American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2026; 27: e953199
DOI: 10.12659/AJCR.953199

Received: 2026.02.23
Accepted: 2026.05.08
Available online: 2026.05.29
Published: 2026.XX.XX

Catheter-Directed Thrombolysis and Direct Oral Anticoagulant Class Switch to Prevent Pulmonary Embolism From Large Inferior Vena Cava Thrombus

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Financial support: None declared
Conflict of interest: None declared

Patient: Female, 46-year-old
Final Diagnosis: Pulmonary embolism with giant IVC thrombus
Symptoms: Chest pain and syncope
Clinical Procedure: —
Specialty: Cardiology

Objective: Rare coexistence of disease or pathology

Background: Inferior vena cava (IVC) thrombosis is an uncommon complication of deep vein thrombosis and may be associated with a high risk of severe pulmonary embolism, particularly in the presence of free-floating thrombi. Although IVC filter placement may be considered to prevent embolization, prolonged filter dwell increases the risk of recurrent venous thrombosis and reduces retrieval success, highlighting the importance of early thrombus clearance. However, evidence regarding optimal interventional and anticoagulation strategies for IVC thrombosis remains limited.

Case Report: A 46-year-old woman with Down syndrome and adjustment disorder presented with sudden-onset chest pain and syncope. On admission, she was hypotensive and hypoxemic. Contrast-enhanced computed tomography revealed bilateral pulmonary emboli and a large floating IVC thrombus extending from below the renal vein to the right common iliac vein. A retrievable IVC filter was placed, and anticoagulation was initiated. No underlying thrombophilia was identified. After 2 weeks, regression of the IVC thrombus was insufficient, and catheter-directed thrombolysis with alteplase and heparin was performed, resulting in marked clinical improvement. The patient was discharged on apixaban. After 2.5 months, the pulmonary arterial thrombi had resolved; however, the IVC thrombus persisted. Switching anticoagulation from apixaban to dabigatran led to complete thrombus resolution 4 months after symptom onset, allowing successful retrieval of the IVC filter.

Conclusions: This case highlights the potential role of alteplase-based catheter-directed thrombolysis for early thrombus reduction and suggests that switching from a factor Xa inhibitor to a direct thrombin inhibitor may be effective in select patients with refractory IVC thrombosis.

Keywords: Catheterization • Dabigatran • Direct Oral Anticoagulants • Inferior Vena Cava • Pulmonary Embolism • Thrombolytic Therapy • Tissue Plasminogen Activator

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Introduction

Inferior vena cava (IVC) thrombosis accounts for approximately 2.6 to 4% of all cases of deep vein thrombosis (DVT) [1]. Free-floating IVC thrombi are associated with a high risk of severe and potentially fatal pulmonary embolism, and placement of an IVC filter may be considered to prevent further embolization [1]. However, prolonged filter dwell increases the risk of recurrent DVT and IVC thrombosis or occlusion, and retrieval success declines markedly beyond 9 weeks [2,3]. Early thrombus clearance is therefore desirable to facilitate timely filter retrieval. In Japan, mechanical thrombectomy devices for venous thromboembolism are not available, and recent shortages of urokinase have further limited therapeutic options. Catheter-directed thrombolysis (CDT), enabling local delivery of thrombolytic agents such as tissue plasminogen activator in close proximity to the thrombus, is primarily used for extensive iliofemoral DVT to achieve early symptom relief and reduce the risk of post-thrombotic syndrome. Reports have also suggested its efficacy in select cases of IVC thrombosis [1,4,5].

Direct oral anticoagulants (DOACs) include factor Xa inhibitors and direct thrombin (factor IIa) inhibitors. In many countries, dabigatran is approved in addition to Xa inhibitors for the treatment of DVT and pulmonary embolism [6]. However, evidence regarding the optimal selection or switching of DOAC classes in patients with refractory venous thrombosis remains limited. We report a case of pulmonary embolism complicated by a large floating IVC thrombus successfully managed with CDT using alteplase, followed by a switch from a factor Xa inhibitor to a direct thrombin inhibitor.

