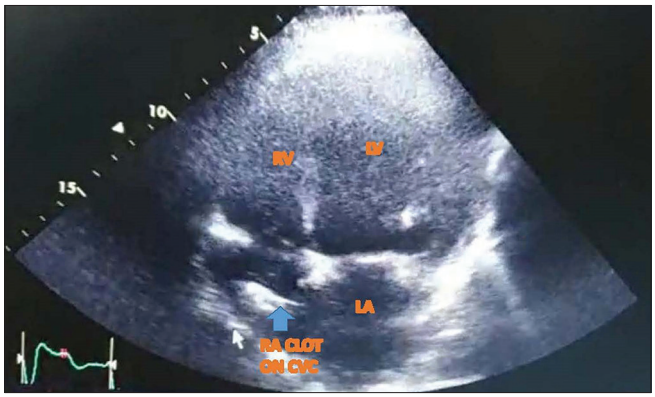

Figure 2: Central venous catheter thrombus in transit.

Case 3

A 17-year-old girl with underlying CKD on MHD, hypertension, and hypothyroidism, came with complaints of altered sensorium, breathlessness, and chest pain and was dialyzed 1 day back. She had low GCS (E1V2M4), hypotension, sinus tachycardia, and severe hypoxemia. The patient was managed with intravenous fluids, broad spectrum antibiotics, vasopressors, mechanical ventilation, and other supportive treatment. The chest X-ray was WNL. ECG showed sinus tachycardia with S1Q3T3 sign. TTE showed a mobile elongated thrombus 3.5 × 0.8 cm in IVC attached proximal to the hepatic vein and extending into RA with RV systolic dysfunction [Figures 3 and 4] TIT with massive PE with obstructive shock. The patient was planned for systemic thrombolysis after computed tomography (CT) head. The upper and lower limb venous Doppler showed no signs of DVT. Vasopressor support continued to increase despite optimal medical management. Unfortunately, patient could not be revived succumbed to her illness.

Case 4

A 65-year-old lady, with COPD and bedridden status for a week because of fractured left humerus and pubic rami, came with chief complains of sudden onset of shortness of breath, low blood pressure, and altered sensorium. ABG showed hypoxemia (Pao2 55 mmHg) with compensated Type 2 failure. The patient was managed with intravenous fluid, supplemental oxygen, inotropic support, broad spectrum antibiotics, and subsequently required ventilator support. TTE showed paradoxical septum, EF-55%, severe TR, PASP-69, and a mass at IVC-RA junction of 1.7 × 2.4 cm clot? mass? (TIT) [Figure 5]. USG abdomen showed cirrhotic liver with a heterogeneous lesion of size 8.4 × 8.3 × 8 cm in the right lobe of the liver with direct tumor invasion to the right hepatic vein and IVC extending up to RA. The investigation showed acute on chronic liver failure (Total Bilirubin – 3.16mg/dl, Direct Bilirubin – 2.21 mg/dl, SGOT – 70 IU/L, SGPT – 98IU/L, and

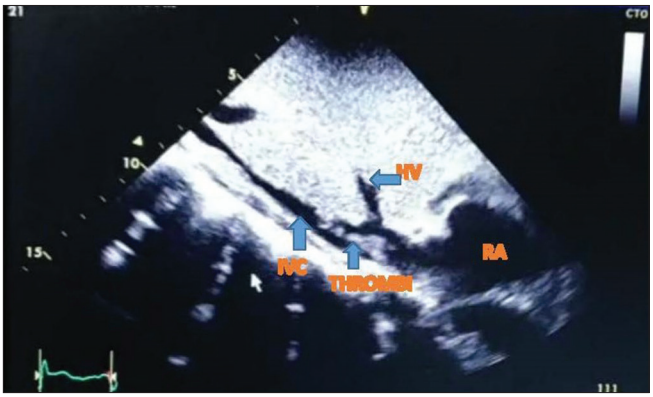

Figure 3: Inferior vena cava thrombus attached proximally to hepatic vein.

