Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Transjugular ultrasound-assisted catheter direct fibrinolysis (EKOS) for relapsed IVC filter thrombosis and phlegmasia cerulea dolens ☆

Arturo Silvio Alaimo, MD[a,*], *Maria Giovanna Di Niso, MD*[a], *Naomi Ciccone, MD*[a], *Antonio Mauro D'Agostino, MD*[b], *Riccardo Corti, MD*[b], *Nicola Cionfoli, MD*[b], *Alessio Consonni, MD*[a], *Pietro Quaretti, MD*[b]

[a] *Department of Radiodiagnostic, IRCCS Policlinico San Matteo of Pavia, University Pavia, Pavia 27100, Italy*
[b] *Interventional Radiology Unit, IRCCS Policlinico San Matteo of Pavia, Pavia 27100, Italy*

ARTICLE INFO

Article history:
Received 29 May 2024
Revised 10 September 2024
Accepted 12 September 2024
Available online 4 October 2024

Keywords:
Inferior vena cava filter
Thrombosis
Phlegmasia cerulea dolens
Inferior vena cava
EKOS
Deep vein thrombosis

ABSTRACT

Phlegmasia cerulea dolens (PCD) is a devastating presentation of deep venous thrombosis (DVT), that may cause venous gangrene, amputation, and death.

A 69-year old male presented with PCD in the lower limbs. Ultrasound (US) and CT-angiogram revealed lower extremities DVT cranially extended to iliac veins and inferior vena cava (IVC) involving an infrarenal IVC filter. In his history, there was 10 years earlier his first occurrence of filter-related PCD, which did require surgical thrombectomy. Currently, we gained access to IVC-filter thrombus from left internal jugular vein and easily placed an EKOS catheter in right femoral vein. Then we started the US-assisted fibrinolysis (EKOS) with low-dose r-TPA. Immediate overnight clinical improvement occurred and a postprocedure venography at 48 hours confirmed complete recanalization.

We report the present case upon PCD to remark 2 unique features. First, we used successfully EKOS by transjugular route for PCD. EKOS combines the effectiveness of low dose r-TPA catheter direct thrombolysis (CDT) with the ultrasound's technology. The descending transjugular approach, previously unreported in this clinical setting, can reduce operative time, invasiveness and risk of filter's displacement in comparison with other thrombectomy devices used via popliteal or femoral approach. Second, we verified for the first time to the best of our knowledge the relapse of PCD in a very long time span (a decade) in the same patient underscoring the significance of vena cava filter as a powerful and persistent risk factor for IVC-thrombosis.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: arturoalaimo20@gmail.com (A.S. Alaimo).

https://doi.org/10.1016/j.radcr.2024.09.058

Introduction

Venous thromboembolism (VTE), which includes DVT, pulmonary embolism, or both, is considered the most common preventable cause of death in hospitals and can lead to significant long-term morbidity [1]. Its incidence can be as high as 1 in 100 in high-risk populations [2]. In cases where anticoagulation therapy is contraindicated, ineffective, or causes complications, the insertion of an IVC filter is considered the primary treatment option for managing VTE.

However, the use of IVC filters has been found to be strongly associated with IVC thrombosis (IVCT), with an estimated incidence of approximately 13% after 8 years of follow-up [3]. Various factors, such as the type of filter used, hypercoagulable conditions, dwell time, and strategies for anticoagulation therapy [4], can contribute to IVCT. To address this issue, retrievable (optional) IVC filters have become increasingly popular, resulting in a significant growing in the rate of IVC filter placements. While the possibility to retrieve these filters has reduced the risk of late complications and raised the rationale for optional filters deployment, the rates of retrieval remain relatively low [2].

The clinical significance of IVCT depends on the rate of IVC patency loss and the development of collateral networks, which can sometimes lead to a rare but potentially life-threatening condition called PCD [5].

There is no consensus or clinical guidelines for treatment of PCD. Its clinical characters may require urgent surgical thrombectomy or fasciotomy while the IVC filter and its related risks of procedural displacement may jeopardize endovascular therapies and the use of large bore thromboaspiration systems via popliteal or femoral approach. We report a patient who suffered for a relapsed PCD without any clear triggering factor, except for being a long-term carrier of an IVC filter. The PCD was straightforwardly resolved with US-assisted catheter fibrinolysis inserted through a jugular route.

Fig. 1 – Contrast-enhanced CT of the abdomen and pelvis showed bilateral lower extremity DVT with extensive thrombosis spreading from the common iliac veins, up to a few millimeters above the IVC-filter (coronal view).