Case Report

A 46-year-old woman with Down syndrome, adjustment disorder, and obesity (body mass index 33.1 kg/m^2) was transported to the emergency department after sudden syncope while working in a seated position, followed by chest discomfort upon regaining consciousness. She had no prior history of chest symptoms, lower-limb pain, or subjective leg swelling. Her regular medication included sertraline. On arrival, she was alert but complained of dyspnea and chest discomfort. Vital signs showed hypotension (90/54 mmHg), heart rate 98 beats/min, tachypnea, and oxygen saturation of 95% on 10 L/min supplemental oxygen. Arterial blood gas analysis revealed a pH of 7.344, partial pressure of carbon dioxide (pCO_2) of 39.2 mmHg, partial pressure of oxygen (pO_2) of 57.4 mmHg, bicarbonate (HCO_3^-) of 20.9 mmol/L, arterial base excess (ABE) of -4.4 mmol/L, and a lactate level of 36.3 mg/dL. Cardiac auscultation was unremarkable, while bilateral lower-leg edema was present. Electrocardiography demonstrated an S1Q3T3 pattern with T-wave inversion in leads V1-V3. Transthoracic echocardiography revealed preserved left ventricular systolic function with marked right ventricular dilatation and left ventricular compression. Contrast-enhanced computed tomography (CT) revealed thrombi in both main pulmonary arteries and a large floating thrombus extending from just below the renal veins within the IVC to the right common iliac vein (**Figure 1**). No mechanical causes of venous obstruction were identified in the lower extremities or along the IVC.

In Japan, thrombus aspiration catheters that are available overseas have not been approved. Systemic thrombolytic therapy is recommended in patients with hemodynamic instability, such as persistent shock or hypotension in the acute phase, or when signs of circulatory deterioration emerge during the clinical course, and intravenous heparin administration is generally undertaken as the initial treatment. Therefore, intravenous unfractionated heparin (5000 units) was administered, and inotropic and vasopressor support with dobutamine and noradrenaline was initiated for hypotension. To prevent further embolization from the floating IVC thrombus, a retrievable IVC filter (Denali) was placed below the renal veins via the right internal jugular vein. Laboratory tests showed preserved hemoglobin (14.4 g/dL) and renal function (creatinine 0.83 mg/dL), with markedly elevated D-dimer levels (23.3 µg/mL). No significant coagulation abnormalities or antiphospholipid antibodies were detected (**Table 1**).

Obesity and reduced physical activity were considered the primary contributors to her venous thrombosis. During the clinical course, no deterioration in hemodynamic status was observed, and catecholamines were rapidly tapered and discontinued; therefore, systemic thrombolytic therapy was not initiated. Anticoagulation with unfractionated heparin was continued, targeting an activated partial thromboplastin time (APTT) of 60-80 s. Follow-up CT demonstrated no significant change in pulmonary or IVC thrombi. Owing to intolerance of prolonged intravenous therapy, anticoagulation was switched to rivaroxaban (15 mg twice daily). One week later, however, the IVC thrombus remained unchanged.

Given the absence of bleeding complications, CDT was initiated on day 16. A pulse-spray infusion catheter (Fountain infusion catheter: Merit Medical) was positioned along the IVC thrombus via the right internal jugular vein, and alteplase was administered as a 2-mg bolus followed by continuous infusion at 0.5 mg/h for 17 h, in combination with low-dose unfractionated heparin (400 U/h). Following alteplase administration, D-dimer levels increased sharply from 8.4 to 73.7 µg/mL and subsequently declined.

Repeat CT on day 19 demonstrated marked regression of the IVC thrombus, and the catheter was removed on day 20. Rivaroxaban might have previously been associated with the development of a cutaneous eruption; therefore, the anticoagulant