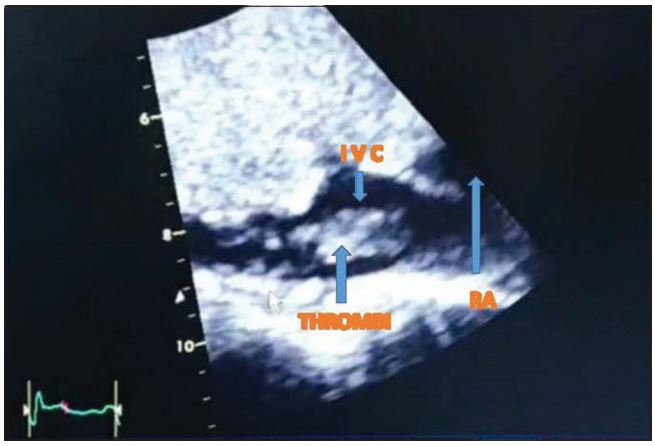

Figure 4: Inferior vena cava thrombus in transit.

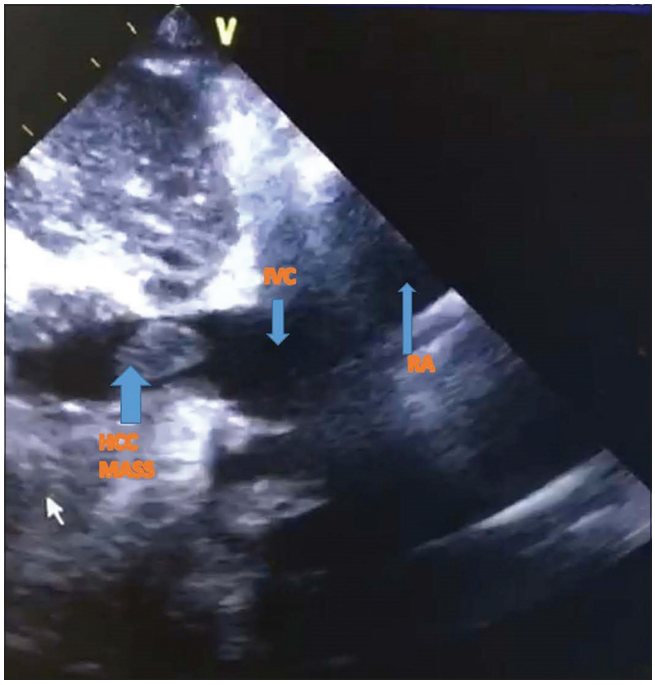

Figure 5: Hepatocellular carcinoma mass in transit.

INR – 2.25), hepatorenal syndrome (Creatinine – 1.8 mg/dl), thrombocytopenia (Hb – 10 gm/dl, TLC – 7000 cells/cubic mm, and Platelets – 65000/mcL), and raised cardiac markers (troponin I – 0.13 ng/ml, NT-pro-BNP – 924 units, and D-dimer – 5055 ng/ml). Alpha-fetoprotein (754 IU/ml) was raised while other tumor markers such as CEA, CEA19-9, CA50, CA19-9, and CA 125 were WNL. Upper and lower limb venous Doppler showed no DVT, TIT with acute PE with obstructive shock with hepatocellular carcinoma (HCC). HCC presentation as pulmonary tumor embolism is extremely rare. The patient was treated with anti hepatic coma regime, albumin, and sorafenib. Patient on a high dose of inotropes could not be shifted for CT head and CTPA. Treatment of choice in advanced HCC with vascular invasion is hepatic resection with removal of tumor thrombus on cardiopulmonary bypass. There is no role of therapeutic anticoagulation and systemic thrombolysis in pulmonary tumor embolism. Liver transplant and cardiac surgery team advised for same but consent was not given and we lost patient.

DISCUSSION

TIT and its etiology

TIT refers to a free-floating clot within the RA, ventricle, superior, or IVC. It usually coexists with massive PE. It is diagnosed only in about 4% of all PE patients according to the International Cooperative PE Registry. The mortality rate associated with TIT is as high as 40%.[1] Etiology of TIT is proximal or distal DVT or right heart clot from atrial fibrillation or cardiomyopathy. TIT e also associated with intravascular foreign bodies such as pacemaker leads, prosthetic tricuspid valves, and central venous catheters, especially hemodialysis catheters. Procoagulant states include antiphospholipid syndrome, protein C, protein S, and antithrombin III deficiencies and systemic vasculitis also predispose to TIT. Incidence of pulmonary tumor embolism is 3–26% of patients with solid tumors.[2] Metastatic spread of malignancies to lungs is common but pulmonary tumor embolism is rare. HCC invasion of IVC and the RA occurs in <2% of the patients.[3]

