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Authors
Braun, Russ
Lin, Michelle

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Clinical Review

ACUTE LIMB ISCHEMIA: A CASE REPORT AND LITERATURE REVIEW

Russ Braun, MD, MPH, MBA, FACEP and Michelle Lin, MD

Department of Emergency Medicine, University of California San Francisco School of Medicine, San Francisco, California
Corresponding Address: Russ Braun, MD, MPH, MBA, FACEP, St Mary's Medical Center, 450 Stanyan Street, San Francisco, CA 94117

□ **Abstract—Background: Acute limb ischemia (ALI), although uncommon, can present with profound symptoms, including disabling pain in the setting of acute vascular and neurologic deficits. The most appropriate diagnostic and therapeutic strategy has evolved with emerging technologies inclusive of less-invasive endovascular diagnostic and therapeutic options. Objective: We present a case of ALI to illustrate the diagnostic and therapeutic approaches with a summary of the most common literature. Discussion: Utilizing the clinical findings applied to the Rutherford classification, the emergency physician, in consultation with a vascular surgeon and interventional radiologist, can strategize a methodical approach for better clinical outcomes, often with less-invasive endovascular interventions, ideally within 6 h of symptom onset. Conclusions: We present a case of ALI to illustrate the diagnostic and therapeutic approach with a summary of the most current literature. Emergency physicians should be aware of optimized clinical outcomes with the use of time-sensitive enhanced endovascular therapies as a recommended option for the best outcomes for the treatment of ALI.** © **2015 Elsevier Inc.**

□ **Keywords—acute limb ischemia; management; interventional; endovascular; thrombolytic; emergency department**

INTRODUCTION

Acute limb ischemia (ALI) is defined as a disruption of arterial blood flow to an extremity occurring within the previous 14 days and is usually caused by thromboembolic pathology. ALI management has evolved over the last decade, with advances in diagnostic capabilities and less-invasive endovascular therapeutic options (1). By approaching and framing the clinical presentation using the Rutherford classification scheme, the emergency practitioner can better articulate the diagnostic and therapeutic options in consultation with a vascular surgeon and interventional radiologist on a high morbidity clinical condition. This review, by case example, provides a detailed summary of the most current literature on managing ALI.

Reprints will not be available from the authors.

CASE REPORT

Patient History

A 54-year-old woman, diagnosed approximately 2 months earlier with lung cancer, stage IIIA non-small cell adenocarcinoma, presented with acute onset left hip and leg pain, arriving by ambulance to the emergency department (ED) within 2 h of symptom onset. Although her history was limited due to her severe discomfort, she indicated that her left foot felt like it was "on fire," and she did not want to bear weight on that side. She denied any trauma, fever, or recent illness. The patient, who denied having any metastatic progression of her disease, reported that she was receiving chemotherapy, and her last treatment was 2 days before presentation. All other review of systems were unremarkable, including no history of palpitations or an irregular heart beat. Her medical history included left leg popliteal fossa varicose veins, in

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addition to the lung cancer. Her social history included a 29-year smoking history.

Physical Examination

The patient appeared older than her stated age and seemed very uncomfortable in the gurney, as evidenced by her writhing in pain from her left hip and proximal leg. The initial vital signs included a blood pressure of 118/56 mm Hg, pulse of 70 beats/min, respiratory rate of 19 breaths/min, oxygen saturation of 100% on room air, and temperature of 37°C. The cardiopulmonary examination was unremarkable. The abdomen was soft and slightly distended. On extremity examination, the patient was able to actively and passively move her left hip and leg, but this was limited because she experienced pain with movement. There were varicosities in the left lower extremity, as documented in the past, as well as mottling of the left lower extremity. On vascular examination, there was no evidence of abdominal or femoral bruits, but there was a diminished pulsation of the left femoral, and delayed pulsation of the left popliteal, arteries, as confirmed by Doppler, compared with the right side. Pedal pulses of the left leg were barely palpable compared to those of the right leg. On neurologic examination, the patient was intact with regard to strength, sensation, and cranial nerve examinations, except for a subjective complaint of numbness and tingling in her entire left foot.