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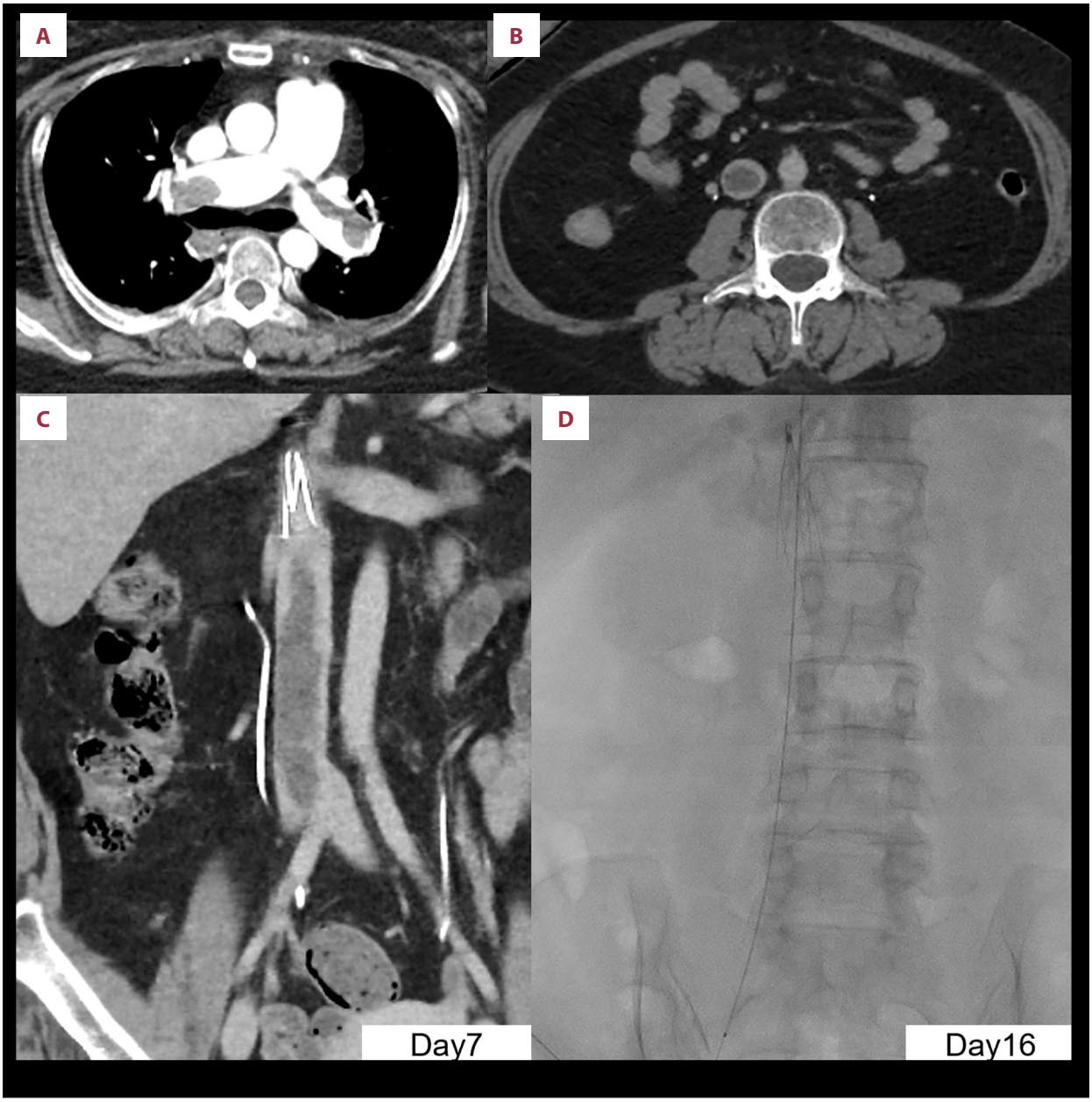

Figure 1. Contrast-enhanced CT findings on admission and at follow-up, and imaging during catheter-directed thrombolysis. On contrast-enhanced CT at admission, thrombi were identified in the bilateral pulmonary arteries (**A**), along with a massive thrombus in the IVC (**B**). One week after IVC filter placement and initiation of anticoagulation, the IVC thrombus remained unchanged (**C**). A pulse-spray catheter (Fountain infusion catheter) was subsequently inserted via the right internal jugular vein, with the side holes positioned across the thrombotic segment of the IVC (**D**). CT, computed tomography; IVC, inferior vena cava.

was switched to apixaban (5 mg twice daily), and the patient was discharged on day 24. As 3 weeks had elapsed since the initiation of treatment, apixaban was administered at the standard dose rather than the high dose. At follow-up CT on day 44, partial regression of the IVC thrombus was observed, although complete resolution had not occurred. By day 72, D-dimer levels had normalized, but the thrombus persisted.

Given the declining retrieval success of IVC filters beyond 9 weeks and the risks associated with prolonged filter placement, anticoagulation was switched to dabigatran (150 mg twice daily). Subsequent APTT prolongation was observed, and CT on day 93 showed resolution of the pulmonary artery thrombi with marked regression of the IVC thrombus. Complete thrombus resolution was confirmed on day 121 (**Figure 2**), enabling

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Table 1. Laboratory data measured on admission.

