

Delirium and Bullae: A Rare Presentation of Chronic Limb-Threatening Ischemia and Undiagnosed Polyvascular Disease

Ashley Shafran, PA-S, Deanna Sgambato, PA-C

Quinnipiac University Physician Assistant Program

Background

- Polyvascular disease is characterized by atherosclerosis in more than one arterial network in the body. The plaque buildup can lead to blockages in cerebral, coronary, and peripheral arteries.¹
- Risk factors for polyvascular disease include diabetes, smoking, hypertension, hyperlipidemia, obesity, and age.²
- Peripheral arterial disease (PAD) occurs when there is atherosclerosis of the arteries supplying the extremities, most commonly the legs.³
- A common symptom of PAD is intermittent claudication, defined as pain while walking that is relieved by rest.³
- Chronic limb-threatening ischemia (CLTI) occurs as a severe manifestation of PAD when there is insufficient blood supply to tissue at rest.⁴
- CLTI can result in ulcerations, amputation, and even death.⁴
- Clinical presentation of CLTI can include rest pain, ulcerations, non-healing wounds, and tissue necrosis.⁵

Case Description

Initial Presentation

- A 73-year-old female with a past medical history of type 2 diabetes, hypertension, and a 35-pack-year smoking history presented to the emergency department (ED) with two days of **altered mental status** and one week of **generalized weakness and headaches**. She denied chest pain, shortness of breath, abdominal pain, dysuria, or recent trauma.
- Vital signs were remarkable for low-grade fever of 37.8°C and heart rate of 121 bpm.

Medical History

- **Past Medical History:** hypertension, type 2 diabetes
- **Home Medications:** glimepiride 4 mg PO once daily, metformin 1000 mg PO twice daily, lisinopril 30 mg PO once daily
- **Allergies:** no known drug allergies
- **Past Surgical History:** no known surgical history
- **Past Social History:** current smoker, 35-pack-year history; denies alcohol or drug use; completes ADLs independently at baseline, lives with daughter

Physical Exam Upon Presentation

- **General:** No acute distress. Minimally verbal with eyes open.
- **Skin:** Warm upper and lower extremities. No rashes or ecchymosis.
- **Cardiac:** S1, S2 appreciated. No murmurs or friction rubs. Radial pulses 2+ bilaterally. Dorsalis pedis pulses 1+ bilaterally. 1+ pitting edema of left lower extremity (LLE).
- **Respiratory:** Non-labored breathing. No wheezing, crackles, or rhonchi.
- **Musculoskeletal:** Moving all extremities with generalized weakness. Exam limited due to inability to follow commands. No nuchal rigidity. Tenderness to palpation of the LLE inferior to the knee.
- **Neurologic:** No facial droop. Pupils equal, round, and reactive to light.
- **Psych:** Alert and oriented to person and place only. Unable to follow commands.

Differential Diagnosis

- Polyvascular disease, acute limb ischemia, chronic limb-threatening ischemia, peripheral arterial disease, cerebrovascular attack, meningitis, bullous pemphigoid, necrotizing fasciitis

Diagnostics

WBCs	13,330 mm ³
Glucose	241 mg/dL
Troponins	47 pg/mL
Serial blood cultures	Negative
Cerebrospinal fluid	No WBCs, no organisms cultured

