Deep vein thrombosis in an elderly patient with chronic limb-threatening ischaemia presented with limb swelling: The role of diagnostic tools and surgical dilemma

AM Omar Mohamed Ozaal and Thanoj Fernando

Abstract
Leg and foot swelling is inherently found in 70% of patients with critical limb-threatening ischaemia due to ischaemia, which does not necessitate any specific intervention. Unilateral leg swelling is a vital sign for the clinical suspicion and diagnosis of deep vein thrombosis and phlegmasia. There is a significant surgical dilemma to delay the diagnosis of deep vein thrombosis or phlegmasia in patients with critical limb-threatening ischaemia when a methodical approach is not followed. We report a case of proximal deep vein thrombosis in an elderly patient with ipsilateral critical limb-threatening ischaemia and discuss the role of diagnostic tools. The role of antiplatelets along with vitamin K antagonists, duration of anticoagulation, iliocaval venous obstruction, compression therapy and inferior vena cava filter is discussed.

Keywords
Lower limb swelling, deep vein thrombosis, critical limb-threatening ischaemia, phlegmasia, surgical dilemma, anticoagulation

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Introduction
Deep vein thrombosis (DVT) is one of the manifestations of venous thromboembolism (VTE), which occurs as a cumulative effect of multiple risk factors. Phlegmasia alba dolens (PAD) and phlegmasia cerulea dolens (PCD) are complications along a spectrum of DVT. Phlegmasia occurs from an acute massive VTE and can progress to critical limb ischaemia and potential limb loss. The lower extremities are commonly affected with phlegmasia, and the iliofemoral segment is almost always occluded.

Seventy percent of patients with chronic limb-threatening ischaemia (CLTI) have distal leg and foot pitting ischaemic oedema. In contrast, unilateral pitting oedema is a vital sign of DVT and phlegmasia. The presence of VTE spectrum of disorders in patients with CLTI can affect the diagnostic clue for the unwary clinician if the patient is not assessed methodically with appropriate diagnostic tools. This can delay the treatment for VTE spectrum disorders and culminate in significant morbidity and mortality. We report a case of DVT in an elderly patient with CLTI, presented with ipsilateral leg swelling, which posed a diagnostic challenge.

Case presentation
A 93-year-old female with previously diagnosed bilateral peripheral artery disease was admitted with acute left leg swelling and calf pain for the 1-week duration. She reported bilateral intermittent claudication for the past 6 months. For 1 month, she had rest pain, and a non-healing ischaemic ulcer of the left lower limb and was scheduled for digital subtraction angiography (DSA) with possible angioplasty. Her comorbidities are hypertension and diabetes mellitus. Her metabolic equivalents (METs) score was 2.

On examination, she was not pyrexic, her heart rate was 82 bpm, her blood pressure was 110/67 mm Hg, and there was pitting oedema from the left foot up to knee level, which was prominent over the distal leg (Figure 1). Tenderness was present over the calf, and there was neither sign of
inflammation nor infection related to the wound. Except bilateral femoral, no other lower limb pulses were palpable. Her right leg did not reveal any swelling, tenderness or wounds apart from diabetic dermopathy and trophic changes.

Her ankle-brachial pressure index (ABPI) was 0.34 and 0.64 in the left and right lower limbs, respectively. Her Well’s score was four on admission, and B-mode ultrasound revealed a non-compressible left common femoral vein with a thrombus in situ along with markedly reduced blood flow in the colour Doppler ultrasound (Figure 2). The common femoral and superficial femoral arteries showed a turbulent abnormal waveform and a high-velocity monophasic waveform with spectral broadening, respectively. Popliteal, anterior and posterior tibial arteries showed significantly dampened monophasic waveforms (Figure 3). Her white cell count and C-reactive protein levels were within normal limits.

The patient was diagnosed with acute DVT of the left lower limb, which was chronically ischaemic and treated with unfractionated heparin (UFH) infusion. Her presenting symptoms reduced significantly over the next 3 days of UFH treatment. She was started with aspirin, long-term anticoagulation with warfarin, compression ultrasound surveillance, wound care and enlisted to DSA with possible angioplasty in 2-month time. She did not report any wound infections or cellulitis during her follow-up period though there was no healing evidence. Unfortunately, she died at home after defaulting her scheduled DSA for 3 months since the

Figure 1. (a–c) Left leg swelling involving the entire leg.

