Venous Ulcers Associated with Deep Venous Insufficiency

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Case Report

A 46-year-old female schoolteacher and non-smoker presented with an ulcer on the medial side of the ankle. The ulcer had persisted for the past year despite compressive dressings at a hospital wound care center. Ulcers in the same general area had occurred intermittently in the past but had healed with local wound care and dressings. The ulcer was very painful, particularly with dependency of the leg (7/10 over a visual analogue scale) and frequently at night. The patient had made a habit of elevating her legs during the day whenever feasible, and to sleep with her legs elevated on a pillow at night. She had been using a nonsteroidal anti-inflammatory drug once or twice a day at work for pain relief, but lately a narcotic prescribed by her physician was required for sleep at night. Even so, on some nights, she had to "walk off" the pain for 20–30 min before she could fall asleep.

Past medical history: She had been hospitalized on two occasions during the past year for cellulitis of the leg, which required intravenous antibiotics. Her saphenous vein was stripped 15 years ago when the ulcer initially appeared. This resulted in healing of the ulcer but it recurred 2 years later. During adolescence, she sustained a closed tibial fracture of the same extremity during a ski accident and was in a plaster cast and crutches for several weeks. Family history: No one in the family had varicose veins or deep venous thrombosis.

Examination: The patient was found to be healthy except for the affected extremity, which had a large 5 Ð 10-cm indolent ulcer on the medial aspect of the lower third of the leg. The ulcer bed had clean granulation tissue with serous drainage. The ulcer was surrounded by a broader area of hyperpigmentation in the "gaiter" area. No obvious varicosities or "blow outs" were noted. Good pedal pulses were present.

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Question 1
Which of the following is *least* likely in this patient?

A. "Primary" deep vein valve reflux
B. Post-thrombotic syndrome
C. Popliteal artery entrapment
D. Recurrent saphenous reflux from neovascularization
E. Perforator incompetence

The patient was referred to the vascular laboratory, where a detailed duplex venous examination was performed. Extensive reflux throughout the deep venous system in the affected extremity was found. Both the femoral and popliteal valves were refluxive, with valve closure times of 7 s and 6 s, respectively. The great saphenous was confirmed absent with no evidence of tributary or collateral reflux around the short sapheno-femoral stump. Neovascularization was not detectable. No significant perforator reflux was found, and the short saphenous vein was not refluxive. The deep venous system was widely patent without evidence of prior thromboses. Air-plethysmography (APG) results were as follows: venous filling index (VFI90) 7 mL/s; venous volume (VV) 135 mL; ejection fraction (EF) 60%; residual volume fraction (RVF) 48%.

Based on the above findings and the clear failure of conservative therapy to heal the ulcer, surgical intervention was discussed with the patient. She consented to this approach. Other preoperative work-up included a hypercoagulation profile and ascending and descending venography.

Question 2
Which of the following statements is true?

A. Duplex is more specific than descending venography in assessing reflux.
B. Valve closure time (VCT) is a reliable quantitative measure of reflux.
C. Venous filling index (VFI90) with APG correlates best with ambulatory venous pressure.
D. Absence of varicosities or "blow outs" on physical examination rules out neovascularization or perforator reflux as a significant source of reflux.
E. Palpable pedal pulses rule out arterial insufficiency as the etiology in patients with painful leg ulcer.

The patient underwent internal valvuloplasty (Kistner technique) of the femoral vein valve under general anesthesia. Postoperative recovery was uneventful. DVT prophylaxis included low-molecular-weight heparin (LMWH) started preoperatively and continued until discharge, intraoperative intravenous heparin (5000 units), and daily warfarin sodium. Pneumatic compression was started during surgery and continued postoperatively when not ambulatory. She was discharged on 5 mg warfarin with instructions to the local physician to maintain the international normalized ratio (INR) at or above 2.5 for 6 weeks, after which the dosage could be lowered for a target INR of 1.7–2.0. The patient was instructed to wear elastic stockings for at least 6 weeks on a daily basis, after which she could adjust the usage as desired.

