Surgery for the Venous Disaster - Phlegmasia Cerulea Dolens

Chien-Hui Lee, MD, Yung-Kun Hsieh, MD
Division of Cardiovascular Surgery, Department of Surgery, Changhua Christian Hospital, Changhua, Taiwan

ABSTRACT
Phlegmasia cerulea dolens is an acute fulminating form of extensive venous thrombosis. Limb loss, post-thrombotic syndrome and life-threatening conditions can occur without appropriate management.

Treatment methods vary; there presently is no consensus on the best form of treatment. Endovascular procedures have been a good option for treating deep vein thrombosis, yet they may be insufficient for patients suffering from phlegmasia cerulea dolens. Venous thrombectomy with the guidance of venography quickly relieves symptoms, hardly causes complications, yields optimal mid-term results, and can be a justifiable treatment for phlegmasia cerulea dolens.

INTRODUCTION
Phlegmasia cerulea dolens (PCD) is a rare and devastating emergency caused by extensive venous thrombosis. A massive thrombus occludes both deep and superficial veins, obstructs the capillary outflow and then elevates the hydrostatic pressure, leading to fluids shifting into the interstitial space and causing substantial tissue edema. The plasma loss can be immense and hypovolemic shock develops as a consequence [Perkins 1996].

The extreme venous hypertension with massive tissue edema impedes the arterial inflow, compromises the tissue perfusion, and ultimately results in venous gangrene, limb loss and death. This ischemic entity is distinguished from the more common non-ischemic venous thrombosis, phlegmasia alba dolens, and is characterized by cyanosis associated with limb swelling and pain [Perkins 1996; Yang 2016; Klok 2013; Wakefield 2009]. Without timely and adequate management, the potentially reversible PCD may become irreversible venous gangrene in 40% to 60% of cases, which bears a 20% to 50% amputation rate; the risk of pulmonary embolism increases with tissue necrosis, and a 20% to 41% mortality rate has been reported [Perkins 1996; Yang 2016; Patel 1998].

METHODS
From May 2016 to May 2018, three patients were diagnosed with PCD in our hospital. They were two males and one female age 49 years to 64 years. All patients had their left lower limbs involved.

Clinical presentations
PCD was the first presentation in all cases, including sudden swelling, pain, and cyanotic appearance of lower extremities (Figure 1). In every case, a weak or missing Doppler signal in the dorsalis pedis and/or posterior tibia arteries was noted and one of the patients had pain extending to the lower back.

Relevant risks were malignancy (2/3) and common iliac vein stenosis (3/3).

We performed computed tomography (CT) imaging directly instead of compression ultrasonography to better identify the arterial or venous lesion as well as the concomitant intra-abdominal pathology. All patients had iliac-femoral-popliteal type deep vein thrombosis (DVT). It extended into the lower inferior vena cava (IVC) in one patient, and in two cases, the blood flow signal below the knee was absent in the arterial phase while present in the venous phase (Figure 2).

No patient displayed symptoms of pulmonary embolism, such as chest pain, hemoptysis, or dyspnea.

Figure 1. Clinical presentations and characteristic imaging of PCD. The PCD affected limb was cyanotic and had tense swelling (Figure 1A). The CT angio demonstrated the decreased artery flow in the affected limb (Figure 1B, white arrow) and a stenotic left CIV (Figure 1C, black arrow) compressed by the right CIA (Figure 1C, white arrow). CIA, common iliac artery; CIV, common iliac vein; CT, computed tomography; PCD, phlegmasia cerulea dolens.
Treatment methods

Fluid resuscitation, anticoagulation, and affected limb elevations were provided as the initial treatment for all patients. The regiment of anticoagulation in our institution is intravenous heparin at an initial bolus of 80 U/kg followed by a continuous intravenous infusion, with dose adjustment to target a partial thromboplastin time prolongation (50 sec~70 sec).

Subsequent management included open venous thrombectomy with the aid of DSA. All patients were well informed about the disease pattern and consented to our surgical treatment policy.

Venous thrombectomy

Venous thrombectomy was performed through the left common femoral vein (CFV) under general anesthesia with the aid of a fluoroscope. After exploring and controlling the CFV, we transversely incised the vein and delivered a 0.035 guide wire up to the IVC under DSA. Proximal thrombus was removed by a dual lumen Fogarty catheterization, and distal thrombectomy was performed by the same method until the competent venous valve impeded the advance of the Fogarty catheter (Figure 3). The more distal segment of thrombus was pushed out by squeezing the lower extremity externally. The Fogarty catheter was replaced by an 8F catheter, through which we performed the intra-operative venography by manually injecting the contrast medium. During the same operation, the abovementioned procedures (thrombectomies-venography) may have been repeated with the presence of residual thrombus.

