

# Venous thrombectomy after failure of catheter-directed thrombolysis for the treatment of three cases of phlegmasia

Fábio Pais<sup>1</sup>, Anita Quintas<sup>1</sup>, Isabel Vieira<sup>1</sup>, Joana Catarino <sup>1</sup>, Ricardo Correia <sup>1</sup>, Rita Bento<sup>1</sup>, Rita Garcia <sup>1</sup>, Joana Cardoso <sup>1</sup>, Tiago Ribeiro<sup>1</sup>, Rita Ferreira<sup>1,2</sup>, Gonçalo Alves<sup>1</sup>, Frederico Bastos Gonçalves <sup>1,2</sup>, Maria Emília Ferreira<sup>1</sup>

<sup>1</sup>Angiology and Vascular Surgery Department, Hospital de Santa Marta, Centro Hospitalar Universitário Lisboa Central, Lisbon, Portugal <sup>2</sup>NOVA Medical School, Universidade NOVA de Lisboa, Portugal.

Received: September 1, 2020; Reviewed: December 20, 2021; Accepted: March 6, 2022

Presented at: Evento Online da SPACV em 2020

## ABSTRACT

**INTRODUCTION:** Phlegmasia cerulea (PC) is a severe form of deep vein thrombosis. In the setting of massive venous thrombosis and severe ischemia, catheter-directed thrombolysis (CDT) or thrombectomy is mandatory. We report three cases of women with PC managed with venous thrombectomy after failure of CDT.

## CASE REPORTS:

1: 20 years-old, with recent intake of oral contraceptive, referred with acute onset of limb swelling, pain and a cold left lower extremity associated with foot pallor, paresthesia and numbness. Doppler ultrasound revealed occlusive thrombosis of the entire deep venous system and the great saphenous vein (GSV). Anticoagulation (AC) and CDT were started. However due to increasing levels of transaminases, creatine kinase and myoglobin, CDT was stopped and venous thrombectomy was proposed. A retrievable inferior vena cava filter (IVC) was implanted and venous surgical thrombectomy. The completion venography showed a Cockett compression that was treated with stenting of the left iliac vein. Thrombophilia tests were positive for anticardiolipin antibodies and hyperhomocysteinemia. At 3-years follow-up, the patient is asymptomatic and under AC. The 3-year Doppler showed normal patency for the iliac stent and a mild femoropopliteal vein insufficiency.

2: 19 year-old, taking oral contraceptives, with acute onset of PCD with acute thrombus in the left iliac, femoral, popliteal veins. CDT was started at admittance but stopped after two days because of very low values of serum fibrinogen and persistence of occlusive thrombus in the iliac vein. A retrievable IVC filter was placed and the thrombus removed with surgical thrombectomy. Phlebography showed no significant residual thrombus and no signs of compression were present. At 1 month follow-up, the patient presented without leg edema or venous claudication symptoms. Thrombophilia testing is awaited.

3: 54 year-old who presented with low back pain, worsening left leg pain and swelling with a cyanosed and colder foot. At doppler ultrasound there were monophasic arterial flow in the left leg. After exclusion of arterial embolism, the first therapeutic approach was CDT, but it was also stopped due to very low fibrinogen levels and an ineffective thrombus lysis in venography controls. After implantation of a retrievable IVC, surgical thrombectomy via femoral vein was performed, with successful thrombus removal. Venography showed Cockett syndrome and a stent was implanted. At 6 months the patient remained without major symptoms, and Doppler confirmed stent patency with non residual obstruction or venous insufficiency.

**CONCLUSION:** Awareness and timely diagnosis of phlegmasia cerulea is necessary to ensure prompt intervention to prevent loss of limb. When CDT is not effective, surgical thrombectomy remains successfully alternative. Iliac venous stenting complement is also crucial to treat associated Cockett syndrome. Endovascular thrombectomy devices may be a reasonable alternative to surgical thrombectomy.