The patient was seen on follow-up at 6 weeks, at which time the surgical incision was well healed and the ulcer had become epithelialized to 90% of the original surface area. She requested and was granted permission to go back to full-time work. When seen in follow-up at 4 months, the patient reported that the ulcer had healed completely 2 weeks after the first clinic visit and had remained healed since. She was free of pain and had abandoned regular use of her stockings. She found it necessary to use them only occasionally when she expected her day to be more strenuous than usual. Physical examination revealed good-quality skin coverage over the previous ulcer, and the limb was free of edema. Interval follow-up duplex examination showed competence of the repaired femoral valve with valve closure time of 0.4 s. Popliteal valve reflux was unchanged. Postoperative APG showed that the VFI90 had been nearly normalized at 2.3 mL/s. Other values were essentially unchanged from preoperative levels.

Question 3
Which of the following is *not* true?

A. Postoperative DVT (30 day) is relatively rare after valve reconstruction procedures for correction of "primary" valve reflux.
B. Arm swelling occurs infrequently after axillary vein harvest for valve reconstruction.
C. Valve reconstruction is contraindicated in post-thrombotic veins.
D. Saphenous vein ablation can be safely undertaken in chronic deep venous obstruction (secondary saphenous varix).
E. In combined obstruction/reflux, stent placement to correct the obstruction alone often results in healing of stasis ulceration.

Commentary

The differential diagnosis of venous ulcers includes ischemic ulcers, diabetic foot ulcers, ulcers related to vasculitis from hypertension or other causes, ulcers related to connective tissue disorders (rheumatoid arthritis, scleroderma, etc.), neuropathic ulcers, Marjolin's ulcer, and numerous other conditions that are clinically quite rare. Popliteal *vein* (not artery) entrapment is a rare cause of venous ulcers. [1] The clinical features of venous ulcers are so characteristic and obvious that a positive diagnosis can be made on the basis of clinical examination alone in all but a few cases. When doubt exists, or when combined pathologies are suspected, a punch biopsy of the skin should be performed without hesitation to clarify the situation. Relevant testing for specific connective tissue, immunological or hematological conditions may be required in some cases. Venous ulcers are differentiated quite easily from arterial (ischemic) ulcers in most instances. The former are indolent and recurring with episodes of healing and breakdown and are generally confined to the gaiter area of the leg. In contrast, the arterial ulcer is progressive without periods of remission and has a wider distribution in the leg with characteristic gangrenous or ischemic appearance devoid of granulation tissue and covered with necrotic tissue. There is seldom the surrounding hyperpigmentation or dermatitis that occurs so

commonly with venous ulcers. Palpable pedal pulses virtually rule out ulcers of ischemic origin, with the notable exception of diabetic foot ulcers and less common entities in which vasculitis or small-vessel disease is often implicated (e.g., collagen disorders such as scleroderma and rheumatoid arthritis). It is usually possible, however, to narrow down the possibilities by a combination of clinical features (history, appearance and location of the ulcer), skin biopsy, and specific testing directed toward suspected non-venous pathology. Ankle/arm arterial index and toe pressure measurements may be required in some cases to clarify the issue. Because of their wide prevalence, venous ulcers can and do occur in combination with the other pathologies listed above. To establish the presence of venous ulcers in concert with other nonvenous pathology, it is necessary to confirm that significant reflux is present based on venous duplex examination and venous hemodynamic tests such as ambulatory venous pressure measurement and/or air plethysmography. In combined arterial/venous ulcers, treatment should be directed initially towards improving arterial perfusion.