For associated venous lesions, transluminal angioplasty was performed through the catheter to assure the venous inflow and to dilate the concomitant stenosis in the iliac vein. IVC filter deployment or catheter-directed thrombolysis (CDT) was required when unignorable stenosis or residual thrombus persisted. The incision of the common femoral vein was sutured closed after the procedure.

All patients were under close surveillance in the intensive care unit and received fluid resuscitation, electrolytes, and renal function monitoring. Heparin infusion was continued and overlapped with oral anticoagulation (warfarin or Rivaroxaban). Oral anticoagulant treatment was kept for at least three months. It was discontinued six months later in one patient because he was symptom-free and had no residual venous lesions on the follow-up imaging study. One patient continued receiving Rivaroxaban as the risk of malignancy persisted.

The outcomes of affected limbs were assessed by clinical pictures and imaging studies (compressive ultrasonography or CT angiography).

RESULTS

All patients had stenotic lesions (>50%) in the left common iliac vein and underwent concomitant endovascular angioplasty. Limb congestion and pain were alleviated immediately after the surgeries. Foot arterial pulses returned to normal, and no perioperative pulmonary emboli occurred.

One patient died of terminal malignancy two months later. An IVC filter was deployed in one patient because the thrombus extended into the distal IVC and intra-operative venography demonstrated residual thrombus persisted after thrombectomies (Figure 4). A multiple side-hole catheter was left in the common iliac vein for Urokinase infusion and was retrieved two days later.
Modified venous thrombectomy remains valuable in extensive venous thrombosis – Lee et al

The patients were followed up for two months to two years (mean duration: 9.6 months). Besides one mortality due to malignancy, the other two had no swelling of their affected extremities, no recurrence of DVT and required no secondary intervention. Details of the patients, interventions, and outcomes are summarized in Table 1.

DISCUSSION

The majority of PCDs occur in the fifth and sixth decades of life [Perkins 1996]. The left lower limbs are involved more frequently than the right lower limbs (45% vs 29%), and both lower limbs are affected in 26% of cases [Perkins 1996; Chinsakchai 2011].

The most well-known risk factors are malignancy, which presents in 1/3 of the cases, and an underlying hypercoagulable state [Perkins 1996]. Other precipitating factors are postoperative or post-traumatic status, postpartum status, use of contraceptive agents, heparin-induced thrombocytopenia, history of DVT, May-Thurner syndrome, prolonged immobility and a variety of inflammatory conditions; approximately 10%–16% of patients have no known risk factors [Perkins 1996; Chinsakchai 2011; Zhang 2018; Ikegami 2016; Onuoha 2015; Mumoli 2012; Warkentin 1997].

In our study all patients had their left lower extremities involved, two had malignancy, and one had May-Thurner syndrome.

The diagnosis is usually clinical. Doppler ultrasound is the recommended tool to assess the pulse of the edematous limbs and exclude the possibility of arterial occlusion [Perkins 1996; Yang 2016; Klok 2013; Chinsakchai 2011]. Venography may be problematic in assessing PCD when the contrast agent is impeded in totally occluded situations [Perkins 1996; Kalagher 2015]. Magnetic resonance imaging and CT are helpful in investigating both vascular and associated intra-abdominal pathology. However, slow arterial blood flow can mimic occlusion and confound the interpretation [Kalagher 2015], which happened in two of our cases (Figure 2). The venous phase of CT is then required for asserting the diagnosis.

There is no definite treatment, but the goal of management is invariable: prevent thrombus propagation, release the venous hypertension, and preserve the collateral circulation and tissue viability [Perkins 1996; Chinsakchai 2011]. The therapeutic strategy depends largely on the clinical picture and experience of the surgeon, and it should be more aggressive with greater extent of tissue ischemia and venous gangrene [Chinsakchai 2011; Rutherford 1997].

Table 1 Summary of the patients’ profiles, interventions and outcomes.