**Keywords:** venous thrombosis; deep venous thrombosis; phlegmasia cerulea; endovascular catheter-directed thrombolysis; Cockett syndrome; thrombectomy.

## Corresponding Author:

Fábio Pais | Tel.: 213594000 | fabiofpais@hotmail.com  
Angiology and Vascular Surgery Department, Hospital de Santa Marta, Centro Hospitalar  
Universitário Lisboa Central, Lisbon, Portugal  
Rua de Santa Marta 1169-024 Lisboa



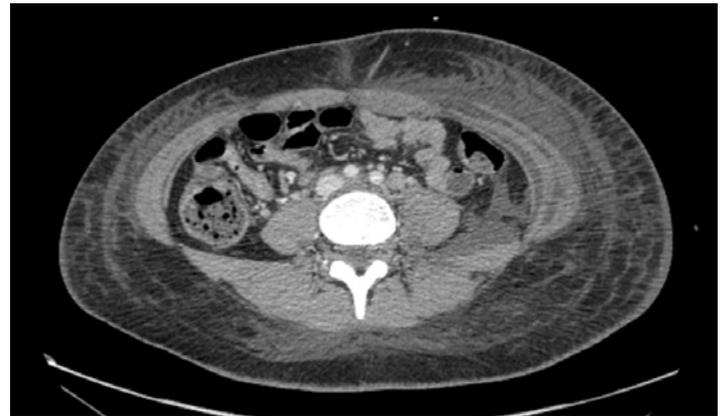
## INTRODUCTION

Extensive deep vein thrombosis (DVT) can lead to life- or limb-threatening diagnosis such as phlegmasia cerulea (PC). PC is an uncommon entity. Clinical signs include a sudden presentation of pain, edema and bluish discoloration of the extremity owing to a massive DVT that impedes venous outflow as a result of extreme venous hypertension and may result in venous gangrene, providing a low likelihood of limb viability.<sup>[1]</sup> The pathogenesis of PC is related to increased hypercoagulability, stasis and/or vascular wall injury, with malignancy as the most common risk factor.<sup>[2]</sup> The left lower extremity is more commonly involved.<sup>[2]</sup> Therapy involves anticoagulation but in cases of massive venous thrombosis presented as phlegmasia cerulea dolens, catheter-directed thrombolysis (CDT) is an additional therapeutic option which leads to thrombus lysis. Thrombectomy is the conventional surgery that allows thrombus removal but it has been associated to complications and was largely overcome with the emergence of endovascular techniques, namely CDT. However, in certain cases of CDT failure associated to limb threatening phlegmasia, thrombectomy is still an option that allows for rapid thrombus removal.<sup>[3,4]</sup>

## CASES PRESENTATIONS

**Case 1:** A 20 years-old woman, without past medical history, except the recent initiation of oral contraceptive pills, presented to the emergency department with acute onset of swelling and cyanosis of the entire limb, associated with pain, foot pallor, paresthesia and numbness. Doppler ultrasound revealed occlusive thrombosis of the left iliac and femoral veins and the great saphenous vein (GSV). Anticoagulation (AC) with unfractionated heparin was started followed by an endovascular approach with CDT: the popliteal vein was approached with ultrasound and a guidewire was advanced and the multiperforated catheter for thrombolysis was placed in the left common iliac vein. Initial venogram demonstrated extensive clotting of the popliteal and femoral venous systems extending into the iliac system. An endovascular catheter was placed in the left common iliac vein without any complication. She was admitted in a semi-intensive care unit to surveillance and due to increasing levels of transaminases, creatine kinase and myoglobin in blood tests associated to absence of clinical improvement, CDT was stopped after 72 hours. A computed tomography angiography (CTA) was performed with persistence of thrombus in the iliac, femoral and popliteal veins and signs of Cockett compression (figure 1). Venous thrombectomy was proposed.