ED Course

This patient was immediately thought to be at high risk for ALI due to the constellation of signs and symptoms, which included an acute onset of extremity pain out of proportion to examination, asymmetrically diminished pulses, and neurologic complaints of left foot paresthesia. In addition, the patient's primary complaint of hip pain and her physical examination with diminished femoral pulses and delayed popliteal pulses weighted our differential toward a vascular occlusion proximal to the femoral artery. However, because the patient presented with no significant risk factors for arterial occlusion, such as atrial fibrillation, we maintained a broad differential diagnosis, including venous thrombosis and pathologic fracture, especially given the recent history of lung cancer.

Emergent phone consultations with a vascular surgeon and interventional radiologist were initiated. Initial portable chest and pelvic x-ray studies were negative for any acute processes, including pathologic fractures. A computed tomography angiogram (CTA) of the abdomen and pelvis with bone windows was performed and demonstrated an acute thrombosis involving the left common iliac and proximal external iliac artery (Figure 1) (2). There was reconstitution in the distal left external iliac artery, which appeared to fill retrograde from collateral vessels. There was no evidence of venous thrombosis or bony pathology.

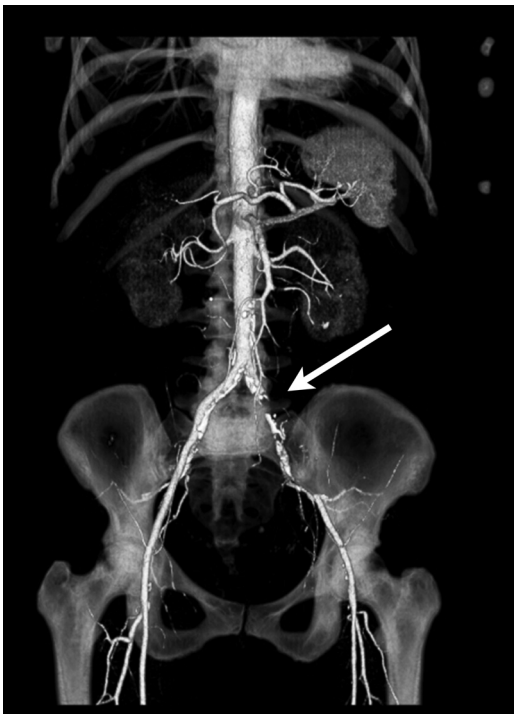

Figure 1. Digital reconstruction of computed tomography angiography of abdomen-pelvis showing a left common iliac and left external iliac thrombosis (arrow).

Because there was no evidence of active bleeding on the CTA, i.v. heparin (bolus of 10,000 U and drip of 1000 U/h) was initiated, and the patient was medicated for pain. Within the first 3 h, the patient was much more comfortable, and it appeared as though perfusion to the left lower leg was improving, based on diminished pain and decreased pallor. For more definitive treatment, it was felt that the patient was a good candidate for intra-arterial thrombolysis.

Hospital Course

In the interventional radiology suite, the patient underwent an infrarenal aortogram, which demonstrated normal flow of the right, but a severe filling defect starting at the left, external iliac artery with poor distal runoff (Figure 2). Catheter-directed therapy, including endovascular clot extraction, was performed on the left external iliac and left common iliac arteries, as well as placement of a lytic infusion catheter just beyond the origin of the left common iliac artery. Intra-arterial tissue plasminogen activator (tPA) infusion at 2 mg/h was initiated and heparin was continued at 600 U/h.

Figure 2. Infrarenal aortogram showing an abrupt disruption of arterial flow at the proximal left external iliac artery (arrow) before treatment.