Figure 2. (a) Ultrasound B mode showing non compressible left femoral vein and (b) colour Doppler ultrasound shows almost no blood flow in the left femoral vein.

*Thrombus in situ.
diagnosis of DVT. We could not find any historical evidence of apparent wound-related infection or recurrent DVT for her death.

**Discussion**

Clinical diagnosis of isolated DVT and associated phlegmasia is challenging. The scenario would be further complicated by adding the history of CLTI. Unilateral leg swelling is a vital clinical sign found in DVT, phlegmasia and CLTI due to various reasons. Unilateral leg swelling or oedema is 97% sensitive and 33% specific for isolated DVT. 70% of the patients with CLTI will have associated leg swelling due to ischaemia. A triad of oedema, pain and blanching without cyanosis or tissue involvement is found in PAD, and it precedes PCD in 50%-60% of patients. PCD is characterized by cyanosis, progression to gangrene with absent pulses, compartment syndrome and pulmonary embolism (PE).
It is paramount and plausible to differentiate phlegmasia in CLTI patients presenting with acute leg swelling over an isolated DVT utilizing clinical aspects aided with imaging. A delay in diagnosing PCD is detrimental as more aggressive treatment approaches, including prompt anticoagulation, leg elevation, fluid resuscitation, thrombolysis and thrombectomy, are indicated in contrast to isolated DVT.  

Anticoagulation is indicated for acute DVT in the initial phase (up to 10 days), principal treatment phase (up to 3 months) and an extended treatment phase (beyond 3 months). These phases are traditionally dominated by UFH and low molecular weight heparin (LMWH), vitamin K antagonists (VKA) and LMWH, and VKA or direct oral anticoagulants (DOAC), respectively. LMWH and VKAs are equally effective for provoked and unprovoked DVT treatment. Although DOACs and VKAs are equally effective for the principal treatment phase of provoked DVT, DOACs are recommended due to their better safety profile. The extended anticoagulation with DOACs followed by VKAs is described in unprovoked DVT because of its high recurrence and continued with no scheduled stop date. Aspirin is not recommended in DVT treatment compared to DOACs and VKAs as it has less reduction in recurrence of DVT. Antiplatelets are strongly recommended in patients with CLTI. Using VKAs and aspirin in our patients is justified with the unavailability of DOACs in our setup. Both provoked and unprovoked DVT require anticoagulation for at least 3 months. It must be extended beyond 3 months regarding the high risk of recurrent DVT in the unprovoked group. Serial compression ultrasound (CUS) surveillance is performed to look for residual venous obstruction (RVO) during extended anticoagulation. The presence of RVO indicates nonresolution of DVT and necessitates the continuation of anticoagulation further. Early thrombus removal with or without stenting in patients with DVT does not reduce the need for anticoagulation.

The risk of PE, post-thrombotic syndrome (PTS) and overall prognosis depends on the involved venous territory, and accurate anatomical classification of proximal and distal DVT is beneficial. Venous duplex ultrasound is sufficient to exclude proximal DVT and acts as the initial test for assessing the iliocaval segment. Risk factors of May–Thurner syndrome and persistent or recurrent symptoms despite adequate anticoagulation are cues for iliocaval venous obstruction (ICVO), which were absent in our patient. Venography with cross-sectional imaging and intravascular ultrasound are highly sensitive for ICVO and are increasingly performed prior to treatment planning. Symptomatic thrombotic ICVO necessitates a venous intervention in addition to anticoagulation. Endovascular angioplasty, stenting and catheter-directed thrombolysis are increasingly performed over open surgery for ICVO. Inferior vena cava (IVC) filters are indicated solely to prevent PE and for patients with DVT where anticoagulation is contraindicated. IVC filters have no positive effects on DVT itself, are associated with subsequent thrombotic complications and are implicated in the occurrence of ICVO.

Early compression therapy in multilayer bandaging or elastic compression hosiery at 30–40 mmHg is recommended for acute DVT. However, it is contraindicated for patients with a history of CLTI with ABPI < 0.5 as in our patient, resulting in limb loss. Elastic below knee compression stocking is helpful in patients with proximal DVT up to 24 months. However, it should be limited to 6–12 months, depending on the Villalta score, to prevent PTS. Post-angioplasty improvement of ABPI to more than 0.5 in a patient with CLTI is acceptable for compression therapy in terms of DVT.

