Phlegmasia Cerulea Dolens With Compartment Syndrome

Aryan Shiari, MD; Ryan Bailey, MD; Jason Beckerman, MD

ABSTRACT

Introduction: Phlegmasia cerulea dolens (PCD) is a rare, severe form of deep vein thrombosis (DVT) characterized by extensive venous thrombosis and significant venous congestion, leading to swelling, cyanosis, and severe pain. Unlike typical DVT, PCD causes secondary arterial compromise via small arteriole collapse, resulting in critical limb ischemia and potential venous gangrene. This compromise, coupled with increased compartment pressures and fluid sequestration, makes PCD a true emergency requiring immediate intervention to prevent irreversible damage and limb loss.

Case Presentation: A 58-year-old woman with a complex medical history presented with severe left hip and lumbar pain following trauma. Examination revealed a swollen, cold, cyanotic, and painful left leg with weak pulses indicating compromised blood flow. Computed tomography confirmed extensive DVT from the left common iliac to the tibial veins, consistent with PCD and concerning for compartment syndrome. Given the critical presentation, fasciotomy was performed without obtaining compartment pressure measurements. The patient received anticoagulation and underwent inferior vena cava filter placement, attempted thrombectomy, and subsequent fasciotomy. Despite these measures, persistent ischemia necessitated a left above-the-knee amputation. Incidental cholangiocarcinoma was subsequently diagnosed, likely contributing to her thrombotic condition.

Conclusions: This case highlights the need for prompt diagnosis and intervention in PCD and its progression to compartment syndrome. Underlying malignancy can complicate the clinical course, necessitating a multidisciplinary approach to care. Immediate anticoagulation, thrombus removal, and supportive measures are essential in preventing further complications and improving outcomes.

INTRODUCTION

Phlegmasia cerulea dolens (PCD) is a severe and rare form of deep vein thrombosis (DVT) characterized by extensive venous thrombosis, significant swelling, cyanosis, and pain. This condition arises from venous obstruction, which increases interstitial pressure, compromises arterial inflow, and leads to ischemia. Notably, a well-documented link exists between venous thromboembolism (VTE) and occult cancer; VTE can be the first sign of undiagnosed malignancy. This heightened risk is due to the hypercoagulable state induced by cancer, involving the release of procoagulant factors, inflammatory cytokines, and tumor-shed microparticles that promote thrombosis.[1]

Distinguishing between unprovoked and provoked VTE is essential for management. Unprovoked VTE occurs without an obvious precipitating factor, while provoked VTE is associated with identifiable risk factors such as trauma. This distinction is important as it can guide the clinical approach to screening for hidden malignancies. When considering conditions like compartment syndrome and phlegmasia, it is important to note that phlegmasia is largely associated with severe venous thrombosis, potentially leading to arterial ischemia due to extensive venous congestion. In contrast, compartment syndrome typically results from trauma and is marked by increased pressure within a closed muscle compartment, which can compromise circulation and cause tissue ischemia.[2,3] In severe cases, PCD can progress to compartment syndrome--a surgical emergency requiring immediate intervention to prevent irreversible damage. PCD represents one

• • •

Author affiliations: Pulmonary, Critical Care, and Sleep Medicine, Mayo Clinic Health System – Northwest Wisconsin Region, Eau Claire, Wisconsin (Shiari); Radiology, Mayo Clinic Health System – Northwest Wisconsin Region, Eau Claire, Wisconsin (Bailey); General and Trauma Surgery, Mayo Clinic Health System – Northwest Wisconsin Region, Eau Claire, Wisconsin (Beckerman).

Corresponding author: Aryan Shiari, MD, 1221 Whipple St, Eau Claire, WI 54703; email shiari.aryan@mayo.edu; ORCID ID 0000-0002-6707-5029

Figure 1. Patient's Legs

Leg was swollen, cold to the touch, cyanotic, and exhibited severe pain and paresthesia.