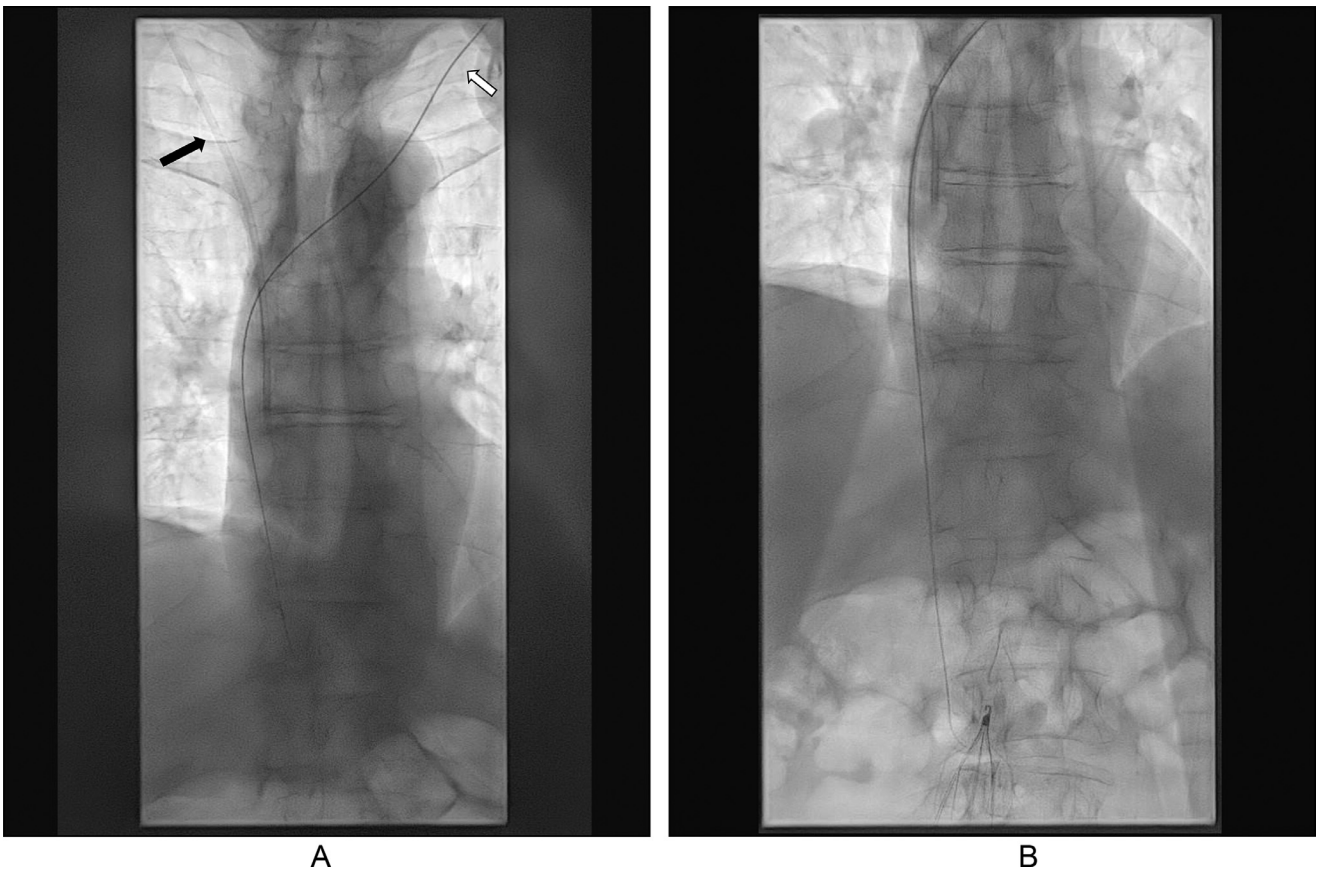

Fig. 2 – (A) Digital fluoroscopy (PA projection). White arrow: guide wire before sheath placement on the left side. Black arrow: central venous catheter on the right side. (B) IVC filter crossing with stiff guidewire (PA projection on fluoroscopy).

Case presentation

A 69-year old male patient presented to the emergency department on January 12, 2023 with acute legs' pain, which increased when the anterior compartment was passively stretched and foot drop was observed. There was severe edema and tenderness in the limbs, which were cold, numb, and weak, with absent pulses in the femoral, popliteal, posterior tibial, and dorsalis pedis arteries. An ultrasound and computed tomographic angiogram revealed bilateral lower extremity DVT with extensive thrombosis spreading from the common iliac veins to the popliteal veins, originating just above the inferior vena cava filter (February 10, 2013), with millimeter involvement of the left renal vein (Fig. 1).

Based on persistent resting pain, decreased sensory and motor function, and increased leg circumference upon physical examination, diagnosis of PCD was made. Serial samples for CPK titration showed an increase from 10,715 to 14,653 mU/mL. Repeated administration of Fentanyl vial was ineffective.