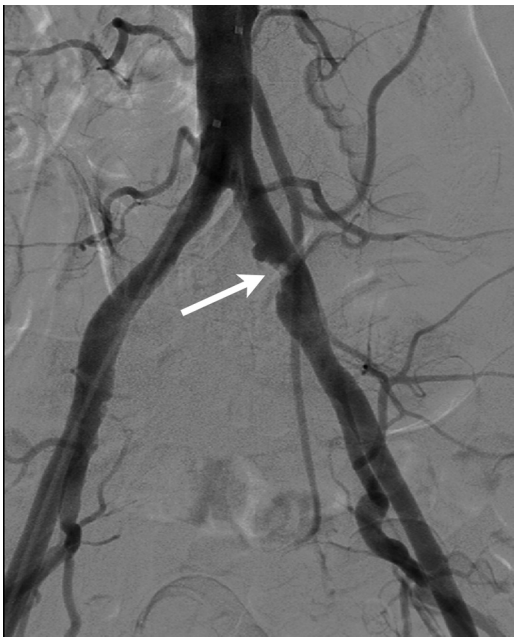

Figure 3. Infrarenal aortogram after catheter-directed thrombolysis and i.v. heparin treatment showing improved arterial blood flow to the left external iliac artery and distal vasculature. An atheromatous plaque remained (arrow), which was eventually stented without complications.

On hospital day 2, there was notable improvement in femoral and dorsal pedal pulses, but there was residual mottling of the plantar aspect of the left fifth toe. A follow-up angiography demonstrated significant flow improvement; however, there was a 50% irregular plaque vs. residual mural thrombus noted in the medial aspect of the mid left common iliac artery. Both the thrombolytic infusion (reduced to 1 mg/h) and i.v. heparin (600 U/h) were continued, with the belief that this lesion represented a significant residual thrombus.

A repeat CTA demonstrated no active extravasation, and a small exophytic irregular filling defect of the left common iliac artery most likely represented an atheromatous plaque (Figure 3) that was successfully excluded by a self-expanding stent. The patient continued to do well and was discharged home on hospital day 4 with the addition of clopidogrel to her regular medications. The patient was evaluated in follow-up clinic with no vascular complaints and resumed chemotherapy for her lung cancer.

DISCUSSION

Case Overview

Our patient was a 54-year-old female with recently diagnosed lung cancer presenting with acute onset of left hip pain radiating to her left thigh associated with distal paresthesias. After stabilization, we were confronted with the challenge of determining the most feasible, highly sensitive, and time-efficient diagnostic study to optimize diagnosis and intervention, while also considering the possibility of a pathologic metastatic fracture. In addition, because her initial presentation of "pain out of proportion to examination," we were also vigilant for vascular emergencies of the arterial and venous systems. Selection of the first diagnostic study may be site-specific, depending on the time of day, one's local practice, and access to studies, therefore, it is important to involve your vascular surgeon and interventional radiologist early in the process when considering an acute vascular emergency in the ED.

Classic Presentation of ALI

This case represents a fairly classic presentation of ALI, which is often a constellation of signs and symptoms described by the six "Ps": acute onset of pain out of proportion to examination, diminished pulses, early skin mottling (pallor), coolness to touch (poikilothermia), distal paresthesias, and paralysis (3). Although this patient presented fairly early (within 2 h of symptom onset), later symptoms might have included progressive limb weakness, paralysis, and absent pulses altogether.

Risk Factors for ALI

As our demographics shift to an aging patient population, we must be aware of chronic disease conditions that can

contribute to a higher prevalence of ALI. In particular, cardiac dysrhythmias (with or without anticoagulation), hypercoagulability secondary to underlying, even treated, malignancy, traumatic injury, low-flow states like sepsis and congestive heart failure and, lastly, patients having undergone previous peripheral vascular procedures inclusive of stenting. Ascertaining any previous vascular procedures inclusive of stenting is critical for diagnostic and management approaches, given the higher risks for stent thrombosis, stent migration, and fistula formation.