Figure 2. Contrast-enhanced Axial Computed Tomography Through the Pelvis at the Level of the External Iliac Vessels

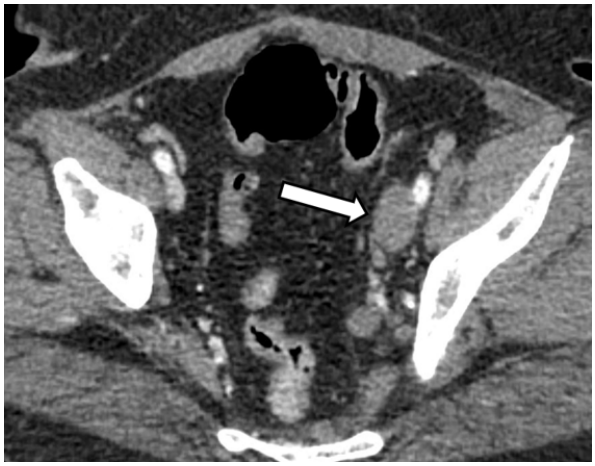
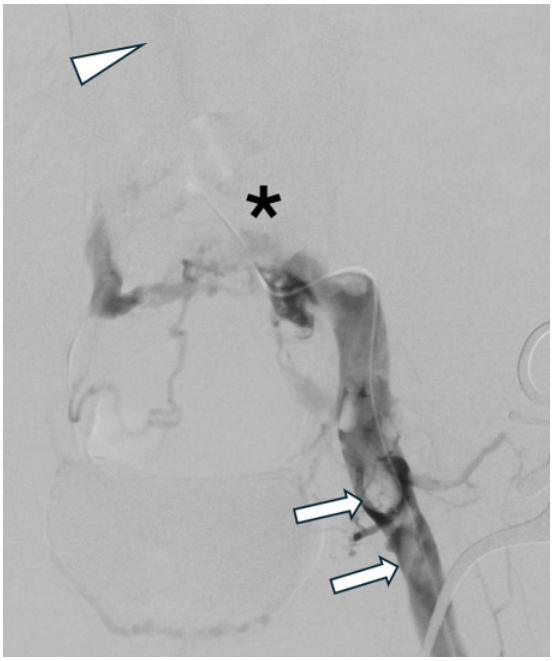


Image demonstrates marked asymmetric enlargement and nonenhancement of the left external iliac vein (arrow) consistent with deep venous thrombosis.

Figure 3. Digital Subtraction Angiography Performed With Catheter Access via Left Superficial Femoral Vein



Angiography demonstrates multiple filling defects in the common femoral and external iliac veins (arrows) with occlusion of the common iliac vein (asterisk) and faint opacification of the IVC (arrowhead) via pelvic collaterals.

of the most severe complications in the spectrum of DVT, where prompt recognition is crucial to prevent progression to compartment syndrome and irreversible ischemic damage.

CASE REPORT

A 58-year-old woman with a complex medical history including diabetes, neuropathy, obesity-related limited mobility (body mass index 44), hypertension, chronic obstructive pulmonary disease, depression, borderline personality disorder, generalized anxiety disorder, chronic pain syndrome, and posttraumatic stress disorder presented with severe left hip and lumbar pain. Symptoms began after her 300-pound son accidentally fell on her 24 hours earlier. There was no evidence of hematoma or rhabdomyolysis from this initial injury. The patient had limited prior medical care and reported no recent hospitalizations, previous surgeries, or chronic pain medication use. Following the trauma, she was advised to rest and limit physical activity to manage her symptoms.

Clinical Examination

Upon examination, the patient's left leg was swollen, cold to the touch, and cyanotic, with severe pain and paresthesia (Figure 1). Pulses in the left lower extremity were weak, indicating compromised blood flow. Her initial creatine kinase (CK) level was 958 U/L.