Ten years earlier, the patient was hospitalized for polytrauma following a car accident. A few days after that hospitalization, a massive pulmonary embolism, treated by rheolytic thrombectomy, along with DVT detection in the left popliteal vein, led to insert a removable IVC filter (DENALI, BARD, February 10, 2013) prior to surgical repair of post traumatic laceration of the right diaphragmatic pillar. Two weeks later, while still in the orthopedics department to treat multiple fractures, the patient experienced symptoms for the first time of PCD and IVC- filter thrombosis. Diagnosis of bilateral DVT with obstruction of the vena cava filter and the development of compartment syndrome (CPK values 27,900 mU/mL, normal range 24-190) was made. Systemic fibrinolytic therapy option was ruled out due to recent trauma and abdominal surgery. Emergent bilateral transverse phlebotomy of the common femoral veins had been made to remove thrombus from the external iliac vein and superficial femoral vein. A coagulation profile test for mutations in factors II, V, and anti-PF4 was negative, while an increased homocysteinemia value was found (29.1 mcmol/L, normal range 5-13.9). The patient was discharged on therapy with Coumadin 5mg/day. The patient discontinued anticoagulation therapy 3 years later due to severe gastric bleeding. Ulcerated gastrointestinal stromal tumor (GIST) was found at esophagogastroduodenoscopy. Gastric GIST causes symptoms secondary to obstruction or hemorrhage; tumor growth outward the overlying gastric mucosa may explain gastrointestinal ulceration and bleeding. After surgical resection of GIST, the patient did not resume anticoagulation therapy. Since then until now, the patient had continued prophylactic therapy with ASA 100 mg/day.

Currently, the patient was brought to angiography suite to execute ultrasound assisted catheter direct fibrinolysis (US-

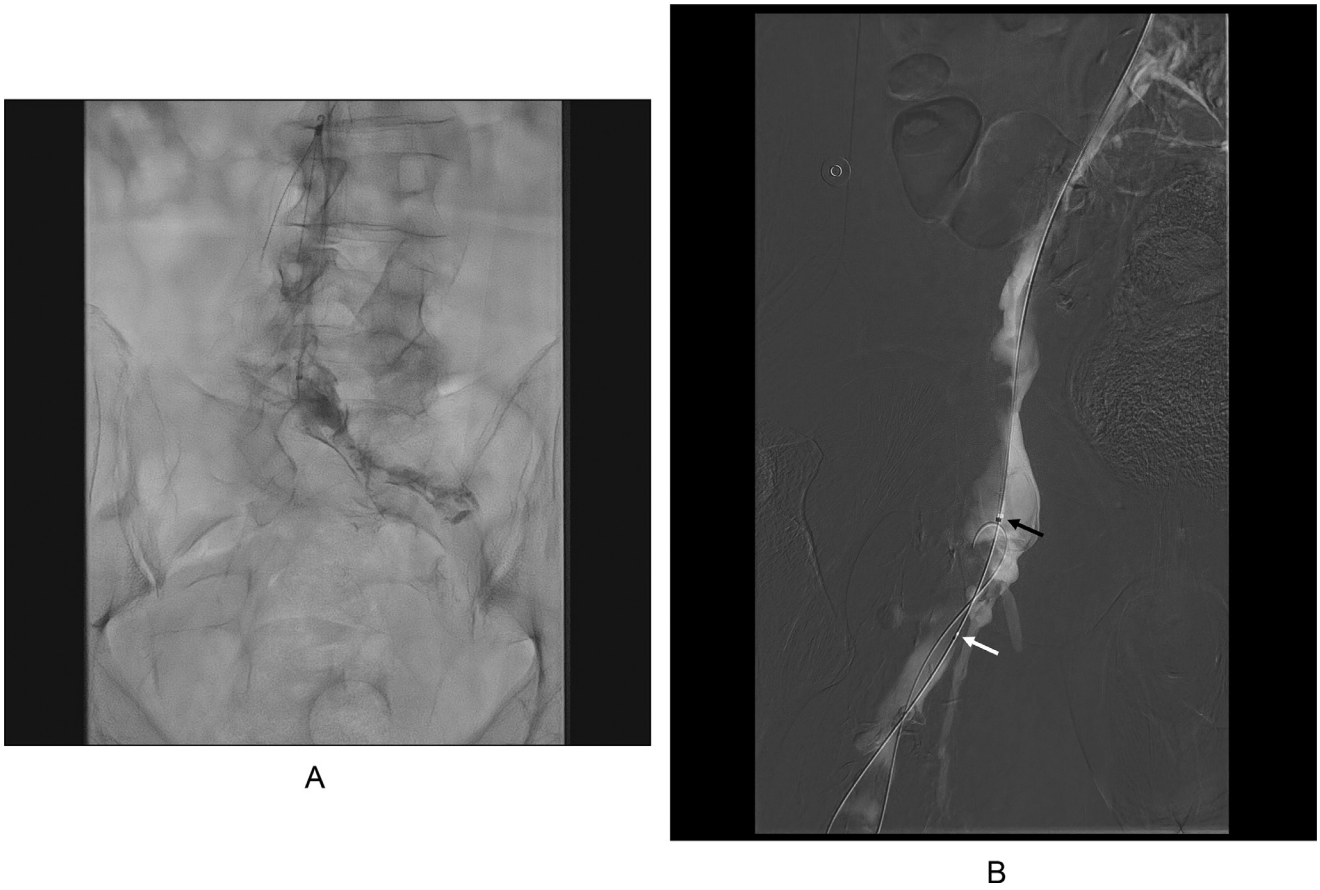

Fig. 3 – (A) Descending venography through the IVC. (Fluoroscopy digital spot) Thrombus is completely occluding the femoral-iliac vein axis up to IVC filter. (B) Descending venography on PA projection through the IVC filter. Distal tip of catheter (Black arrow) placed in right common femoral vein. White Arrow points a marker on the guidewire.