Value of Ankle-Brachial Index

Doppler examination was performed in the ED and again by the vascular surgeon, with both examinations demonstrating a delayed Doppler signal in the femoral and popliteal regions, supporting a diagnosis of ALI. While formal ankle-brachial indexes (ABIs) were not obtained in this case, they can be helpful in detecting vascular insufficiency (3). ABIs of the lower extremities are measured by obtaining the ratio of the systolic blood pressure of the affected extremity (using the higher value between the dorsalis pedis and posterior tibialis) divided by the higher of the brachial systolic blood pressures (Figure 4). An ABI value < 0.9 is considered abnormal, and a value < 0.5 is consistent with severe occlusion.

Diagnostic Considerations

In the presented case, after obtaining an initial pelvis x-ray study that did not show any obvious fractures and, in consultation with the radiologist and vascular surgeon, it was decided that an abdominal-pelvic CTA would be the most practical, highest yield, next diagnostic study. This modality enabled us to exclude bone metastases and venous thromboses, and also diagnose ALI of the common iliac artery. In addition, CTA digital reconstructions can be invaluable to the vascular surgeon to help plan a less-invasive approach in the endovascular suite (2). An alternative initial management approach might have been to perform a digital subtraction angiography in the interventional radiology laboratory without a CTA, but this would have been less reliable in detecting other nonvascular etiologies of acute left leg pain in a patient with lung cancer. Other diagnostic modalities considered included duplex ultrasonography, but it is less sensitive for detection of vascular pathology proximal to the inguinal ligament, as well as magnetic resonance angiography, but this was not accessible on an emergent basis.

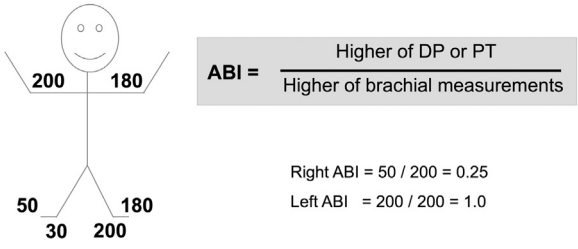

Figure 4. Example of an ankle brachial index calculation. ABI = ankle-brachial index; DP = dorsalis pedis; PT = posterior tibialis.

Treatment: Aspirin and Heparin

Current recommendations include administration of 325 mg aspirin, unless there is a contraindication (4). Most practitioners recommend immediate i.v. heparin to prevent clot propagation, however, this may be initiated in the interventional radiology laboratory after obtaining arterial access if you anticipate that the patient will be sent rapidly for diagnostic angiography (5,6). Appropriate heparin dosing, including addition of a loading dose, may be patient- and surgeon-specific and the vascular surgeon should be involved in this decision. The literature supports reduced-dosed adjuvant heparin administration with intra-arterial thrombolytic infusions to minimize the risk of bleeding. One consensus group recommended a heparin bolus of 2500 U, followed by continuous infusion of 500 U/h to maintain the partial thromboplastin time between 1.25 and 1.5 times control (7).

Treatment Decision-Making Process

After a diagnosis of ALI is made, heparin should be initiated (5). The Rutherford classification for ALI (Table 1) is a helpful management guide, as defined by the Society for Vascular Surgery and the International Society for Cardiovascular Surgery (8). ALI can be categorized as Viable (class I), Threatened (class II), and Irreversible (class III). Management varies depending on the severity and timing of ischemia. The critical branch point on the Rutherford criteria regarding severity of presentation is the presence of muscle weakness. Generally, preserved muscle strength usually indicates presence of a class I or IIA lesion. Although not an absolute indicator, muscle weakness suggests progression of ALI to class IIB or III. This division in classification between class I to IIA and IIB to III is important, because it traditionally mirrors the decision for an endovascular approach vs. an open operative intervention, respectively (6). Of note, for patients presenting with class III (irreversible ALI), immediate revascularization is not indicated. Instead primary amputation is the recommended course.