Investigations

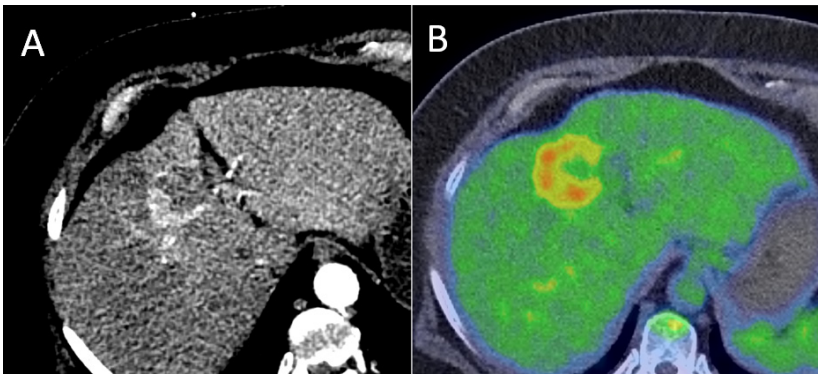
Computed tomography (CT) confirmed a substantial DVT extending from the left common iliac to the tibial veins. A contrast-enhanced axial CT through the pelvis demonstrated marked asymmetric enlargement and nonenhancement of the left external iliac vein, consistent with DVT (Figure 2).

As part of the trauma evaluation, abdominal and pelvic CT revealed a peripherally enhancing mass in the right hepatic lobe

with associated capsular retraction and probable slight peripheral biliary dilation (Figure 4A). The CA 19-9 level was normal at 15 U/mL.

Digital subtraction angiography via the left superficial femoral vein demonstrated multiple filling defects in the common femoral and external iliac veins, occlusion of the common iliac vein, and faint opacification of the inferior vena cava (IVC) via pelvic collaterals (Figure 3). These findings led to a clinical diagnosis of PCD with a high suspicion of compartment syndrome. Although intercompartmental pressure measurement is an important diagnostic tool, the acute presentation necessitated immediate intervention, making it a secondary consideration.

Figure 4. Contrast-enhanced Computed Tomography and Fluorodeoxyglucose (FDG) Positron Emission Tomography-CT (PET-CT) Findings of Cholangiocarcinoma



A. Contrast-enhanced CT through the level of the liver demonstrates the arterially enhancing lesion (arrow) in the right hepatic lobe. B. FDG PET-CT demonstrates increased FDG uptake within the peripheral enhancing component of the biopsy-proven cholangiocarcinoma. Decreased central FDG uptake is consistent with central necrosis and fibrotic changes typical of cholangiocarcinoma.

Treatment

Intravenous heparin was initiated, and the patient underwent sequential IVC filter placement, attempted thrombectomy, and subsequent fasciotomy. Despite these surgical interventions, her left lower extremity remained immobile, with minimally detectable posterior tibial pulses and absent dorsalis pedis pulses on Doppler examination. Her CK levels continued to rise, reaching 11 427 U/L within 24 hours of admission. Due to unsuccessful nonoperative management and progressive ischemia, the decision was made to proceed with a left above-knee amputation.

Pathology and Oncological Findings

Pathological examination of the amputated limb revealed organizing thrombus within the posterior tibial, popliteal, and femoral veins. Post-procedure, the patient's clinical condition stabilized, and CK levels normalized within 48 hours. She remained hemodynamically stable, and further workup was initiated to determine if the causative event was trauma or underlying malignancy.

CT-guided biopsy of the right hepatic mass revealed a well-differentiated carcinoma with clear cell features associated with dense fibrosis. The tissue sample exhibited positive staining for cytokeratin 7 (CK7), OSCAR keratin, albumin in situ hybridization (ISH), and Ki-67 (indicating increased cellular proliferation), and negative staining for CD10, CDX2, CK5/6, CK20, estrogen receptor (ER), GATA3, MelA, PAX8, S100, TTF1, Hep Par-1, and arginase. The immunohistochemical profile was consistent with cholangiocarcinoma.

With malignancy confirmed, the thrombotic condition was likely provoked by the underlying malignancy and subsequent trauma, highlighting the complexity of the patient's medical condition. Further diagnostic workup with positron emission tomography (PET)/CT imaging revealed no evidence of metastasis. Following multidisciplinary tumor board discussion and consultation with the patient, the decision was made to treat the cholangiocarcinoma with radiation therapy alone (Figure 4B). She was not a surgical candidate due to comorbidities and performance status, as noted by the general surgery and medical oncology teams. She also had experienced significant deconditioning since admission. Interventional radiology (IR) assessed the possibility of ablating the primary cholangiocarcinoma lesion but concluded that they could not achieve a full ablation, making IR procedures unsuitable. Finally, the patient expressed a strong preference against chemotherapy, citing concerns about potential side effects and its impact on quality of life. Thus, it was determined that palliative radiation therapy would offer the most benefit by alleviating symptoms and improving quality of life. She preferred this choice, focusing on palliation rather than curative intent.