ACDF). We choose the left jugular vein approach because on the right side there was placed a central venous catheter. Under ultrasound guidance, a 6Fr sheath was placed in the left jugular vein (Figs. 2A and B) and descending venography through the IVC filter was carried out, revealing a thrombus completely occluding the popliteal veins bilaterally, extending proximally up to the femoral-iliac veins and IVC filter (Figs. 3A and B).

USACDF started by inserting a 5Fr 106 cm long EKOS catheter (EkoSonic® Endovascular System; Washington, USA). The 18 cm long PROBE was positioned in correspondence of the thrombosis, followed by r-TPA infusion. A continuous infusion of r-TPA (20 mg of r-TPA in 1000 mL of normal saline solution at 75 mL/hour, 1.5 mg of r-TPA per hour for 10 hours, then reduced to 40 mL/hour, 0.8 mg per hour) was started. Simultaneously, normal saline solution was continuously infused (at 30 mL/hour) through the central lumen of the catheter to dissipate heat generated by the ultrasound energy (Fig. 4).

The patient was transferred to the intensive care unit (ICU) for monitoring. Overnight, the patient experienced progressive improvement of symptoms, with restoration of limb color, temperature, strength, sensitivity, and pulses. The patient was closely monitored in the ICU for any signs or symptoms of complications, such as pulmonary embolism or bleeding. Blood samples were taken every 12 hours to monitor hematocrit levels, hemoglobin levels, partial thromboplastin time, fibrinogen levels, and platelet counts. A postprocedure venography at 48 hours, prior to removing the introducer, confirmed complete recanalization without any complications (Figs. 5-7).

Finally, the patient was transferred to the vascular surgery ward. He was offered the option to remove the filter, but after we explained the risks bound to removal of a long time dwelling IVC filter, such as vena cava laceration and hemorrhagic shock, he refused.

Discussion

PCD is a rare and potentially devastating presentation of extensive DVT, often involving the iliac-femoral veins and inferior vena cava. This medical condition requires urgent management due to its significant association with morbidity and mortality (25%-40%) [6]. The most serious complication of PCD is pulmonary embolism, which has a mortality rate of 50% [7] and an incidence between 12 and 40%. Additionally, PCD can lead to secondary compartment syndrome, necessitating fasciotomy, and in cases where thrombosis affects capillaries and

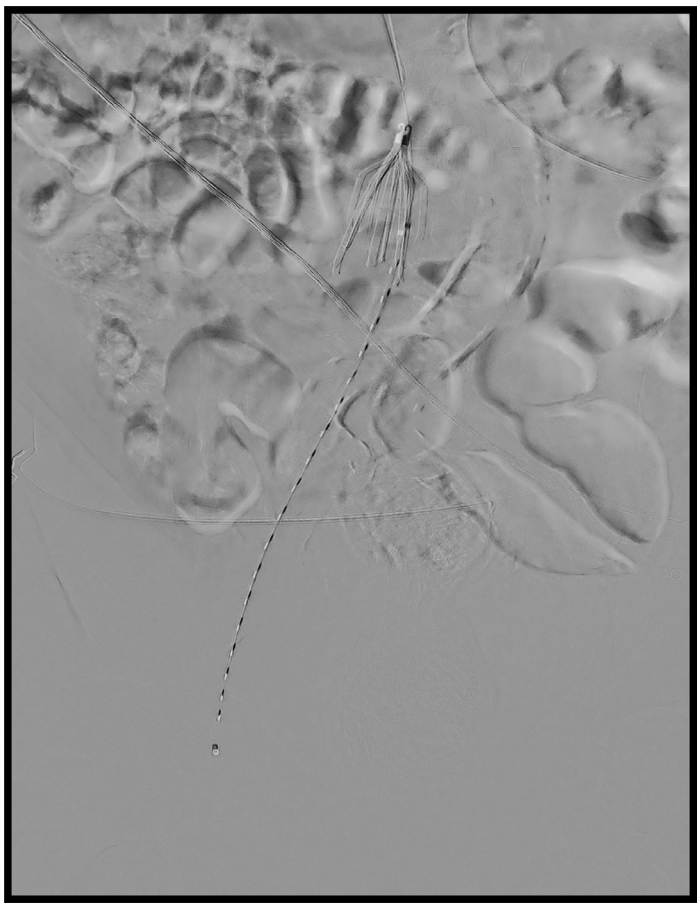

Fig. 4 – PA projection of digital venography. The 18 cm long PROBE (1marker /cm) was positioned in correspondence of iliac thrombosis through IVC-filter.