Our patient had a left lower limb ischaemic wound that failed to heal with suitable wound dressings without angioplasty. Our experience confirms that the wound healing is suboptimal in patients with CLTI, even with good collaterals. Non-healing is multifactorial and lies on par with literature. Intermittent pneumatic compression in CLTI showed varying wound healing (4%–96% at 3 months) without any mortality benefit and worst outcome in patients with renal failure in terms of limb salvage and mortality. There is a lack of evidence to support non-revascularisation methods in CLTI though widely used in real-world practice when the traditional methods of revascularization are unsuitable or failed.

Conclusion

Differentiating phlegmasia from isolated DVT in patients with CLTI is challenging to the unwary clinician as they all have leg swelling as an essential clinical sign. Although antiplatelets are not indicated for DVT, they can be combined with anticoagulants in patients with CLTI treated for DVT. Resolution varies in provoked versus unprovoked DVT and can be picked up with RVO in venous ultrasound on post-DVT surveillance, which is an important factor determining the duration of anticoagulation. The presence of ICVO should be promptly identified with imaging in patients with proximal DVT, as this necessitates early venous interventions in addition to anticoagulation. Compression therapy is beneficial for DVT patients with CLTI when their ABPI is optimized above 0.5 with angioplasty.

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ORCID iD
AM Omar Mohamed Ozaal https://orcid.org/0000-0002-4709-8178

References
1. Hardy TJ and Bevis PM. Deep vein thrombosis. Surgery 2019; 37(2): 67–72.
2. Chinsakchai K, Ten Duis K, Moll FL, et al. Trends in management of phlegmasia cerulea dolens. Vasc Endovascular Surg 2011; 45(1): 5–14.
3. Khiabani HZ, Anvar MD, Rostad B, et al. The distribution of oedema in the lower limb of patients with chronic critical limb ischaemia: a study with computed tomography. Vasa 1999; 28(4): 265–270.
4. Jette M, Sidney K and Blumchent G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation. Clin Cardiol 1990; 13(8): 555–565.
5. Wells PS and Owen C. Does this patient have deep vein thrombosis? JAMA 2014; 295(2): 199–207.
6. Sandler DA, Martin JF, Duncan JS, et al. Diagnosis of deep-vein thrombosis: comparison of clinical evaluation, ultrasound, plethysmography, and venoscan with X-ray venogram. Lancet 1984; 2(8405): 716–719.
7. Gardella L and Faulk J. Phlegmasia alba and cerulea dolens. Treasure Island, FL: StatPearls Publishing, 2022, https://www.ncbi.nlm.nih.gov/books/NBK563137/
8. Andras A, Tenna AS and Stewart M. Vitamin K antagonists versus low-molecular-weight heparin for the long term treatment of symptomatic venous thromboembolism. Cochrane Database Syst Rev 2017; 2017(7): 1–83.
9. Kakkos SK, Kirkilesis GI and Tsolakis IA. Editor’s choice – efficacy and safety of the new oral anticoagulants dabigatran, rivaroxaban, apixaban, and edoxaban in the treatment and secondary prevention of venous thromboembolism: a systematic review and meta-analysis of phase III trials. Eur J Vasc Endovasc Surg 2014; 48(5): 565–575.
10. Kakkos SK, Gohel M, Baekgaard N, et al. Editor’s choice – European Society for Vascular Surgery (ESVS) 2021 clinical practice guidelines on the management of venous thrombosis. Eur J Vasc Endovasc Surg 2021; 61(1): 9–82.
11. Marik PE and Cavallazzi R. Extended anticoagulant and aspirin treatment for the secondary prevention of thromboembolic disease: a systematic review and meta-analysis. PLoS ONE 2015; 10(11): e0143252.
12. Conte MS, Bradbury AW, Kolh P, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. Eur J Vasc Endovasc Surg 2019; 58(1): S1–S109.e33.
13. Mousa A. Overview of iliocaval venous obstruction (ed I Davidson, J Eidt, J Mills, et al.). UpToDate, 2020, https://www.uptodate.com/contents/overview-of-iliocaval-venous-obstruction
14. Villalta S, Picolli A, Lensing A, et al. Assessment of validity and reproducibility of a clinical scale for the post thrombotic syndrome. Haemostasis 1994; 24: 157.
15. Moran PS, Teljeur C, Harrington P, et al. A systematic review of intermittent pneumatic compression for critical limb ischaemia. Vasc Med 2015; 20(1): 41–50.