DISCUSSION

The management of PCD and its progression to compartment syndrome in this case underscores the complex clinical decision-making required in such critical conditions. Although rare, PCD carries significant risks due to complications, including venous gangrene, pulmonary embolism, and circulatory shock, with mortality rates ranging from 20% to 40%. Additionally, the high risk of amputation, affecting up to 50% of cases, highlights the need for urgent intervention to prevent severe ischemia and tissue necrosis.[4-6]

In this case, the progression from PCD to compartment syndrome was primarily attributed to a malignancy-induced prothrombotic state further exacerbated by trauma. Immediate anticoagulation with intravenous unfractionated heparin (UFH) was initiated to prevent further thrombus propagation. This step is crucial in managing PCD; the activated partial thromboplastin

time (aPTT) ratio should be maintained between 1.5 and 2.5 times the control value to achieve therapeutic levels, following standard guidelines.[7,8]

Thrombus removal was a central component of the management strategy, especially given the limb-threatening nature of the condition. Catheter-directed thrombolysis (CDT) and mechanical thrombectomy were employed as key interventions. An IVC filter was placed prior to mechanical thrombectomy to prevent distant embolization, a decision supported by studies demonstrating the effectiveness of retrievable IVC filters in capturing emboli during CDT, thereby reducing the risk of iatrogenic pulmonary embolism. For instance, Lee et al reported successful emboli capture in 31.4% of patients undergoing CDT, with no pulmonary embolism cases in those with filters.[9] Similarly, the FILTER-PEVI trial highlighted a significant reduction in iatrogenic pulmonary embolism risk with IVC filter placement during percutaneous endovenous intervention.[10] However, the potential bleeding risks associated with IVC filters must be weighed carefully.

Endovascular interventions, such as single-stage endovascular thrombectomy combined with iliac vein stenting, provide a minimally invasive approach with high technical success and symptom relief, particularly relevant when PCD is due to iliac vein lesions. In scenarios where compartment syndrome developed and pressures remained elevated despite restoring venous outflow, a fasciotomy was considered necessary. While it relieves pressure, fasciotomy carries significant risks, including blood loss--especially when combined with thrombolytic therapy and anticoagulation.[8,11,12] Therefore, it is reserved for situations where other interventions fail to reduce compartment pressures.

In cases such as the one presented, where endovascular interventions and mechanical thrombectomy, along with anticoagulation therapy and fasciotomy, fail to salvage the limb, the severity of the condition often leads to irreversible ischemic damage. In such severe cases, where all attempts to restore adequate circulation and reduce compartment pressures fail, amputation becomes necessary to prevent further systemic complications and to preserve the patient's overall health.[4,5,13] This outcome underscores the importance of early recognition and aggressive management of PCD, although even with optimal care, limb loss can still be unavoidable in the most severe presentations. Supportive measures, including fluid resuscitation, leg elevation, and effective pain management, are essential components of the treatment plan. Continuous monitoring for signs of compartment syndrome—including severe pain, paresthesia, and motor deficits—is crucial to ensure timely intervention and prevent long-term complications.[14]

CONCLUSIONS

This case of PCD progressing to compartment syndrome highlights the importance of rapid diagnosis and intervention in managing severe venous thrombosis. Despite the complexity of the patient's condition, exacerbated by underlying malignancy and trauma, this case illustrates the necessity of a multidisciplinary approach in such emergencies. While immediate interventions, including anticoagulation, thrombus removal, and supportive measures, are essential to prevent further complications, limb salvage is not always possible. The need for amputation in this patient reflects the severe nature of PCD and its potential for irreversible damage. This case also reinforces the need for vigilance in patients with underlying malignancies, as they are at increased risk for thrombotic events, necessitating a proactive and coordinated approach to care.