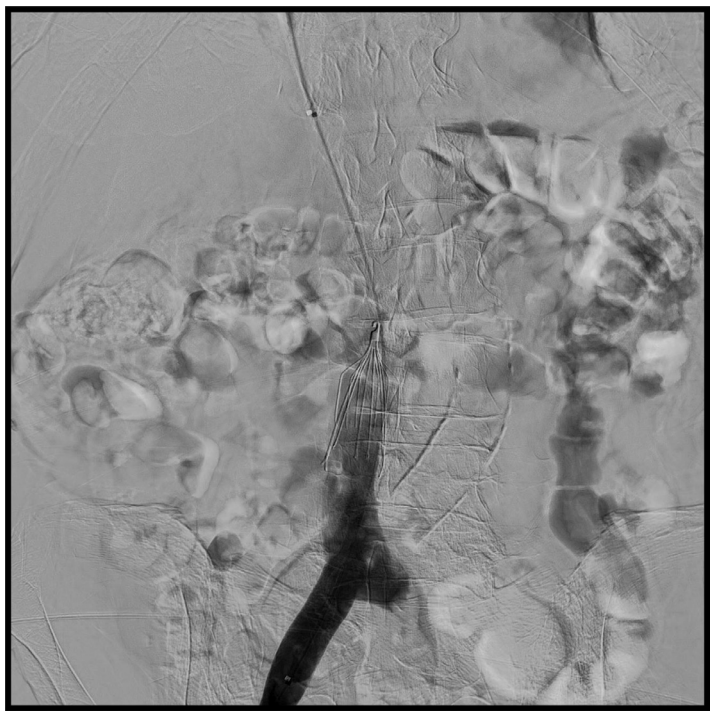

Fig. 5 – Postprocedure venography confirmed complete recanalization (PA projection).

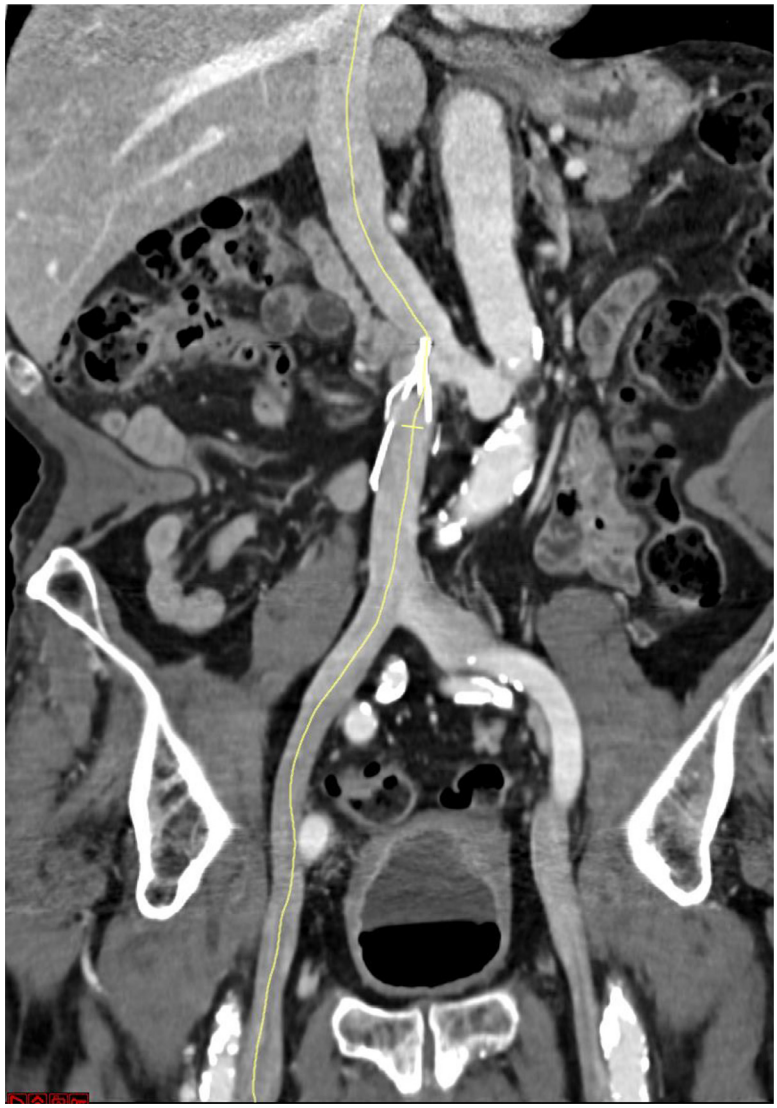

Fig. 6 – Contrast-enhanced CT of the abdomen (coronal view). Complete recanalization of thrombosis.

causes irreversible tissue ischemia and venous gangrene, amputation may be required (22%-68% of cases) [8].

Some of the most important risk factors for PCD include malignancy, immobilization, oral contraceptive use, May Turner syndrome, recent major surgery, or trauma [9]. PCD has been rarely associated with vena cava filters thrombosis [10]. In our case report, the patient developed his first manifestation of PCD requiring surgical thrombectomy 17 days after the placement of a vena cava filter, likely due to a combination of risk factors such as contraindication to anticoagulation, immobilization, recent severe polytrauma, and major surgery. The patient discontinued anticoagulant drugs for the last 7 years. At the time of the second occurrence of PCD, the patient did not have any known risk factors. Approximately 10%-16% of patients with PCD do not have identifiable risk factors [11]. While rare, there have been a few reported cases of PCD in patients with chronic indwelling IVC filters in the absence of apparent triggering factors [12].