<table>
<thead>
<tr>
<th>Case</th>
<th>Comorbidities</th>
<th>Presentations</th>
<th>Thrombus Lesions</th>
<th>Definite treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(M) 60y</td>
<td>May-Thurner syndrome, Diabetes</td>
<td>Lt lower limb: cyanosis, tense, cold, swelling</td>
<td>Lt CIV to PopV, Lt CIV and EIV stenosis</td>
<td>VT PTA on Lt EIV CIV and EIV (8mm balloon)</td>
<td>Fair* 2nd intervention: no</td>
</tr>
<tr>
<td>(F) 64y</td>
<td>Malignancy, Renal failure, Diabetes</td>
<td>Lt lower limb: cyanosis, tense, and swelling</td>
<td>Lt CIV to PopV, Lt CIV and EIV stenosis</td>
<td>VT PTA on Lt CIV (10mm balloon), Lt EIV (7mm balloon); IVC filter deployment</td>
<td>Expired two months later of terminal stage malignancy. 2nd intervention: no</td>
</tr>
<tr>
<td>(M) 49y</td>
<td>Malignancy</td>
<td>Lt lower back pain, Lt lower limb: cyanosis, cold, swelling</td>
<td>Lower IVC to Lt PopV, Lt CIV stenosis</td>
<td>VT PTA on Lt CIV (12mm balloon); CDT in Lt CIV</td>
<td>Fair* 2nd intervention: no</td>
</tr>
</tbody>
</table>

CIV, common iliac vein; EIV, external iliac vein; EVRF, endovenous radiofrequency ablation; F, female; GSV, great saphenous vein; Lt, left; M, male; PopV, popliteal vein; PTA, percutaneous transluminal angioplasty; VT, venous thrombectomy; y, years old.

*Fair means “No limb edema and no recurrent venous thrombosis”
The first-aid management consists of fluid resuscitation, anticoagulation, and adequate limb elevation [Perkins 1996; Chinsakchai 2011; Onuoha 2015]. For those who fail to respond with systemic anticoagulation within 6hrs–12hrs, vascular specific interventions may be beneficial [Perkins 1996; Chinsakchai 2011; Weaver 1988]. On occasion, the presence of compartment syndrome associated with progressive gangrene necessitates emergent fasciotomy, and the amputation rate is highest in this circumstance [Perkins 1996; Chinsakchai 2011; Onuoha 2015].

Surgical thrombectomy correlates well with the treatment goal by promptly reducing the thrombus load and decreasing the compartment pressure. This prevents pulmonary embolism and venous gangrene and also achieves good mid-term and long-term outcomes [Perkins 1996; Yang 2016; Chinsakchai 2011; Zhang 2018; Comerota 2012; Casey 2012; Goyal 2013]. However, poor clearance of distal thrombus, high re-thrombotic rates, and the possibility of minimal improvement in post-phlebitis syndrome due to a venous valve injury make an open thrombectomy less preferable [Perkins 1996; Chinsakchai 2011; Zhang 2018; Laohapensang 2013; Lansing 1968]. CDT with or without percutaneous mechanical thrombectomy is less invasive and has been the preferred management for DVT [Perkins 1996; Zhang 2018; Amin 2014; Meissner 2012; Jaff 2011]. Nevertheless, endovascular interventions for PCD can be limited by ineffectiveness in clearing totally occluded venous segments and an increase in the incidence of pulmonary embolism resulting from manipulating the catheter and clot fragmentation during the procedure [Perkins 1996; Chinsakchai 2011; Thery 1990]. The time-consuming nature can defer tissue reperfusion and thereby worsen the outcome.

Combining open thrombectomy with endovascular techniques not only possesses merits of open thrombectomy, but also avoids later venous insufficiency. The hybrid strategy proves valuable and may be a potential option when treating ischemic limbs affected by PCD [Yang 2016; Zhang 2018; Laohapensang 2013; Igari 2014; Sarwar 2009; Norgren 2007; Meissner 1999].

We suggest an aggressive attitude of venous thrombectomy for PCD with the aid of DSA, combined with angioplasty or CDT for associated lesions. From our experiences, this hybrid technique quickly dredged the inflow channel and dilated the stenotic venous segments so that the congestion was resolved and disease recurrence was prevented.

In our cases, swelling immediately was resolved and no patient so far has displayed post-thrombotic syndrome.

**CONCLUSION**

Rapid restoration of tissue perfusion is the principle management for PCD. Interventions usually are required to keep the patency of venous outflow and to prevent gangrene.

In the current study, three PCD patients were treated successfully with open thrombectomy under DSA combined with angioplasty or CDT for associated lesions. This hybrid strategy is considered as a treatment option for the management of PCD. However, further research on its effectiveness in a larger population of patients is needed.

**REFERENCES**