However obvious the diagnosis, patients with venous ulcers should be evaluated through a detailed assessment protocol to assess severity and form a base for later outcome assessment. Use of CEAP classification [2] and venous clinical severity scoring [3] provides a standardized format to accomplish this. Quality-of-life assessment methodologies [4] in venous disease have been validated and provide a way for outcome assessment from the patient's perspective. **[Q1: C]**

Many patients with chronic venous insufficiency will not volunteer information such as relief of leg pain with leg elevation and stocking use, night leg cramps and restless legs, or their developed habit of sleeping with the leg elevated at night, unless specifically asked. Perhaps because of the chronicity of the condition, these details have become an integral part of their daily lives and may not be mentioned as complaints without direct questioning. Even potentially important information, such as previous attacks of cellulitis or "phlebitis" that occurred years or decades ago and required hospitalization and a period of anticoagulant treatment may not be forthcoming unless specifically inquired, because the patient has forgotten the episode or does not consider it relevant to their current condition. Besides solidifying the diagnosis of venous ulcer, such information may be important in narrowing down the differential diagnosis in doubtful cases or combined pathologies. For example, ischemic rest pain at night is often relieved by hanging the leg over the side of the bed at night, whereas patients with venous pain seldom resort to this practice. Pain of claudication (arterial or venous) worsens with ambulation, whereas patients with limb pain from venous reflux have often learned to "walk off" their nocturnal pain. Venous claudication is estimated to occur in about 15% of patients with chronic venous insufficiency. Climbing up stairs is particularly difficult for these patients. Pain out of proportion to clinical signs is a characteristic of deep venous pathology. Pain, nocturnal leg cramps or restless legs may be the only clinical feature(s) in some patients. Recording the level of pain preoperatively by a visual analogue scale [5] is a simple reliable tool in severity assessment. The type and frequency of analgesic use (narcotic, non-narcotic, non-steroidal) is also useful. Past and current list of medications, particularly estrogen-type hormones and anticoagulants/platelet inhibitors, are relevant parts of the history and useful information in future management.

Limb swelling is a frequent manifestation of venous disease. It is hard to quantify by examination except in very gross terms. Plethysmographic techniques including the commonly used limb circumference measurement are unreliable as swelling is quite variable during the day with the extent of orthostasis. Patients' own perception of limb swelling is strongly influenced by the degree of accompanying pain. Patients themselves may not be aware of swelling obvious to the examiner if painless; conversely, even mild swelling, when painful, may be rated as severe by the patient. For these reasons, quantification of swelling either by history or by examination is subject to considerable variance and error. Although some clinical features are described as unique to lymphedema in texts, differentiation of venous from lymphatic swellings on clinical grounds alone is generally not possible. Furthermore, the two pathologies frequently coexist. Lymphatic dysfunction appears to be secondary to venous obstruction in many cases; relief of venous obstruction can reverse the lymphatic dysfunction. [6] A thorough venous investigation is essential even when lymphoscintigraphy is abnormal.

The investigation of venous ulcers is directed toward positive establishment of venous etiology, identification of regional pathology, and assessment of hemodynamic severity. Hypercoagulability work-up provides guidance to the institution of anticoagulation, its duration and intensity. Duplex examination has replaced venography as the primary investigation for both screening and definitive assessment of chronic venous insufficiency. Overall accuracy of duplex ultrasound is superior to that of descending venography in the assessment of reflux [7, 8]. Duplex examination in the erect position yields more accurate results than does examination in the sitting or recumbent position [9]. Quick inflation/deflation cuffs with pressures set for various levels provide for standardized compression maneuvers and allow measurement of valve closure times; reflux is present when these exceed threshold values for the various valve stations. Disappointingly, valve closure times do not correlate with clinical or hemodynamic severity of reflux [10] and cannot be used in a quantitative way as originally hoped. The size and location of perforators can be assessed by duplex and is superior to physical examination. Patency of venous structures can be confirmed positively and post-thrombotic changes can be identified. Despite evolving refinement, duplex remains a largely qualitative morphologic technique.