A comprehensive list of contraindications to the use of anticoagulant drugs is beyond the scope of our case report. However, when there are no contraindications and the original indication for filter placement is no longer clinically relevant, retrievable filters should be removed according to the 2010 FDA safety recommendations [13]. Furthermore, emerging literature also supports the removal of chronic indwelling IVC filters when they are no longer necessary [14–16]. In fact, IVC filters inherently increase the risk of DVT due to their composition, design, and dwell time of placement [17,18]. IVC filter thrombosis occur in 2%-30% of patients [16,19,20], with only 13% of cases being symptomatic, as observed in our presented case according to the PRECIP study . The incidence of filter thrombosis, even in the absence of symptoms, justifies the recommendation to remove vena cava filters when they are no longer needed.

PCD poses a significant therapeutic challenge as management decisions are still evolving, and there are no estab-

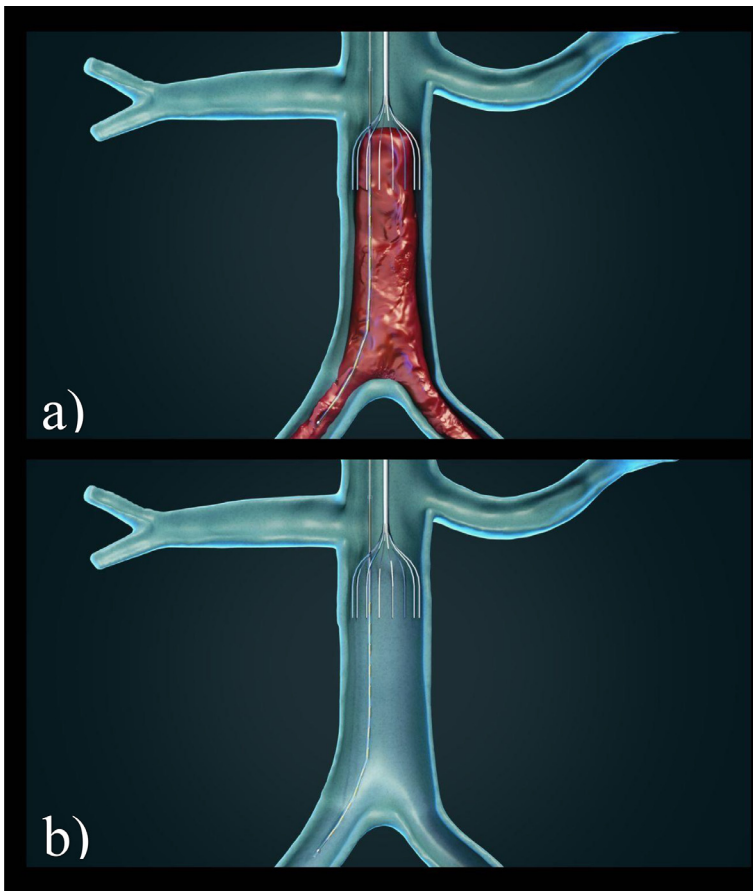

Fig. 7 – Schematic illustration pre- and postprocedure. (A) EkoSonic® Endovascular System positioned through the thrombus. (B) After UACDF and complete recanalization.

lished guidelines to follow. However, it is widely accepted that medical management alone is insufficient. The goal is to remove the thrombus as soon as possible, primarily through minimally invasive endovascular interventions such as CDT, pharmaco-mechanical catheter-directed thrombolysis, or percutaneous thrombectomy using mechanical or aspiration techniques [21]. CDT has become the standard of care in the treatment of proximal DVT. In our case, we used transjugular CDT with EKOS, which combines the effectiveness of CDT with the powerful technology of EKOS. The use of alteplase, a recombinant tissue plasminogen activator, is common in CDT to degrade fibrin complexes within the thrombus [22]. EKOS is an ultrasound-accelerated catheter system that enhances thrombolysis and accelerates recovery [23]. In our patient CDT enhanced by ultrasound successfully restored blood flow and resolved the massive thrombosis and its symptoms within 48 hours without hemorrhagic complications. EKOS has already been proposed for IVC-filter related thrombosis but always by ascending way with bilateral popliteal access [24], such as for mechanical thrombectomy systems [10,24,26].

Table 1 shows treatment modalities and relative outcomes achieved from 2008 to date in patients with PCD. It is noteworthy that 2 patients with IVC-filter thrombosis not treated by EKOS died [10,28] while all patients [27,29,24], and present patient, treated by EKOS had improved outcome. Instead, even if large CAVA trial failed to show significant reduction of PTS after USACDF in comparison to standard therapy in patients with iliac-femoral thrombosis, a significant reduction in symptom severity expressed by Villalta score and PTS reduction in >50% of patients with successful fibrinolysis, occurred [25] (Table 1).

The transjugular route we chose, previously unreported, may offer unique and simplified access. Due to the low profile of the introducer, the trans-filter single passage of the device was faster and straightforward reducing the risk of filter dislocation and tilting in comparison with time-consuming and potentially dangerous maneuvers needed with manual or assisted thrombectomy devices. Further, the planned reduction of scheduled r-TPA infusion, likely in ULTIMA trial [26], may have reduced the possibility of hemorrhagic complications. This management may represent an effective treatment method with high clinical success for IVC filter's thrombosis PCD-related.