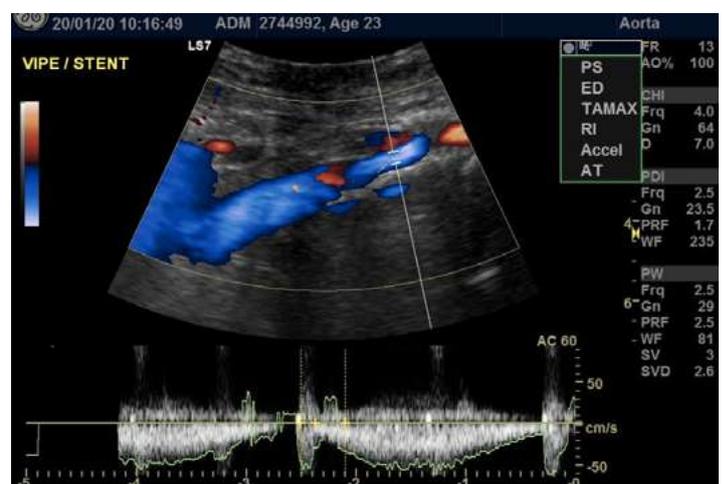
**Figure 1:** Diagnostic CTA – case 1.



CTA showing signs of Cockett compression in which the left common iliac vein is compressed when it passes between the right common iliac artery and the spine.

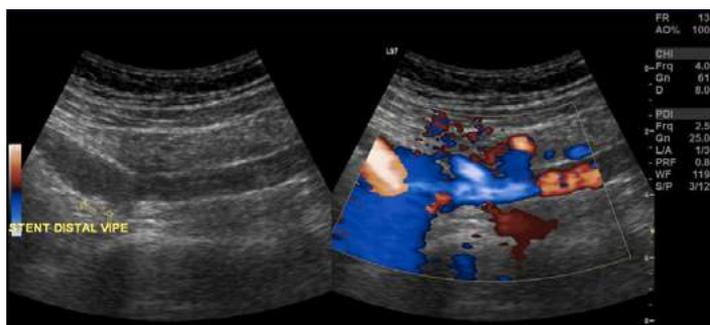
An inferior vena cava filter (IVC) was firstly implanted and venous surgical thrombectomy was performed through femoral vein cutdown using a 5F Fogarty catheter. Venography confirmed a Cockett compression that was treated with iliac vein stenting (Zilver Vena®). The final venogram revealed no obstruction in flow and no further intervention was performed. The postoperative course was uneventful, with clinic condition and blood tests' resolution. Further investigation revealed positive thrombophilia tests for anticardiolipin antibodies and hyperhomocysteinemia. At 3-years follow-up, the patient maintains asymptomatic under AC treatment in with rivaroxaban in therapeutic dose ad eternum. The 3-year Doppler ultrasound showed normal patency for the iliac stent (figure 2A and 2B) and a mild femoropopliteal vein insufficiency.

**Figure 2 A:** Doppler ultrasound performed 3 years after the surgical intervention.



Doppler ultrasound showing good patency of the iliac stent.

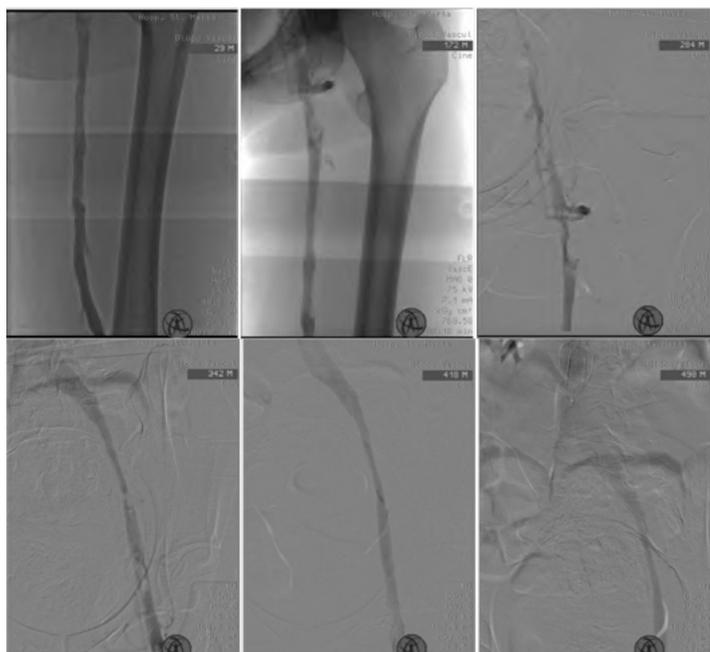
**Figure 2 B:** Doppler ultrasound performed 3 years after the surgical intervention.