Descending venography can document reflux through valve stations. The best results are obtained when the test is performed in the near-erect position with standardized Valsalva maneuver [11]. Comparison with duplex has led to the realization that the test, though sensitive, is not very specific. Descending venography is easily combined with transfemoral ascending venogram for assessment of the iliac veins, which may not visualize adequately by pedal injections of contrast. Even transfemoral venogram is only about 50% sensitive for detection of iliac vein obstructions [12]. Intravascular ultrasound (IVUS) is the gold standard for assessment of iliac veins for stent placement [13].

Ambulatory venous pressure is a global test of venous function. About 25% of patients with venous stasis ulceration have normal ambulatory venous pressure measurement parameters. Factors other than venous reflux, such as compliance, ejection fraction and arterial inflow, affect ambulatory venous pressure [14]. The latter factors are often abnormal in patients with chronic deep venous insufficiency.

Consequently, ambulatory venous pressure often improves after valve reconstruction surgery but complete normalization is less frequent [15]. Measurement of ambulatory venous pressure via the dorsal foot vein has been believed to accurately reflect deep venous pressure changes with calf exercise. Recent data throw considerable doubt on this long-held assumption [16].

Air-plethysmography is a non-invasive test of calf venous pump and can be used to assess surgical outcome [17]. Residual volume correlates with ambulatory venous pressure. However, venous filling index (VFI90) has been a more consistent index of reflux with normalization after corrective surgery [18, 19].

Venous endothelial injury that occurs with deep venous surgery takes about 6 weeks to heal [20]. Patients should be anticoagulated adequately during this vulnerable period. With proper management, the thromboembolic complication rate is surprisingly low [21]. Patients who have suffered from previous bouts of thromboembolism and those with known hypercoagulable abnormalities are under increased risk of recurrent thrombosis and are candidates for long-term or even permanent anticoagulation. **[Q2: A]**

Once thought a rarity, primary deep venous reflux comprises about 30–40% of all deep venous reflux in centers active in deep venous reconstruction. Differentiating "primary" deep venous reflux from secondary or post-thrombotic reflux is problematic. The presentation and clinical features may be similar. Negative history for prior DVT may be unreliable as some thromboses are silent; and others might have been overlooked, ascribing limb pain to trauma or orthopedic surgery that initiated it. Preoperative venography is a poor guide, and surgical exploration of the valve station is often the final arbiter [22]. Some patients with primary reflux develop actual distal thrombosis that can be recurrent. Correction of proximal reflux in this group of patients may alleviate these recurrent symptoms [23]. Conversely, deep venous thrombosis initiates by unknown mechanisms eventual development of reflux in adjacent and remote valve stations [24].

Correction of primary deep venous reflux by internal valvuloplasty was first described by Kistner in 1964. Subsequently, he described an external technique as well. A variety of open and closed techniques for correction of primary and post-thrombotic deep venous reflux are currently in use [25, 26]. The internal valvuloplasty technique has provided excellent results [21, 23, 27–29] and remains the standard. The newer techniques provide a wider choice that may be more appropriate in certain circumstances, and yield clinical results similar to the original internal technique [21, 30]. Direct valvuloplasty may be feasible in some cases of post-thrombotic reflux where the valves have escaped destruction [22, 31]. Axillary vein valve transfer is the standard commonly used for correction of post-thrombotic reflux. It can be used with some modifications even in trabeculated veins with surprisingly good long-term patency and clinical success [32]. Arm swelling after axillary vein harvest is rare. **[Q3: C]**

The recent introduction of vein stent technology has decreased the number of valve reconstructions in our institution. Surprisingly, stent application appears to yield excellent clinical results in a broad spectrum of symptomatic chronic venous disease patients, including those with severe associated reflux [33]. This finding portends a major paradigm shift in the treatment of chronic venous disease. In the last three centuries the diagnosis and treatment of chronic venous disease had