In conclusion, IVC-filter thrombosis causing PCD is a challenging condition to manage, and there are no established guidelines for its treatment. Prompt removal of the thrombus is crucial, and minimally invasive endovascular interventions, such as CDT with EKOS, may offer promising results. The use of inferior vena cava filters should be carefully evaluated before insertion, and removal when they are no longer necessary

Table 1 – Treatments of PCD and clinical results.

	PCD	IVC Filter	Treatment	EKOS	Result
Shem et al. [10]	1 patient	+	MTA and r-TPA	No	Death
Oguzkurt et al. [27]	7 patients	+ 3/7	MTA 7/7 CDT 2/7	No	1 limb amputation
Khan et al. [28]	1 patient	-	Reolitic thrombectomy and r-TPA	Yes (Both arterial and venuos)	Discharged with AC
Bagenal et al. [29]	1 patient	+	-	No	Death
Salam et al. [30]	1 patient	+	r-TPA	Yes (popliteal bilateral)	Discharged with AC
ELsaid et al. [31]	1 patient	-	Fasciotomy and CDT	No	Discharged with AC
Maruthi et al. [24]	1 patient	+	MTA and CDT	Yes (popliteal)	Patency and no PTS
Taniguchi et al. [32]	1 patient	+	Fasciotomy	No	Discharged with AC
Present study	1 patient	+	r-TPA	Yes (transjugular)	Patency and no PTS

AC, Anti-coagulant therapy; CDT, catheter direct thrombolysis (without US assistance); MTA, mechanical thrombo aspiration; PTS, post thrombotic syndrome.

should be recommended to reduce the risk of complications, as IVC thrombosis may relapse after a long time. Further research and clinical experience are necessary to establish standardized management protocols for PCD.

Patient consent

The patient has consented to his medical course being used for a case report and educational purposes.

REFERENCES

[1] SHull RD, Raskob GE, Hirsh J. Prophylaxis of venous thromboembolism. An overview. Chest 1986;89:374S–383S.

[2] Heit JA. Venous thromboembolism epidemiology: implications for prevention and management. Semin Thromb Hemost [Internet] 2002;28(Suppl 2):3–13 Available from:. doi:10.1055/s-2002-32312.

[3] Greenfield LJThe PREPIC Study Group. Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) Randomized Study. Perspect Vasc Surg Endovasc Ther [Internet] 2006;18(2):187–8 Available from:. doi:10.1177/1531003506290863.

[4] W Shi, W Lou. In: X He, C Liu The management of filter-related caval thrombosis complicated by heparin-induced thrombocytopenia and thrombosis.

[5] Wongsakorn C, Osaree A Cerulea dolens with compartment syndrome.

[6] Jensen J, Ladner J, Mann R, Kitley C. Successful thrombectomy and thrombolysis of deep vein thrombosis in a patient with acute phlegmasia cerulea dolens with May-Thurner anatomy. Radiol Case Rep [Internet] 2021;16(3):631–7 Available from:. doi:10.1016/j.radcr.2020.12.035.

[7] Chinsakchai K, ten Duis K, Moll FL, de Borst GJ. Trends in management of phlegmasia cerulea dolens. Vasc Endovascular Surg [Internet] 2011;45(1):5–14 Available from:. doi:10.1177/1538574410388309.

[8] Perkins JM, Magee TR, Galland RB. Phlegmasia caerulea dolens and venous gangrene. Br J Surg [Internet] 1996;83(1):19–23 Available from:. doi:10.1002/bjs.1800830106.

[9] Feinman LJ, Meltzer AJ. Phlegmasia cerulea dolens as a complication of percutaneous insertion of a vena caval filter. J Am Osteopath Assoc [Internet] 1989;89(1):63–8 Available from:. doi:10.1515/jom-1989-890111.

[10] Shem K. Phlegmasia cerulea dolens: rare complication of vena cava filter placement in man with paraplegia. J Spinal Cord Med [Internet] 2008;31(4):398–402 Available from:. doi:10.1080/10790268.2008.11760743.

[11] Sequeira Gross HG, Jimenez Y, Ciobanu C, Tarekegn K, Colon Ramos A, Lazar J. Phlegmasia cerulea dolens: a new perspective on management. Cureus [Internet] 2021:e16257 Available from. doi:10.7759/cureus.16257.

[12] Kiefer CS, Colletti JE. Phlegmasia cerulea dolens in a patient with an inferior vena cava filter. J Emerg Med [Internet] 2013;44(1):e95–7 Available from:. doi:10.1016/j.jemermed.2012.01.018.

[13] US Food and Drug Administration. Removing retrievable inferior vena cava filters: initial communication. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm221676.htm. [accessed 01.06.13].

[14] Kaur S, Suri P, Bryan W, Kitley C. Laser-assisted permanent greenfield filter removal with ileocaval stent reconstruction following filter thrombosis, a case report. Radiol Case Rep [Internet] 2023;18(12):4449–57 Available from:. doi:10.1016/j.radcr.2023.09.043.