Doppler ultrasound showing good patency of the iliac stent.

**Case 2:** A 19 year-old woman, with recent intake of oral contraceptives, presented with acute onset of left lower limb swelling, pain, pallor, poikilothermia and cyanosis. Doppler ultrasound revealed acute thrombus in the left iliac, femoral, popliteal veins and in the GSV. After starting heparin, CDT was planned. With local anesthesia and sedation, the popliteal vein was approached and a guidewire was advanced and the multiperforated catheter for thrombolysis was placed in the left common iliac vein, with the proximal extremity at the level of the 5th lumbar vertebra and the distal extremity below the inferior ischial ramus. CDT was stopped after two days due to very low values of serum fibrinogen, absence of clinical improvement and persistence of occlusive thrombus in the iliac vein (figure 3). A retrievable IVC filter was placed and the thrombus was removed with surgical thrombectomy using a 5F Fogarty catheter. Phlebography showed no significant residual thrombus and no signs of iliac vein compression were present (figure 3).

**Figure 3:** Left-lower-limb venography after 48-hours of catheter-directed thrombolysis.



The left lower extremity venogram demonstrates the persistence of thrombus in the iliac vein (top images and bottom left). After surgical thrombectomy, successful thrombus removal was achieved and no signs of Cockett compression were observed (bottom middle and right).

At 1-month of follow-up, the IVC filter was removed and the patient presented without leg edema or venous claudication symptoms. Thrombophilia testing is awaited and the patient is under rivaroxaban 20mg per day.

**Case 3:** A 54 year-old woman without know risk factors for venous thromboembolism, presented with low back pain, worsening left leg pain and swelling with a cyanosed and colder foot. At doppler ultrasound an occlusive thrombosis of the iliac, femoral and popliteal veins was found. After exclusion of arterial embolism, the first therapeutic approach was CDT. Approaching the small saphenous vein with puncture guided with ultrasound, a guidewire was advanced through the vein axis and the multiperforated catheter for thrombolysis was placed in left common iliac vein. Thrombolysis was also stopped due to very low fibrinogen levels and an ineffective thrombus lysis in venography controls after 11 hours. After implantation of a retrievable IVC through the right femoral vein, surgical thrombectomy via left femoral vein was performed using a 5F Fogarty catheter with successful thrombus removal. Venography showed left iliac vein stenosis compatible with Cockett syndrome and a stent was implanted, with resolution of the remaining obstruction in final venogram. In the postoperative, the patient had a hematoma in the right femoral access, that was managed with local compression and blood transfusion. At 5 months of follow-up, the patient underwent an endovascular procedure to remove the IVC, but without success. At 6 months of follow-up, the CTA showed the IVC, in infrarenal topography, with normal radiologic appearance and the patency of the iliac stent. Doppler ultrasound confirmed also stent patency and no residual obstruction or venous insufficiency were present. Thrombophilia testing was negative and the patient was referred her primary care unit to ruleout paraneoplastic syndrome. The patient is under anticoagulation with rivaroxaban 20mg per day.

## DISCUSSION

The authors report three cases of successful venous thrombectomy in PC after CDT failure.

This is a description of three cases of typical presentation of PC in young patients, admitted in our emergency department, with unknown risk factors for venous thromboembolism besides recent intake of oral contraceptives in two patients. However, further investigation revealed positive tests for thrombophilia in 1 patient yet. The diagnosis was made by clinical and ultrasound evaluation.