WBC, $\times 10^2/\mu L$	67	hsTnI, pg/mL	89.3
Hemoglobin, g/dL	14.4	BNP, pg/mL	60.4
Platelets, $\times 10^4/\mu L$	14.7	APTT, s	26.8
AST, IU/L	35	PT-INR	0.96
ALT, IU/L	20	Fibrinogen, mg/dL	320
LDH, IU/L	252	Antithrombin-III,%	76
T.Bil, mg/dL	0.6	PC activity,%	101
CK, IU/L	35	PS activity,%	72
BUN, mg/dL	12.7	LA (Russell's viper venom time)	1.1 (negative)
Creatinine, mg/dL	0.83	Anti-CLβ2GPI antibody, U/mL	1.2 (negative)
eGFR, mL/min/1.73 m^2	58.6	Anti-β2 GPI IgG antibody, U/mL	0.7 (negative)
hsCRP, mg/dL	4.9	Anticardiolipin IgG antibody, U/m	4.0 (negative)
		Antinuclear antibody	<1: 40 (negative)

β2 GPI, beta-2 glycoprotein 1; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CK, creatine kinase; CLβ2GPI, cardiolipin-beta2 glycoprotein 1 complex; eGFR, estimated glomerular filtration rate; hsCRP, high sensitivity c-reactive protein; IgG, immunoglobulin G; hsTnI, high-sensitivity troponin I; LA, lupus anticoagulant; LDH, lactate dehydrogenase; PC, protein c; PS, protein s; PT-INR, prothrombin time-international normalized ratio; T.Bil, total bilirubin; WBC, white blood cells.

successful IVC filter retrieval on day 126. No bleeding complications occurred, and no recurrence of venous thromboembolism has been observed.

Discussion

Floating IVC thrombi pose a substantial risk of massive pulmonary embolism, and prophylactic IVC filter placement is commonly performed. However, failure of thrombus resolution may preclude filter retrieval, exposing patients to long-term complications associated with permanent filter placement [3]. Early thrombus reduction is therefore a key therapeutic goal.

CDT allows local delivery of thrombolytic agents directly to the thrombus and has been shown to reduce thrombus burden in iliofemoral DVT, with potential benefits in preventing post-thrombotic syndrome [4]. Its use in IVC thrombosis remains less well established but may be considered in select patients with low bleeding risk. Furthermore, Gong et al reported that, in patients with subacute proximal venous thrombosis, CDT with alteplase achieved successful thrombus lysis earlier than regimens using urokinase [5]. Regarding dosing, continuous alteplase infusion at 0.01 mg/kg/h, with a maximum total dose of 24 mg over 24 hours, has been reported, and this regimen was referenced in the present case [1]. In the present case, alteplase-based CDT resulted in rapid biochemical and radiological evidence of thrombus lysis, as reflected by a marked transient increase in D-dimer levels. Previous studies have suggested that substantial D-dimer elevation following thrombolysis indicates effective fibrin degradation [7]. Despite initial improvement, complete thrombus resolution was not achieved with factor Xa inhibitor therapy. Dabigatran (a direct thrombin inhibitor) has been shown to be at least equal in efficacy to warfarin for venous thromboembolism treatment [6]. Reports have described successful thrombus resolution after switching from Xa inhibitors to dabigatran in patients with recurrent thromboembolic events [8,9]. In this case, APTT prolongation following dabigatran initiation suggested enhanced thrombin inhibition, which may have contributed to the complete thrombus resolution in our patient [10].

Conclusions

In patients with pulmonary embolism complicated by a large floating IVC thrombus refractory to standard anticoagulation, CDT using alteplase may facilitate early thrombus reduction. Additionally, switching from a factor Xa inhibitor to a direct thrombin inhibitor in the subacute phase may constitute an effective treatment strategy when thrombus resolution is insufficient, potentially enabling timely IVC filter retrieval.