Timing of intervention relative to limb salvage is as critical as severity of presentation. In a retrospective review of 822 cases with acute peripheral arterial emboli, logistic regression analysis indicated that patients

Table 1. Rutherford Classification Scheme for Acute Limb Ischemia (8)

Class	Category	Prognosis	Sensory Loss	Muscle Weakness	Arterial Doppler	Venous Doppler
I	Viable	No immediate limb threat	None	None	Audible	Audible
IIA	Marginally threatened	Salvageable if treated promptly	Minimal- to none	None	+/-Audible	Audible
IIB	Immediately threatened:	Salvageable if treated immediately	More than just toes	Mild-moderate	Rarely audible	Audible
III	Irreversible	Limb loss or permanent damage	Profound, anesthetic	Profound, paralysis	Inaudible	Inaudible

presenting with > 6 h between symptom onset and intervention were 40 times more likely to undergo amputation than the group of patients presenting with < 6 h (9).

In conjunction with mapping the patient's examination findings to the Rutherford classification, determining whether the ischemic limb was due to an embolic vs. thrombotic etiology can also be helpful in guiding management. The majority (80% to 90%) of arterial emboli originate in the heart, with many of these patients having underlying heart disease (10). Dysrhythmias, especially in patients with atrial fibrillation who are not anticoagulated, have a high propensity for embolic disease. Arterial disease, including proximal aneurysms and proximal atherosclerotic disease, can both generate emboli leading to arterial occlusion. Generally, embolic lesions fall into the more severe Rutherford class IIB or III, which traditionally requires operative management. This occurs because patients have not formed significant collateral vessels to compensate for the acute disruption in arterial blood flow.

In comparison to acute embolic ischemia, a thrombotic occlusion (typically with underlying atherosclerosis) causing ALI generally has more of a subacute clinical course and delayed presentation. These patients usually have risk factors for, or a known history of, peripheral arterial disease. Over time, they develop compensatory collateral circulation. Consequently, patients with thrombotic ALI tend to present with less severe ischemic signs (Rutherford class I or IIA). Catheter-directed therapy should be considered as the first-line treatment because the patients can presumably tolerate the slower regimen, which can take 12 to 24 h to take effect. Classic clinical manifestations differentiating embolic from thrombotic occlusion are summarized in Table 2 (10).

In this case report, the patient was classified as class IIB ALI because of a combination of sensory changes ascribed to the whole foot (not limited to just toes) and very diminished femoral and delayed popliteal arterial Doppler pulses, despite there being no gross muscle weakness. Instead of electing for an operative approach, a catheter-directed embolectomy was first attempted. Subsequently, catheter-directed therapy with tPA was performed (11). A combined approach of mechanical and pharmacologic catheter-based techniques are becoming more prevalent as an alternative to more invasive and open surgical approaches that typically incur a higher morbidity and mortality, especially as these patients often are older and with comorbidities (10).

The management approach in our case is supported by a 2002 Cochrane review on the initial management of ALI, which determined that there was no significant difference between thrombolysis vs. surgical management with regard to limb salvage or mortality at 30 days, 6 months, and 1 year. This review included five trials (published during 1992 to 1998) and included a total of 1283 patients (12). Complications were higher among the patients receiving the less-invasive thrombolytic approach (tPA or urokinase) vs. surgery, including stroke at 30 days (1.3% vs. 0%), major hemorrhage (8.8% vs. 3.3%), and distal embolization (12.4% vs. 0%). However, initial management with surgery compared to thrombolysis was found to more often require subsequent operative intervention at 30 days (odds ratio = 5.37; 95% confidence interval 3.99−7.22). Furthermore, surgical intervention for ALI in elderly patients was associated with mortality rates as high as 29% (13). Overall, despite similar outcomes, the authors concluded that the higher overall complication rate with thrombolysis must be balanced against the risk of surgery in each patient (8).

