Diagnosis Of Leg Ulcers
A Khachemoune, C Kauffman

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Abstract
In the United States, leg ulcers present a significant clinical problem, occurring at a rate of approximately 600,000 new cases per year. (1) The most common types are venous, arterial, and neuropathic ulcers. Venous hypertension is the primary culprit in venous ulcerations. Peripheral vascular disease due to atherosclerosis with microvascular or macrovascular changes leads to ischemic ulcers. Sensory impairment with loss of protective sensation in the foot and repetitive trauma lead to neuropathic ulcers. Unusual causes of leg ulcers must be considered in the differential diagnosis. To arrive at the diagnosis, the clinician must perform a thorough history and physical examination, and order relevant investigative studies. Good management of chronic leg ulcers depends on correction of identified underlying conditions, long-term multidisciplinary care effort, and integrating traditional and new wound-healing technologies. Most patients with chronic leg ulcers benefit from the use of compression bandaging at a level appropriate to their vascular status. Venous ulcers must be managed with an arsenal of strategies to control venous insufficiency, heal the wound, and prevent recurrence. Surgery with revascularization remains the treatment of choice for chronic ischemic leg ulcers. In the absence of vascular compromise, up to 90 percent of neuropathic ulcers will heal with proper ulcer debridement, treatment of infection, saline wet-to-dry dressings, and relief of weight from the ulcerated area. The available armamentarium for wound care includes over 2000 wound dressing products and elastic compression wraps. Chronic leg ulcer treatment options have been expanded by alternatives available to treating these wounds. These alternatives include hyperbaric oxygen therapy, bioengineered skin substitutes, recombinant platelet-derived growth factors and vacuum assisted wound closure. Patients with large leg ulcers may benefit from skin grafting. Other patients may benefit from ligation and stripping of superficial veins or subfascial interruption of perforating veins.

VENOUS ULCERS
Venous ulcers represent up to 80% of all lower extremity ulcers. (2) Venous ulcers develop slowly. Symptoms may include aching, heaviness, leg-tiredness, cramps, itching, burning, and swelling. These symptoms often worsen with prolonged standing and improve with leg elevation.

When taking the medical history, special attention should be paid to the duration, location and previous history of the ulcers. A history of long duration varicose veins, and/or deep venous thrombosis (DVT) is often present. Acquired and genetic factors known to increase the risk for DVT formation are summarized in table 1. (3) Other causes of venous ulcers include neoplastic obstruction, congenital or acquired arteriovenous fistulae.

Table 1: Acquired and Genetic Risk Factors for Venous Thrombosis

<table>
<thead>
<tr>
<th>Acquired</th>
<th>Genetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>Factor V Leiden*</td>
</tr>
<tr>
<td>Trauma</td>
<td>Prothrombin G20210A mutation*</td>
</tr>
<tr>
<td>Immobilisation</td>
<td>Antithrombin deficiency*</td>
</tr>
<tr>
<td>Obesity</td>
<td>Protein S deficiency*</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Protein C deficiency*</td>
</tr>
<tr>
<td>Hepatic syndrome</td>
<td>Hyperhomocysteinemia*</td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td></td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td></td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyperhomocysteinemia</td>
</tr>
</tbody>
</table>


* Laboratory screening for these factors may be appropriate in patients with the history of recurrent deep venous thrombosis (DVT).

On physical examination, venous ulcers are usually located...
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in the malleolar area. (Picture 1) A typical venous ulcer is usually superficial with irregular or shaggy borders. The drainage is often moderate to heavy. There is often presence of fibrinous material at the ulcer bed. (Table 2) Other findings may include telangiectasia, reticular or varicose veins, edema, and hyperpigmentation, lipodermatosclerosis, venous stasis dermatitis, and atrophie blanche.

Figure 2
Picture 1: Typical venous ulcer, located at the internal malleolus

Figure 3
Table 2: Main characteristics of venous, arterial and neuropathic leg ulcers

