Recurrent Intermediate High-Risk Pulmonary Embolism While on Therapeutic Apixaban: A Case of Anticoagulation Failure and Concurrent May-Thurner Syndrome

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Background

- **Pulmonary embolism (PE) recurrence:** 11% at one year and 40% at ten years after discontinuing anticoagulation.[1]
- PE recurrence during active anticoagulant therapy, particularly with factor Xa inhibitors, occurs in approximately 2–3% of patients. [2]
- Predisposing risk factors for recurrent venous thromboembolism (VTE) include anatomical variants such as May-Thurner syndrome.
- **May-Thurner syndrome (MTS):** compression of the left common iliac vein by the overlying right common iliac artery.[3]
- MTS is disproportionately prevalent in young women and predisposes to left-sided deep vein thrombosis (DVT).[3]

Case Presentation

Setting: Hospitalized tertiary-care intensive care unit and inpatient family medicine service.

Patient: A woman in her mid-40s with a history of unprovoked bilateral DVT and PE presents with sudden-onset substernal chest pain with associated dyspnea, diaphoresis, and nausea. She reported full compliance with apixaban 5 mg twice daily since her discharge 3 months prior.

Prior Hospitalization: Patient presented with acute extensive DVT involving the inferior vena cava (IVC), bilateral iliac veins, and the left common femoral and superficial femoral veins.

Present Hospitalization: CT pulmonary angiography confirmed bilateral pulmonary emboli involving the distal main, segmental, and subsegmental branches with significant right ventricular (RV) strain identified; RV:LV > 1.0.

- Acute: IV unfractionated heparin → Bilateral catheter-directed thrombolysis (EKOS) and tPA infusion following SEATTLE II protocol
- Non-acute: Extensive workup + heparin bridge to warfarin with higher INR target (2.5-3.5)

Investigation and Treatment

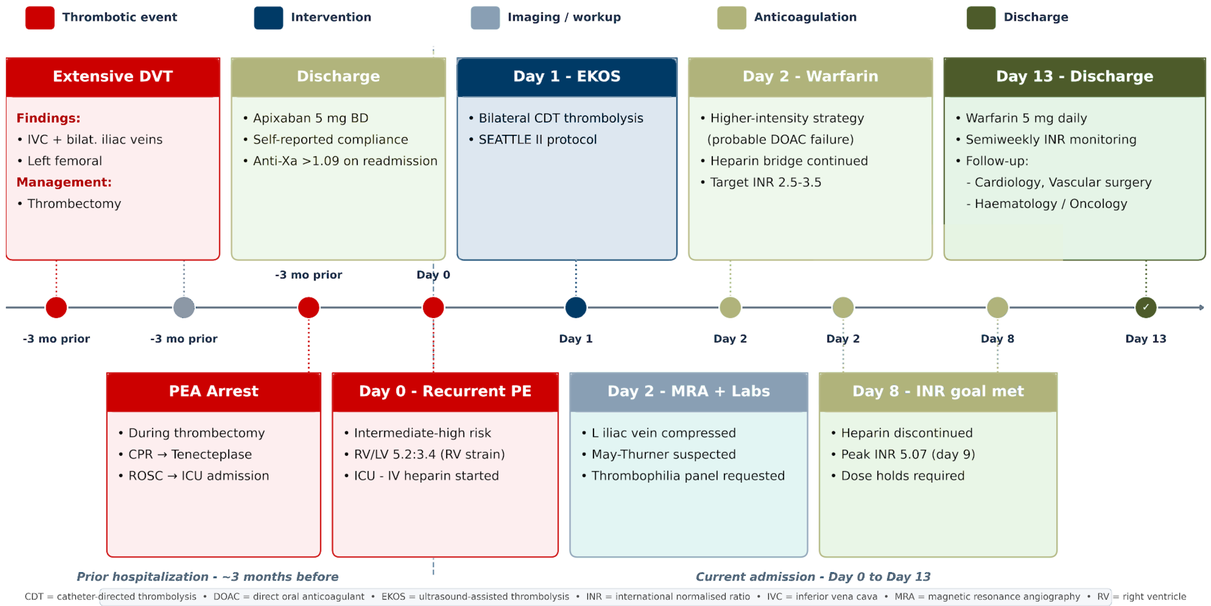


Figure 1. Clinical timeline

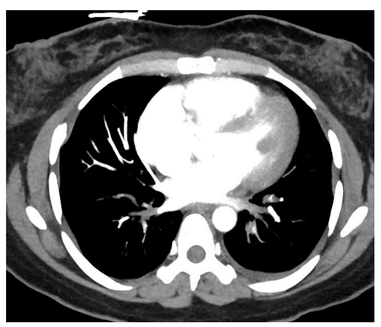


Figure 2a. Axial contrast-enhanced CTPE at the pulmonary hilum. Mediastinal window shows right-sided enlargement relative to the left ventricle, consistent with right heart strain. Filling defects within bilateral subsegmental pulmonary vessels are indicative of acute thromboembolic occlusion.



Figure 2b. Axial contrast-enhanced CTPE at the pulmonary hilum. Lung window shows well-aerated parenchyma without consolidation, infarction, or pleural effusion. Subsegmental pulmonary vessels are visible near the right and left hila, where the corresponding filling defects seen on the mediastinal window localize to the distal subsegmental branches.



Figure 3. Coronal MRA with and without contrast of the pelvis demonstrating features suggestive of May-Thurner syndrome. The left common iliac vein is compressed by the right common iliac artery. There is a filling defect extending from the right common femoral vein to the junction of the right common iliac vein and the inferior vena cava indicative of a non-acute, non-occlusive thrombosis.

References. Please scan QR code for a list of our references!

Discussion

- Thrombophilia workup: normal homocysteine and complement levels, negative JAK2, lupus anticoagulant and antiphospholipid antibodies.
- MR venography (MRV) is insufficient to diagnose MTS → intravascular ultrasound (IVUS) is the gold standard.[4]
- There is an absence of definitive anticoagulant alternative in the setting of failed direct oral anticoagulant (DOAC) therapy. Warfarin with a higher INR target of 2.5–3.5 was opted for our patient, a strategy analogous to that used in triple-positive APS.[5]
- The persistence of RV dysfunction (elevated RVSP at 55 mmHg), an independent predictor of VTE recurrence, reinforces the need for close outpatient follow-up and sustained anticoagulation.[6]
- **Limitations:** Absence of DOAC plasma level measurement prevents confirmation of apixaban concentration and thus compliance. Thrombophilia testing during an acute thrombotic event and while on heparin therapy may compromise reliability. Lack of confirmation of May-Thurner syndrome.

Takeaways

- Recurrent VTE during active DOAC therapy is rare and warrants systematic evaluation for anatomical and hypercoagulable etiologies.
- MTS is an under-recognized risk factor for anticoagulation failure and recurrent VTE.
- Warfarin with a higher INR target is a reasonable strategy in cases of DOAC failure with unclear etiology. Further prospective research is needed for definitive guidance.
- **Key roles of family medicine physicians:**
  - Recognizing anticoagulation failure
  - Coordinating multidisciplinary evaluation
  - Ensuring longitudinal care post-discharge