Table 2. Classic Differentiating Features in the Clinical Presentation of Acute Arterial Embolism Versus Thrombosis (9)

	Embolism	Thrombosis
Cardiac dysrhythmia	Yes	No
Onset	Sudden	Sudden or slower onset
Severity of signs and symptoms	Severe	Less severe
History of claudication or rest pain	No	Yes
Risk factors for peripheral vascular disease*	No	Yes
Contralateral pulse exam	Normal	Abnormal
Exam findings of chronic limb ischemia†	No	Yes

* Risk factors include cardiac disease, prior myocardial infarction, hyperlipidemia, stroke, family history of peripheral vascular disease, smoking, and diabetes mellitus.
† Diminished hair growth, thin skin, thick nails, and arterial ulcerations.

There has also been an expanding body of literature on the efficacy of catheter-directed therapy for the treatment for ALI of < 14 days duration. Unfortunately, given the diversity of techniques, thrombolytic agents used, and outcome indicators in retrospective reviews, it has been difficult to generate a consensus statement. There are, however, known predictors for success in catheter-directed therapy, defined by > 75% removal of thrombus with antegrade flow. These predictors include the following: previously received catheter-directed therapy, thrombolytics, ABI > 0.33, no loss of motor function, presence of cardiac dysrhythmia, and occluded vascular graft (as opposed to a native artery) (14,15).

It is believed that with current technologies and improved experience with endovascular techniques subsequent to the original 2002 Cochrane review, there may be better outcomes with fewer complications favoring an endovascular approach for Rutherford class I, IIA, and even select IIB ALI patients. Ultimately, the treatment decision by the emergency physician and vascular surgeon should weigh all of these risk-to-benefit factors, as well as the relative feasibility and access to the interventional radiology vs. operative suite. More prevalent today are hybrid operating rooms with angiographic capability. Interventions for ALI will more often involve a multimodal approach, as in the case presented (8).

CONCLUSIONS

The presentation of ALI, although uncommon, requires rapid diagnosis and appropriate management, often in consultation with a vascular surgeon and interventional radiologist, to determine the best diagnostic and therapeutic strategy for optimal results. We presented a case of class IIB ALI and the decision to perform both a mechanical catheter embolectomy and catheter-directed therapy. Additionally, we have provided a comprehensive review of the management of ALI with a focus on risk stratification, the Rutherford classification scheme, and different treatment modalities. Emergency physicians should be aware of advances in endovascular therapies as a recommended option for the treatment of ALI.

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ARTICLE SUMMARY

1. Why is this topic important?

Acute limb ischemia (ALI), although uncommon, can present with profound symptoms, including disabling pain in the setting of acute vascular and neurologic deficits. The presentation of ALI requires rapid diagnosis and appropriate management by the emergency physician, often in consultation with a vascular surgeon and interventional radiologist, to determine the best diagnostic and therapeutic strategies for optimal results.

2. What does this study attempt to show?

Utilizing the clinical findings applied to the Rutherford classification, the emergency physician, in consultation with a vascular surgeon and interventional radiologist, can strategize a methodical approach for better clinical outcomes and often with less-invasive endovascular therapies. We present a case of ALI to illustrate the diagnostic and therapeutic approaches with a summary of the most current literature.

3. What are the key findings?

We have provided a comprehensive review of the management of ALI with a focus on risk stratification, the Rutherford classification scheme, and different treatment modalities. Emergency physicians should be aware of advances in endovascular therapies as a recommended option for the treatment of ALI. The case presented provides an example of class IIB ALI and the decision approach to perform both a mechanical catheter embolectomy and catheter-directed therapy in the interventional suite.

4. How is patient care impacted?

ALI management has evolved during the last decade with advances in diagnostic capabilities and less-invasive endovascular therapeutic options. By approaching and framing the clinical presentation using the Rutherford classification scheme, the emergency practitioner can better articulate the diagnostic and therapeutic options in consultation with a vascular surgeon and interventional radiologist on a high morbidity clinical condition. This review, by case example, provides a detailed summary of the most current literature on managing ALI.