<table>
<thead>
<tr>
<th></th>
<th>Venous ulcer</th>
<th>Arterial ulcer</th>
<th>Neuropathic ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>Past history of venous issues + DVT, trauma, surgery in leg, or multiple pregnancies.</td>
<td>History of smoking, intermittent claudication.</td>
<td>History of excision, pressure, and ulcer classification.</td>
</tr>
<tr>
<td>Location</td>
<td>Between the malleolus and the lower calf. Majority of venous ulcers are located above the malleolus.</td>
<td>Frequently occurs distally and can be painful.</td>
<td>Sites of pressure (e.g., metatarsal heads, heel, naso).</td>
</tr>
<tr>
<td>Ulcer bed</td>
<td>Fibrinous material at the ulcer bed with moderate to heavy exudate.</td>
<td>Dry necrotic base.</td>
<td>Variable depth partial thickness of source ulcer involving tendon, fascia, joint capsule or the bone itself.</td>
</tr>
<tr>
<td>Appearance</td>
<td>Sharply defined, irregular margins that can vary from small to nearly encircling the leg. Margins are either flat or have a slight step elevation.</td>
<td>Soaped or punched out with a sharply demarcated border.</td>
<td>Surrounding callus. May be site of tract formation. Prolonged bacterial infection may be associated with underlying osteomyelitis.</td>
</tr>
<tr>
<td>Capillary refill time</td>
<td>Normal (≤3 seconds)</td>
<td>A prolonged capillary refill time (&gt;4-5 seconds)</td>
<td>Normal if no associated arterial disease.</td>
</tr>
<tr>
<td>Surrounding skin</td>
<td>Pigmented (the macular deposition), edema, hypoactive hair (white scar formation), infiltrated lipodermatosclerosis.</td>
<td>Pale, loss of hair, shiny and atrophic skin, cool, dry, weak or absent dorsalis pedis pulse.</td>
<td>Freely palpable.</td>
</tr>
<tr>
<td>ABI* measured by Doppler ultrasonography</td>
<td>Normal. An ABI of ≥0.9 or higher is normal.</td>
<td>ABI of 0.8 or less indicates severe arterial disease.</td>
<td>Normal if no associated arterial disease.</td>
</tr>
</tbody>
</table>

*ABI: (ankle/brachial index): The ankle-to-brachial blood pressure ratio.

PATHOPHYSIOLOGY OF VENOUS ULCERS

Venous hypertension in both the superficial and deep venous systems may be due to one or a combination of the following causes: valve dysfunction, venous obstruction (e.g., DVT), and failure of calf muscle pump function. The mechanism of ulceration in patients with venous insufficiency is unclear. Pericapillary fibrin cuff formation, trapping of white blood cells and growth factors have been proposed as possible mechanisms of ulcerations. (4) Trapping of leukocytes within the microcirculation leads to their subsequent activation. Endothelial cells, presumably activated by hypoxia or other causes, stimulate adherence of leukocytes. The activated leukocytes then release toxic products, with subsequent surrounding tissue injury.

ARTERIAL ULCERS

Arterial ulcers are most worrisome, because of the threat of limb loss. The frequent involvement of the coronary arteries
Diagnosis Of Leg Ulcers

with atherosclerosis is also of concern. Arterial ulcers often affect the toes or shin or occur over pressure points (Picture 2). Arterial ulcers are often seen in elderly. These patients often present with a history of intermittent claudication or a rest pain, which is usually relieved by dependent position. Some patients report that in order to ease the pain to their limbs they have to sit on the edge of the bed and dangle their legs. The patient medical history is often positive for smoking and other risk factors for atherosclerosis like hypertension, hyperlipidemia, and diabetes. A history of minor trauma to the leg initiating the ulcer is frequently reported.

Figure 4
Picture 2: Necrotic leg ulcer (arterial) located at the shin area

On physical examination, the ulcers usually are located on bony prominences. A typical arterial ulcer is deep and has circular or well-demarcated “punched out” margins. The ulcer base is covered with a black, dry necrotic material with minimal or poor granulation tissue. Other findings include weak or absent peripheral pulses, dependent rubor and elevational pallor of the foot, and thickened nails. The skin of the affected leg is often shiny, atrophic, dry, and cold to the touch. Examination of the leg should include palpation of pulses, and determination of range of hip, knee, and ankle movements. Involvement of these articulations with an inflammatory process may explain the pain, which should be differentiated from pain caused by arterial insufficiency. Reduced mobility from arthritis is a factor that is known to prevent healing of ulcers. Also calf muscle pump failure due to musculoskeletal deficiency is often overlooked as a component of venous, as well as mixed arterial and venous ulcers. Arterial ulcers are mainly due to atherosclerosis of large vessels.