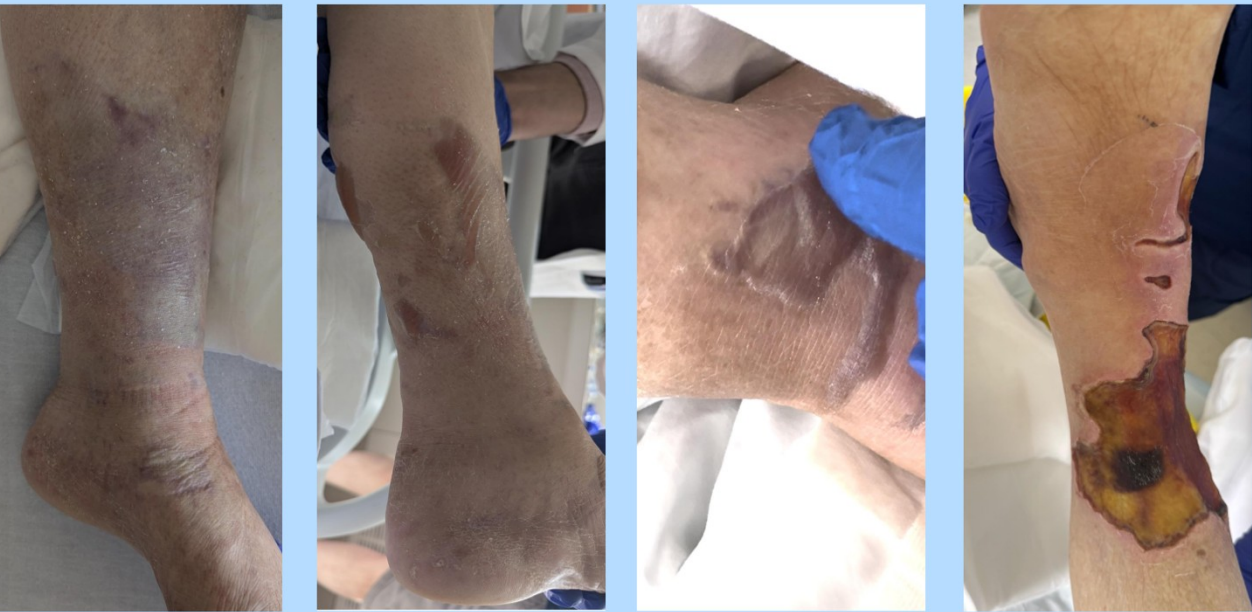
Imaging

ECG	Sinus tachycardia
Duplex ultrasound of LLE	Negative for DVT
Head CT	Negative for acute processes
CT angiogram of head and neck	Atrophic and small vessel ischemic changes with severe atherosclerotic calcification
CT of LLE	Negative for fracture, subcutaneous edema, or focal collections
Punch biopsy of bullae on LLE	Negative
Arterial duplex ultrasound of bilateral lower extremities	High-grade stenosis and monophasic flow of the left superficial femoral artery
CT angiogram of abdomen with runoff	Diffuse tibial artery disease bilaterally with tibial artery occlusions of bilateral lower extremities
Cardiac catheterization	Chronic total occlusion of RCA at the ostium collateralized by the LAD and calcified 80% stenosis in the proximal LAD

Patient Outcome

- Patient was admitted for altered mental status with concern for sepsis and meningitis
- The patient was empirically treated for meningitis with IV ceftriaxone, ampicillin, vancomycin, and acyclovir
- On day two of hospitalization, the patient's mental status returned to baseline of A&O x 4, but her distal LLE became **exquisitely painful**, and an area of **bluish ecchymosis** was noted (Figure 1. Day 2)
- Left foot remained warm and the dorsalis pedis pulse was detectable by hand-held Doppler with easily audible biphasic sound
- Numerous clear small **flaccid bullae** developed around the circumferential distal LLE (Figure 1. Day 3) that then increased in size (Figure 1. Day 7)
- The bullae ruptured and developed into **well-demarcated necrotic areas** (Figure 1. Day 25)
- Due to elevation of troponins on admission and abnormal left ventricle perfusion on cardiac stress testing, patient underwent high risk **percutaneous intervention (PCI) with stenting** prior to revascularization of the LLE
- **Revascularization of bilateral lower extremity** occurred after numerous delays in care
- Following the revascularization, the patient was moved to the surgical intensive care unit for monitoring

Figure 1. Progression of Left Lower Extremity Throughout Hospitalization Days



Day 2 → Day 3 → Day 7 → Day 25

Discussion

- In the United States, approximately 11-20% of individuals 65 years and older have PAD.^{6,7}
- Prevalence of PAD in those that have concomitant diabetes is as high as 31%.⁶
- Up to 40% of patients with PAD are asymptomatic, often delaying diagnosis and treatment.⁸
- Active smoking is highly associated with development of PAD, with active smokers being 2.7 times more likely to develop PAD than non-smokers.⁹
- Among all preventable risk factors, smoking has the greatest impact on development of PAD and progression to CLTI.⁴
- Polyvascular disease and type 2 diabetes together significantly increase the risk of major adverse cardiovascular events (MACE).¹⁰
- Delirium can be an associated symptom of CLTI.¹¹
- Diagnosis of acute limb ischemia can be made by ankle-brachial index, duplex ultrasound, computed tomography angiogram, and magnetic resonance angiography.^{4,12}
- Treatment of acute limb ischemia includes endovascular revascularization, bypass graft, embolectomy, and amputation.^{4,5}
- CLTI increases the risk of mortality at 2 years by 40%, and the risk of amputation at 5 years is as high as 43.4%.⁴
- Those with polyvascular disease in addition to PAD have a substantially increased risk of MACE compared to those that have PAD alone.¹⁴