PC is a vascular emergency that requires early recognition and treatment to prevent venous gangrene of the extremity, limb amputation and even death. It is characterized by extensive thrombosis, often occurring in iliac-femoral type DVT with rapid disease progression and total venous outflow occlusion.<sup>[4]</sup> The complete pathophysiology is not fully understood, but with the complete obstruction of the venous returns (both the superficial and deep system), there is an increase of the limb venous pressure and of the interstitial tissue pressure, ultimately with arrest of the capillary flow, and arterial collapse under pressure, leading to an acute insufficiency in blood supply.<sup>[4]</sup> PC often occurs in the left lower extremity and can be induced by malignancy, hypercoagulable states, femoral vein catheterization and May-Turner Syndrome.<sup>[7]</sup>

The diagnosis of PC is based in the clinical signs of

sudden and massive leg edema, pain out of proportion and discoloration, followed by erythrocyanosis, sensorial and/or motor involvement and finally arterial impairment.<sup>[5]</sup> The first diagnostic modality for DVT is the venous ultrasound. However, as PC can involve iliac thrombosis, the computed tomography (CT) venography can be used as to better characterize the extent of the proximal thrombus.<sup>[9]</sup>

In these case reports, a decision to CDT was immediately made due to presence of limb threatening phlegmasia and absence of bleeding risk factors. Although evidence is scarcer, since CDT did not work and limb threatening maintained, a surgical thrombectomy was performed to allow a rapid thrombus removal and improvement of ischemic clinical presentation.

In PC, a faster course of action is required above anticoagulation alone to prevent venous gangrene and potentially death. According to the recent American College of Radiology Appropriateness Criteria of Radiologic Management of Iliofemoral venous thrombosis, in acute iliofemoral DVT and limb-threatening ischemia, depending on the state of the threatened limb, techniques for rapid thrombus resolution have included surgical thrombectomy, percutaneous mechanical thrombectomy and CDT. Because of the rare nature of the condition, there is no relevant literature comparing outcomes between medical, catheter-based, or surgical therapies with prospective randomized controlled trials.<sup>[10]</sup>

In recent years, endovascular techniques as CDT are safe and effective for the treatment of PC. Absolute contraindications include active internal bleeding, previous stroke, neurosurgical intervention and intracranial hemorrhage within three months. A limited number of reports have suggested that CDT can resolve the venous thrombosis, with a good preservation rate for most patients with PC, and therefore recommends as a first-line treatment.<sup>[11,12,13]</sup> However, CDT is a lengthy process and will increase the risk of bleeding. For these rapidly progressive PC cases, CDT may delay treatment, resulting in irreversible limb necrosis and therefore is not recommended. Therefore, thrombectomy may be an effective option for the treatment of PC.<sup>[14]</sup>

Venous thrombectomy provides rapid relief of venous hypertension and prevents further thrombus propagation. Nowadays in the operating room, the availability of the digital subtraction angiography, can greatly improve the success rates of thrombectomies, with the results of thrombectomies and the outflow assessed simultaneously, allowing treatment of iliac vein compression with stent placement, improving clinical efficacy of the procedure.<sup>[15,16]</sup>

In all cases described above, an IVC filter was placed to prevent pulmonary embolism due to thrombus migration with thrombectomy. Thrombus in the iliac vein was removed by Fogarty catheterization and a control venography was performed in all cases. In two of the cases, after the thrombus removal, stent implantation was performed simultaneously to relieve iliac vein occlusion, thereby treating the cause of the disease - the Cockett syndrome. With the venous flow restored, the severity of swelling did relieve greatly. Thereby, after failure of CDT, and in the absence of other adjuvant endovascular technologies for thrombus removal (mechanical or pharmacomechanical) surgical thrombectomy via femoral vein combined with endovascular treatment can be an option, allowing a rapid removal of the thrombus and resolving the iliac vein compression, when present. Another clinical report had similar results, stating that it allows a quickly improvement

of the venous outflow with less bleeding, shorter hospital stays, a low recurrence of thrombosis and a low incidence of long-term post-thrombotic syndrome.<sup>[10]</sup>