NEUROPATHIC ULCER

Diabetics are more prone to develop neuropathic ulcers. Vascular changes are also common causes of diabetic foot ulcers, and both conditions may be present in the same patient. Sensory neuropathy often leads to a loss of protective sensation. Motor neuropathy leading to small muscle wasting leads to an imbalance between flexors and extensors of the lower limb, causing clawing of toes and prominence of the metatarsal heads, thus providing appropriate conditions for ulceration. Sympathetic autonomic neuropathy leads to dry, cracked, and fissured skin over the lower leg. Rarer conditions responsible for neuropathic ulcers include chronic alcoholism with malnutrition, leprosy, tabes dorsalis, spina bifida, and syringomyelia.

Location is important in evaluating the cause of a neuropathic foot ulcer. Usually, plantar ulcers are the result of moderate repetitive trauma underneath a metatarsal head. Medial, lateral, and digital ulcers are often the result of pressure from shoes overlying such osseous abnormalities as bunions and hammertoes. (Pictures 3, 4, and 5)
In patients with ulcers on the sole of the foot, the sole should be examined for signs of ascending infection, including proximal tenderness and appearance of pus on proximal compression of the sole. Surrounding calluses are typical of neuropathic ulcerations, and sinus track formation should be explored by probing the wounds. (7)

Determining the point at which loss of protective sensation develops, and thus the risk of injury increases, is important. The loss of protective sensation is defined as the inability to perceive testing with a 5.07 Semmes-Weinstein monofilament (SWM) standardized to deliver a 10-g force. (11) The SWM is pressed against the skin to the point of buckling. Measurements are usually taken at each of 10 sites on the foot annually. (11) Inability to perceive 4 or more sites is associated with a higher risk of loss of sensation and concomitant risk of ulceration. (11,12) A simplified monofilament examination using only 4 sites per foot (total 8 sites) has been used. (13)

Less common causes of leg ulcers have a wide range of etiologies. Investigation and management of such types of ulcers vary with the underlying causes and often need a multidisciplinary team including a wound specialist.

INITIAL ASSESSMENT OF PATIENTS WITH LEG ULCERS

Most of the information about the etiology of leg ulcers is obtained from the patient’s history and physical examination. If arterial insufficiency is suspected, with the use of a hand-held Doppler the physician can assess the arterial system in the lower extremities. The ankle brachial index (ABI) is determined by dividing the ankle systolic
pressure by the brachial systolic pressure obtained at the same time. This will provide an objective estimate of arterial insufficiency, and will help in making the decision as to whether compression therapy is appropriate. The ABI of a normal artery ranges from 0.9 to 1.2.

Initial laboratory investigations may include a complete blood cell count (to rule out underlying hematologic disorders), erythrocyte sedimentation rate (which is elevated in patients with many diseases including connective tissue diseases and associated vasculitic ulcers, and infectious processes), and a fasting blood glucose. Serum albumin and transferrin levels are very helpful in assessing the nutritional status in elderly patients.

INVESTIGATING LEG ULCERS
NON-INVASIVE INVESTIGATIONS
VENOUS ULCERS

In patients with the history of recurrent DVT screening for selected acquired and inherited risk factors for deep venous thrombosis may be appropriate. (3,14) (See table 1)

Exercise programs, the use of compression stockings, smoking cessation and avoidance of estrogen therapies can greatly reduce risks of recurrent DVT. Long term anticoagulation may be necessary in these patients. (3)

Certain non-invasive methods are useful to confirm the diagnosis of venous ulcers and clarify the anatomical and functional defect. This will help determine further diagnostic and therapeutic strategies. Color duplex ultrasound scanning which is becoming the de facto standard for evaluation of venous obstruction is also used to assess the location and extent of reflux.

ARTERIAL ULCERS

The ABI is a basic test, which can be performed at the initial office visit. Severe ischemia may occur at less than 0.5. (15) In patients with arterial media calcification (mostly diabetics) the ABI may be elevated (> 1.3) due to incompressible vessels. Arterial duplex ultrasound is also used to assess the leg arterial system, and information regarding areas of stenosis is obtained using this technique.

Patients with severe arterial insufficiency, e.g. ABI<0.5 or severe areas of arterial stenosis documented on duplex ultrasound should be referred to a vascular surgeon.

Plethysmography performed in a vascular laboratory with measurements taken at the thigh, calf, ankle, metatarsal, and digital levels will assess disease progression through volume recordings, which are quantified through the pulse volume recorder. This procedure measures the small volume changes that occur in tissues during systole. (8,16)

The transcutaneous pressure of oxygen (TcPO2) is used to help determine the degree of microvascular perfusion, which reflects the metabolic state of the limb. It may be measured with an oxygen electrode coupled directly to the skin of the foot or leg. The limb is adequately perfused when TcPO2 >30 mm Hg. TcPO2 measurements are also obtained to assess improvement after hyperbaric oxygen therapy.