Institution Where Work Was Done

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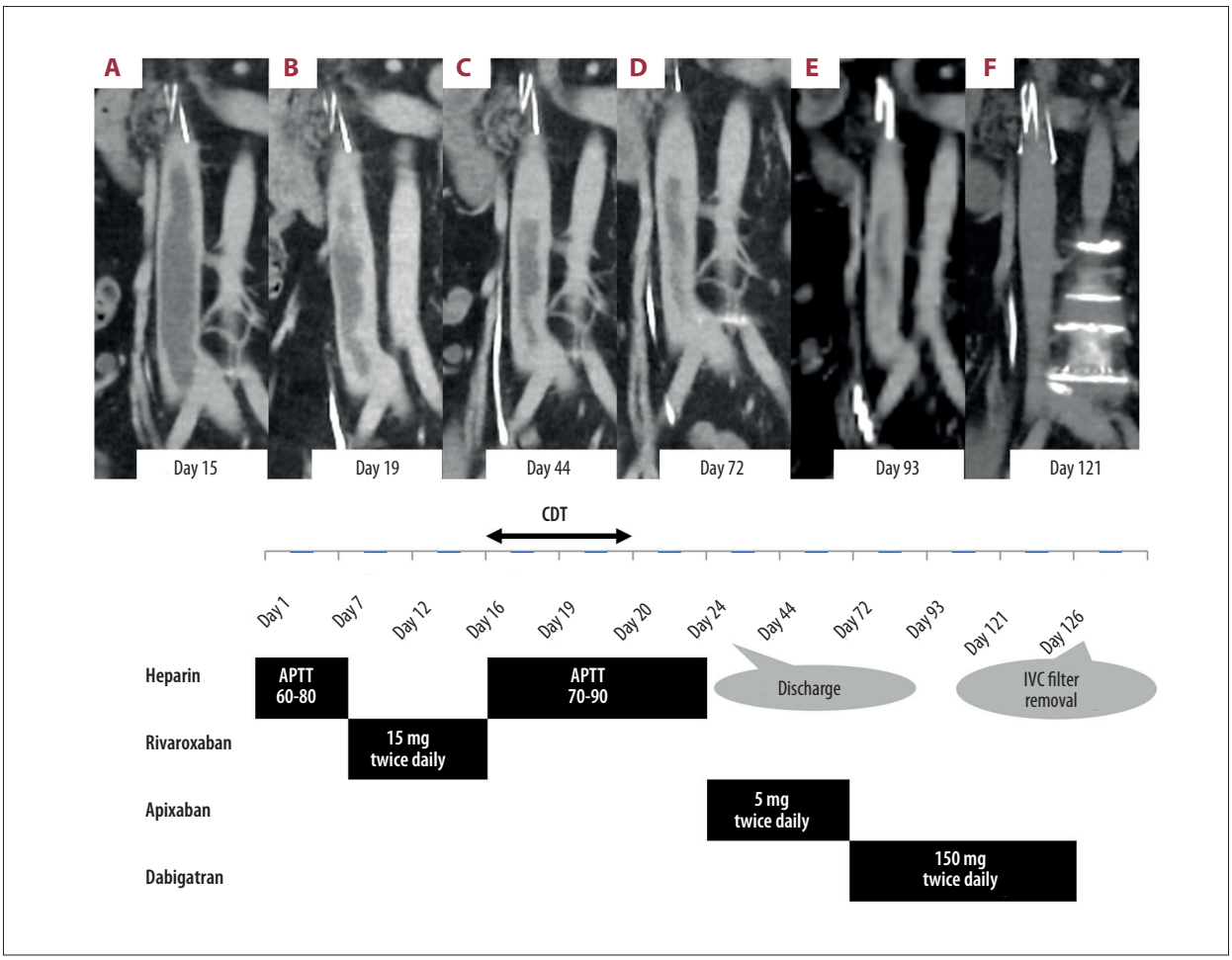

Figure 2. Clinical course during hospitalization. The IVC thrombus showed minimal regression (**A**). CDT was initiated on day 16, consisting of a 2-mg local bolus of alteplase followed by continuous infusion at 0.5 mg/h for 17 h in combination with unfractionated heparin (400 U/h). After completion of alteplase therapy, the unfractionated heparin dose was increased via the pulse-spray catheter, with continuous infusion (days 16-20). Follow-up contrast-enhanced computed tomography demonstrated regression of the IVC thrombus (**B**). Although oral apixaban was continued after discharge, the IVC thrombus did not resolve (**C, D**). After switching to dabigatran on day 72, further thrombus regression was observed (**E**), with complete resolution confirmed on day 121 (**F**), followed by successful retrieval of the IVC filter. APTT, activated partial thromboplastin time; CDT, catheter-directed thrombolysis; IVC, inferior vena cava.

Statement of Patient Consent

Written informed consent was obtained from the patient and patient's family for publication of this case report.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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