## CONCLUSION

Awareness and timely diagnosis of phlegmasia cerulea is necessary to ensure prompt intervention to prevent loss of the limb. These three cases demonstrate acute iliofemoral DVT and limb-threatening ischemia, in which surgical thrombectomy, after failure of CDT, rapidly removed the thrombus, improved the venous outflow and improved the limb preservation rate. Iliac venous stenting complement is also crucial to treat associated Cockett syndrome when present. Although the use of an endovascular technique for the treatment of phlegmasia cerulea has been frequently reported in recent years as first line therapy, when it does not work, surgical thrombectomy combined with stent implantation seems to be an effective and safe method for phlegmasia cerulea.

**Acknowledgements** None

**Conflicts of interest** None

**Funding** None

## REFERENCES

1. Vysetti S, Shinde S, Chaudhry S, et. al.: Phlegmasia cerulea dolens—a rare, life-threatening condition. *Sci World J* 2009;9:1105-6.
2. Chaochankit W, Akaraborworn O: Phlegmasia cerulea dolens with compartment syndrome. *Ann Vasc Dis* 2018;11:355-7.
3. Yang SS, Yang SS, Yun WS: Surgical thrombectomy for phlegmasia cerulea dolens. *Vasc Specialist Int* 2016;32:201-4.
4. ACR Appropriateness Criteria Radiologic Management of Iliofemoral Venous Thrombosis. *J Am Coll Radio* 2020;17;5:S255-64.
5. Klok F.A., Huisman M.V.: Seeking optimal treatment for phlegmasia cerulea dolens. *Thromb Res* 2013;131:372-3.
6. Chinsakchai K., Ten Duis K., Moll F.L., et. al.: Trends in management of phlegmasia cerulea dolens. *Vasc Endovascular Surg* 2011;45:5-14.
7. Veltchev LM, Kalniev MA, Todorov TA: Phlegmasia cerulea dolens - risk factors and prevention. *J IMAB* 2009;15:89-91.
8. Patel NH, Plorde JJ, Meissner M: Catheter-directed thrombolysis in the treatment of phlegmasia cerulea dolens. *Ann Vasc Surg* 1998;12:471-5.
9. Schroeder M, Shorette A, Singh S, Budhram G: Phlegmasia cerulea dolens diagnosed by point-of-care ultrasound. *Clin Pract Cases Emerg Med* 2017;13:104-7.
10. Zhang Z, Chen Z, Sun Y, Xu M. Surgical Thrombectomy and Simultaneous Stenting for Phlegmasia Cerulea Dolens Caused by Iliac Vein Occlusion. *Ann Vasc Surg* 2018;51:239-45.
11. AbuRahma A.F., Perkins S.E., Wulu J.T., et. al. Iliofemoral deep vein thrombosis: conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. *Ann Surg* 2001;233:752-60.
12. Amin V.B., Lookstein R.A. Catheter-directed interventions for acute ilio caval deep vein thrombosis. *Tech Vasc Interv Radiol* 2014;17:96-102.
13. Meissner M.H. Rationale and indications for aggressive early thrombus removal. *Phlebology* 2012;27:78-84.
14. Mewissen M.W., Seabrook G.R., Meissner M.H., et. al.: Catheter-directed thrombolysis of lower extremity deep vein thrombosis: report of a multicenter registry. *Radiology* 1999;211:39-49.
15. Rodríguez L.E., Aboukheir A., Figueroa-Vicente R., et. al.: Hybrid operative thrombectomy is noninferior to percutaneous techniques for the treatment of acute iliofemoral deep venous thrombosis. *J Vasc Surg Venous Lymphat Disord* 2016;5:177-84.
16. Kou C J, Batzlaff C, Bezzant M L, et al. (June 12, 2020) Phlegmasia Cerulea Dolens: A Life-Threatening Manifestation of Deep Vein Thrombosis. *Cureus* 12(6):e8587.