NEUROPATHIC ULCERS

Plain radiographs to rule out osteomyelitis are suggested when there is sinus tracking or when probing to bone is possible. (17) It is important to evaluate underlying blood flow characteristics and determine the need for surgical consultation. Low ABI and TcPO2 significantly increase the odds ratio of amputation in diabetics. (18)

INVASIVE INVESTIGATIONS

Venography may be performed as an investigational procedure prior to valvular surgery. Lower extremities arteriography is indicated in patients with ischemic rest pain, intolerable claudication, impending gangrene, or the presence of non-healing ulcers of suspected arterial origin. (16)

Because leg ulcers are neither sterile nor need to be sterile to heal, a quantitative bacterial culture is more specific, and should be performed once wound infection is suspected. (19) This is performed by curetting or biopsying the bed of the ulcer. The quantitative biopsy is the current gold standard for assessing the quality and quantity of microbial pathogens within a wound. Quantitative biopsies containing greater than 10^5 organisms per gram of tissue are considered significant, and systemic antibiotherapy should be considered. (20)

Ulcers that probe to bone should be considered osteomyelitic until proven otherwise. Radiographs will usually show characteristic changes such as translucency corresponding to areas of osteolysis. The sensitivity, specificity, and likelihood ratios of probing to bone are better than those of plain radiograph and bone scan but are worse than those of 111indium scanning and magnetic resonance imaging. (21) More specific tests such as white blood cell scans are more sensitive than bone or gallium scan.(19) In a comparative study of 107 patients, Sommezoghi et al. (22) found that
99mTc-labeled ciprofloxacin (Infecton) has a better specificity for bacterial infections than WBC scans in detecting infectious foci in bones and joints.

One should keep in mind that even in the presence of osteomyelitis, constitutional symptoms and leukocytosis may be lacking in immunocompromised and some diabetic patients.

**INVESTIGATING ATYPICAL LEG ULCERS**

Guided by the medical history and physical examination, some specific laboratory investigations and procedures may be performed. Significantly elevated antinuclear antibodies, rheumatoid factors, or other more specific immunologic tests may tend to support the diagnosis of vasculitic process. Serologic tests for syphilis, or polymerase chain reaction for mycobacterium DNA may be performed on specimens from an ulcer suspected of being of mycobacterial origin (e.g., erythma induratum of Bazin: Mycobacterial panniculitis with subsequent ulceration usually involving the calves). Cryoglobulins may be associated with hepatitis C and leg ulceration. Therefore, hepatitis C serologies and serum level of cryoglobulins may be helpful tests. Like cryoglobulins, cryofibrinogen may be associated with recurrent leg ulcers, especially if there is a history of worsening of symptoms with exposure to cold. Ulcers due to cryofibrinogenemia may be treated with an anabolic steroid, stanozolol (Winstrol).

Leg ulcers of atypical presentation or those that fail to heal should alert the clinician to consider uncommon etiologies. (1) When a wound fails to heal after three to four months of conventional treatment, biopsy of the ulcer edge (either excisional or multiple punch biopsy techniques) should be performed to rule out malignancy. The most common type of cancer developing in chronic wounds is squamous cell carcinoma. Pyoderma gangrenosum is a non-infective ulcer, which usually presents with undermined borders. It may be associated with inflammatory bowel disease, inflammatory arthropathies, or myeloproliferative disorders. Appropriate work up for associated disease should be considered in patients with pyoderma gangrenosum. Patients with leg ulcers are prone to developing contact dermatitis to dressings. When necessary a patch testing should help determine specific allergens.

**CONCLUSION**

Leg ulcers are very common and physicians should be familiar with the common methods used for their diagnosis and management. Some laboratory investigations may be helpful and can be ordered as part of the baseline work up. Unusual leg ulcers need more specific tests. The management of leg ulcers will be described in “Management of Leg Ulcers”. The Internet Journal of Dermatology, Volume 1 Number 2, 2002.

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**References**

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Author Information

Amor Khachemoune, MD, CWS
Medicine, Division of dermatology, Georgetown University Medical Center

Catharine Lisa Kauffman, MD
Chief, Medicine, Division of Dermatology, Georgetown University Medical Center