Conclusion

- Chronic limb-threatening ischemia can present atypically with findings such as delirium and bullae
- Polyvascular disease is strongly correlated to diabetes and smoking
- With high rates of amputation and mortality, it is critical that chronic limb-threatening ischemia is diagnosed and treated early

References

1. Susskind MD, Mehta RJ, Stebbins A, et al. Polyvascular disease and increased risk of cardiovascular events in patients with type 2 diabetes: insights from the EXSCAL trial. *Aliment Pharmacol Ther*. 2021;33(1-6):doi:10.1016/j.alpt.2021.10.011
2. Golligorsky J, Vito R, Quigley F, et al. Cohort study examining the prevalence and relationship with outcome of standard modifiable risk factors in patients with peripheral artery occlusion and aneurysmal disease. *Eur J Vasc Endovasc Surg*. 2022;63(2):301-313. doi:10.1016/j.ejvs.2021.10.039
3. Porras CP, Roth MJ, Tera M, et al. Differences in symptom presentation in women and men with confirmed lower limb peripheral artery disease: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg*. 2022;63(4):602-613. doi:10.1016/j.ejvs.2021.12.039
4. Fisher A, Eberhardt RT. The current state of critical limb ischemia: a systematic review. *JAMA Surg*. 2016;151(11):1070-1077. doi:10.1001/jamasurg.2016.2018
5. Senthil JD, Senthil SM. Chronic critical limb ischemia: diagnosis, treatment and prognosis. *Ann Fam Physician*. 1999;59(7):1899-1908
6. Yoon MJ. The current U.S. prevalence of peripheral arterial disease. *Vasc Dis Manag*. 2023;20(4):67-73
7. Sigwart B, Lundin F, Wahlberg E. The risk of disease progression in peripheral arterial disease is higher than expected: a meta-analysis of mortality and disease progression in peripheral arterial disease. *Eur J Vasc Endovasc Surg*. 2016;51(3):395-403. doi:10.1016/j.ejvs.2015.10.022
8. Alhabib F, Wang AT, Elayeh TA, et al. A systematic review for the screening for peripheral arterial disease in asymptomatic patients. *J Vasc Med Biol*. 2015;51(3):425-535. doi:10.1016/j.jvmb.2014.12.002
9. Lu L, Mackay DF, Pell JP. Meta-analysis of the association between cigarette smoking and peripheral arterial disease. *Heart*. 2014;100(5):414-423. doi:10.1136/heart-2013-304082
10. Bonnes MP, Gutierrez JA, Cannon C, et al. Polyvascular disease, type 2 diabetes, and long-term vascular risk: a secondary analysis of the IMPROVE-IT trial. *Lancet Diabetes Endocrinol*. 2018;6(12):934-943. doi:10.1016/S2213-8587(18)30390-0
11. Meulenbroek AL, Lammens G, Fourneau I, et al. Prehabilitation for delirium prevention in elderly patients with chronic limb threatening ischemia. *J Vasc Med Biol*. 2025;31(2):450-459. doi:10.1016/j.jvmb.2024.10.034
12. Anand SS, Cannon P, Edebo BM, et al. Major adverse limb events and mortality in patients with peripheral artery disease: the COMPELL Trial. *J Am Coll Cardiol*. 2018;71(20):2306-2315. doi:10.1016/j.jacc.2018.03.008
13. Bonnes MP, Gutierrez JA, Cannon C, et al. Polyvascular disease, type 2 diabetes, and long-term vascular risk: a secondary analysis of the IMPROVE-IT trial. *Lancet Diabetes Endocrinol*. 2018;6(12):934-943. doi:10.1016/S2213-8587(18)30390-0
14. Gutierrez JA, Mulder H, Jones WS, et al. Polyvascular disease and risk of major adverse cardiovascular events in peripheral artery disease: a secondary analysis of the EUCLID trial. *JAMA*. 2018;1(7):e185239. doi:10.1001/jama.2018.5239