Financial disclosures: None declared.

Funding/support: None declared.

REFERENCES

1. Falanga A, Russo L, Milesi V, Vignoli A. Mechanisms and risk factors of thrombosis in cancer. *Crit Rev Oncol Hematol.* 2017;118:79-83. doi:10.1016/j.critrevonc.2017.08.003

2. Mrozinska S, Cieslik J, Broniatowska E, Malinowski KP, Undas A. Prothrombotic fibrin clot properties associated with increased endogenous thrombin potential and soluble P-selectin predict occult cancer after unprovoked venous thromboembolism. *J Thromb Haemost.* 2019;17(11):1912-1922. doi:10.1111/jth.14579

3. Kyriazi V, Theodoulou E. Assessing the risk and prognosis of thrombotic complications in cancer patients. *Arch Pathol Lab Med*. 2013;137(9):1286-1295. doi:10.5858/arpa.2012-0490-RA

4. Aydemir B, Hoyle C, Hakmeh W. Phlegmasia cerulea dolens causing compartment syndrome. *Am J Emerg Med*. 2022;61:234.e1-234.e3. doi:10.1016/j.ajem.2022.08.009

5. Chang G, Yeh JJ. Fulminant phlegmasia cerulea dolens with concurrent cholangiocarcinoma and a lupus anticoagulant: a case report and review of the literature. *Blood Coagul Fibrinolysis*. 2014;25(5):507-511. doi:10.1097/MBC.0000000000000057

6. Lipe DN, Cuthbert D. Rare case of unilateral phlegmasia cerulea dolens with bilateral deep vein thrombosis at a community military hospital emergency department. *Mil Med.* 2017;182(5):e1823-e1825. doi:10.7205/MILMED-D-16-00346

7. Chang CT, Chang CD. Successful treatment of phlegmasia cerulea dolens with percutaneous thrombectomy and catheter-directed thrombolysis: a case report. *Medicine (Baltimore)*. 2022;101(47):e31483. doi:10.1097/MD.0000000000031483

8. Meissner MH, Gloviczki P, Comerota AJ, et al. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg*. 2012;55(5):1449-1462. doi:10.1016/j.jvs.2011.12.081

9. Lee SH, Kim HK, Hwang JK, et al. Efficacy of retrievable inferior vena cava filter placement in the prevention of pulmonary embolism during catheter-directed thrombectomy for proximal lower-extremity deep vein thrombosis. *Ann Vasc Surg.* 2016;33:181-186. doi:10.1016/j.avsg.2015.10.034

10. Sharifi M, Bay C, Skrocki L, Lawson D, Mazdeh S. Role of IVC filters in endovenous therapy for deep venous thrombosis: the FILTER-PEVI (filter implantation to lower thromboembolic risk in percutaneous endovenous intervention) trial. *Cardiovasc Intervent Radiol.* 2012;35(6):1408-1413. doi:10.1007/s00270-012-0342-z

11. Erdoes LS, Ezell JB, Myers SI, Hogan MB, LeSar CJ, Sprouse LR 2nd. Pharmacomechanical thrombolysis for phlegmasia cerulea dolens. *Am Surg.* 2011;77(12):1606-1612. doi:10.1177/000313481107701230

12. Gutierrez JR, Volteas P, Skripochnik E, Tassiopoulos AK, Bannazadeh M. A case of phlegmasia cerulea dolens in a patient with COVID-19, effectively treated with fasciotomy and mechanical thrombectomy. *Ann Vasc Surg*. 2022;79:122-126. doi:10.1016/j.avsg.2021.07.034

13. Mesfin A, Lum YW, Nayfeh T, Mears SC. Compartment syndrome in patients with massive venous thrombosis after inferior vena cava filter placement. *Orthopedics*. 2011;34(3):229. Published 2011 Mar 11. doi:10.3928/01477447-20110124-23

14. Chaochankit W, Akaraborworn O. Phlegmasia cerulea dolens with compartment syndrome. *Ann Vasc Dis.* 2018;11(3):355-357. doi:10.3400/avd.cr.18-00030

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 2379-3961) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.