[15] Tamrazi A, Wadhwa V, Holly B, Bhagat N, Marx JK, Streiff M, et al. Percutaneous retrieval of permanent inferior vena cava filters. Cardiovasc Radiol [Internet] 2016;39(4):538–46 Available from:. doi:10.1007/s00270-015-1214-0.

[16] Grewal S, Chamarthy MR, Kalva SP . Complications of inferior vena cava filters. Cardiovasc Diagn Ther [Internet] 2016;6(6):632–41 Available from:. doi:10.21037/cdt.2016.09.08.

[17] Angel LF, Tapson V, Galgon RE, Restrepo MI, Kaufman J. Systematic review of the use of retrievable inferior vena cava filters. J Vasc Interv Radiol [Internet] 2011;22(11):1522–1530.e3 Available from:. doi:10.1016/j.jvir.2011.08.024.

[18] Morrow KL, Bena J, Lyden SP, Parodi E, Smolock CJ. Factors predicting failure of retrieval of inferior vena cava filters. J Vasc Surg Venous Lymphat Disord [Internet] 2020;8(1):44–52 Available from:. doi:10.1016/j.jvsv.2019.07.010.

[19] Martin MJ, Blair KS, Curry TK, Singh N. Vena Cava filters: current concepts and controversies for the surgeon. Curr Probl Surg [Internet] 2010;47(7):524–618 Available from:. doi:10.1067/j.cpsurg.2010.03.004.

[20] Milovanovic L, Kennedy S, Midia M. Procedural and indwelling complications with inferior vena cava filters: frequency, etiology, and management. Semin Intervent

Radiol [Internet] 2015;32(01):034–41 Available from:. doi:10.1055/s-0034-1396962.
[21] Said A, Sahlieh A, Sayed L. A comparative analysis of the efficacy and safety of therapeutic interventions in phlegmasia cerulea dolens. Phlebology [Internet] 2021;36(5):392–400 Available from:. doi:10.1177/0268355520975581.
[22] Karnabatidis D, Spiliopoulos S, Tsetis D, Siablis D. Quality improvement guidelines for percutaneous catheter-directed intra-arterial thrombolysis and mechanical thrombectomy for acute lower-limb ischemia. Cardiovasc Radiol [Internet] 2011;34(6):1123–36 Available from:. doi:10.1007/s00270-011-0258-z.
[23] Owens C. Ultrasound-enhanced thrombolysis: EKOS EndoWave infusion catheter system. Semin Intervent Radiol [Internet] 2008;25(1):037–41 Available from:. doi:10.1055/s-2008-1052304.
[24] Maruthi R, Zlotshewer B, Singh M, Forfia P, Lakhter V, Bashir R. Bilateral phlegmasia cerulea dolens related to inferior vena cava filter thrombosis. J Am Coll Cardiol [Internet] 2022;79(9):2925 Available from:. doi:10.1016/s0735-1097(22)03916-x.
[25] Notten P, de Smet AAEA, Tick LW, van de Poel MHW, Wikkeling ORM, Vleming L-J, et al. CAVA (ultrasound-accelerated catheter-directed thrombolysis on preventing post-thrombotic syndrome) trial: long-term follow-up results. J Am Heart Assoc [Internet] 2021;10(11):4–8 Available from:. doi:10.1161/jaha.120.018973.
[26] ULTIMA: randomised, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism.
[27] Oguzkurt L, Ozkan U, Demirturk OS, Gur S. Endovascular treatment of phlegmasia cerulea dolens with impending venous gangrene: manual aspiration thrombectomy as the first-line thrombus removal method. Cardiovasc Radiol [Internet] 2011;34(6):1214–21 Available from:. doi:10.1007/s00270-010-0042-5.
[28] Khan IR, Reeves JG, Riesenman PJ, Kasirajan K. Simultaneous arterial and venous ultrasound-assisted thrombolysis for phlegmasia cerulea dolens. Ann Vasc Surg [Internet] 2011;25(5):696.e7–696.e10 Available from:. doi:10.1016/j.avsg.2011.02.005.
[29] Bagenal JD, Nasralla D. Bilateral phlegmasia cerulea dolens in an occluded inferior vena cava filter. BMJ Case Rep [Internet] 2013;2013(apr10 1):bcr2013009302 Available from:. doi:10.1136/bcr-2013-009302.
[30] Sana Salam, H Hashmi, David Toups, S Khan Phlegmasia Cerulea Dolens: A Complication of Filter Use in the Inferior Vena Cava, Successfully Treated With Ultrasound-Assisted, Catheter-Directed Thrombolysis.
[31] ELsaid AS, AlQattan AS, Elashaal E, AlSadery H, AlGhanmi I, Aldhafery BF. The ugly face of deep vein thrombosis: phlegmasia cerulea dolens—case report. Int J Surg Case Rep [Internet] 2019;59:107–10 Available from:. doi:10.1016/j.ijscr.2019.05.021.
[32] Taniguchi T, Matsui Y, Furukawa Y. Phlegmasia cerulea dolens with lower leg compartment syndrome. Eur Heart J [Internet]. 2023;44(27):2499 Available from:. doi:10.1093/eurheartj/ehad255.