Clinical presentation and diagnosis

Clinical presentation can range from asymptomatic to massive PE. TTE is the diagnostic modality of choice which is easily available, done bedside and can be repeated to assess the effects of therapeutic intervention. Transesophageal echocardiography considered when TTE is suboptimal or non-diagnostic pulmonary angiography is the gold standard for thromboembolic disease but has poor sensitivity and specificity for pulmonary tumor emboli.[4] Pulmonary tumor emboli diagnostic gold standard is demonstration of tumor cells in the pulmonary vasculature.

Treatment

Treatment modality chosen depends on the site and burden of thrombus, hemodynamic and oxygen status, underlying comorbidities, and expertise available in the institution. Guidelines for PE (2019) provide an overview of the management of TIT with extension to pulmonary circulation. Treatment for TIT includes therapeutic anticoagulation, systemic thrombolysis, percutaneous embolectomy, and CDT and surgical embolectomy. First step in hemodynamically unstable PE is supplemental oxygenation and inotropic support for RV failure along with therapeutic anticoagulation. Systemic thrombolysis within 48 h (if no absolute contraindications) gives maximum benefits. Thrombolysis done up to 14 days if symptomatic

patients. Systemic thrombolysis advantages are easy availability and simple bedside administration. Meta-analysis of thrombolysis trials showed significant reduction in the combined outcome of mortality and recurrent PE in massive PE. Risk of severe bleeding and intracranial hemorrhage with systemic thrombolysis was 9.9% and 1.7%, respectively.[5] In hemodynamically stable PE with RV dysfunction and elevated troponin levels, thrombolysis causes significant reduction in the risk of hemodynamic decompensation but increases the risk of severe extracranial and intracranial bleeding (PE thrombolysis trial. Percutaneous embolectomy and CDT become crucial in scenario of hemodynamic instability, high thrombus burden, contraindications for systemic thrombolysis, failed thrombolysis, or shock likely to cause death before systemic thrombolysis may take effect. Success rates of percutaneous mechanical thrombectomy with CDT has reached up to 87% in expert hands. ULTIMA, SEATTLE II, PERFECT trial showed favorable results in massive and submassive PE. Surgical embolectomy is recommended for contraindications or failed thrombolysis. Vena cava filters recommended for absolute contraindication to anticoagulant, recurrent PE on anticoagulation, or free floating thrombi.

Long-term anticoagulation

Therapeutic anticoagulation for up to 3 months is recommended for whom major transient and reversible factor is identified and modified. Therapeutic anticoagulation for an indefinite period is recommended for cancer patients, recurrent VTE, and for patients with no or minor identifiable risk factors. Drugs used for therapeutic anticoagulation are Vitamin K antagonists (VKA) or non-Vitamin K oral anticoagulants (NOACs). The use of NOACs is increasing nowadays for good safety profile, no coagulation profile monitoring and comparable bleeding risk to VKAs (major bleeding = 1%& clinically relevant non-major bleeding = 6%.[5] VKAs recommended for antiphospholipid syndrome. NOACS safety profile not established in chronic liver disease Child Pugh B and C and CKD with creatinine clearance <15 ml/min. NOACs are preferred in CKD Stages 1–3 but in Stage 4, the choice of warfarin versus NOACs depends on drugs pharmacokinetics and patient profile. Warfarin remains first-line treatment in ESRD. Warfarin in CKD is associated with calciphylaxis and nephropathy characterized by tubular obstruction by red cell casts following glomerular hemorrhage. Anticoagulation with heparin is safe in non-dialysis-dependent CKD, but remains a challenge in the hemodialysis patients.

CONCLUSION

Systemic thrombolysis is treatment of choice for TIT with hemodynamic instability. Mechanical thrombectomy and CDT will now play a bigger role with availability of expertise in tertiary care centers. NOACs are becoming the drug of choice for long-term anticoagulation nowadays with increasing use of them even in CKD Stage 1–3.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflict of interest.

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