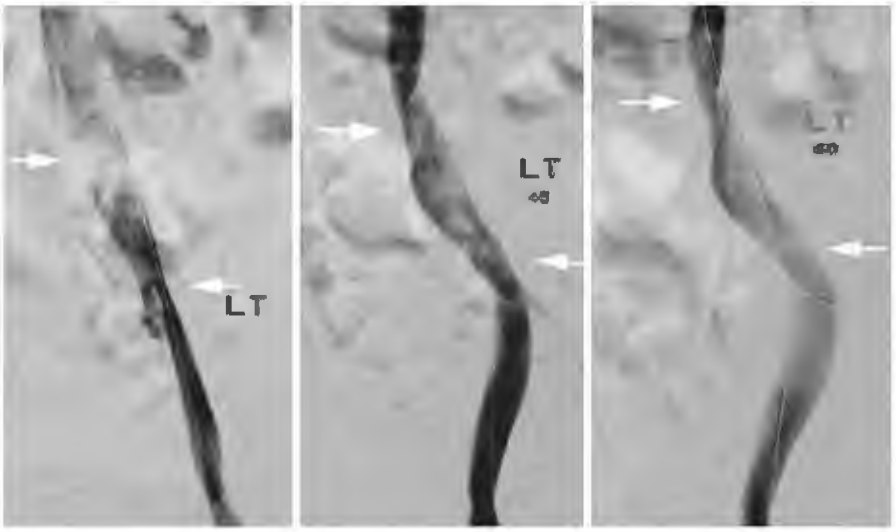

Fig. 51.1 Proximal and distal NIVL. Notice appearance and disappearance of the lesions as the projection is rotated from frontal to oblique lateral [36]

focused on the reflux component. It appears that the prevalence and importance of obstructive component present in iliac veins had been underestimated in the past [34]. This is mainly due to deficiencies of traditional diagnostic modalities. The diagnostic sensitivity of venography even using transfemoral injection of contrast is only about 50% in frontal projections [12, 33]. Higher diagnostic yield may be obtained by using biplane projections (Fig. 51.1). Specialized duplex techniques are required for examination of iliac veins [35] and are not routinely carried out in most institutions.

Post-thrombotic syndrome is now known to be due to a combination of obstruction and reflux in the majority of patients [37]; iliac obstructive lesions are commonly present. Use of intravascular ultrasound (IVUS) has shown Cockett's syndrome (alias May–Thurner syndrome, iliac vein syndrome) is surprisingly frequent in "primary" reflux as well [36]. These lesions may be extrinsic compression, intrinsic webs and membranes or often a combination. The generic term "Non-thrombotic iliac vein lesion (NIVL)" has been suggested instead for this reason [36]. They are thought to result from injury of repetitive pulsations of the proximate artery [12]. Lesions have been detected in all age groups, both sexes, both sides of the limb and in distal as well as proximal iliac vein segments. Retro inguinal lesions may also be present in some patients. Iliac vein lesions are pathogenic in about 30–40% of patients without associated reflux [33]. Absence of reflux or presence of only trivial reflux (e.g. single station segmental reflux) by duplex examination in the context of symptoms should prompt investigation of the iliac vein segment [38]. Modern imaging techniques have shown such lesions to be present in over half the general population [39], most remaining silent during lifetime. The very high incidence (>90%) of these lesions in symptomatic limbs suggests a "permissive" role [36] allowing symptom expression when additional pathology such as trauma, infection, venosclerosis or onset of reflux is superimposed. Permissive lesions are known to play a role in

many disease processes such as, for example, patent foramen ovale (PFO) associated stroke. PFO in silent form is present in about 25% of the general population and becomes symptomatic when paradoxical embolus occurs.

Correction of the obstructive component with stent placement in thrombotic and non-thrombotic cases results in excellent relief of pain and swelling and improvement in quality of life measures. Long-term cumulative stent patency rate is excellent (93% in 603 limbs at 6 years in one series) [8–10]. Stent occlusions are exclusive to postthrombotic limbs and very rare in primary disease.

Even totally occluded iliac veins (Fig. 51.2) and even more extensive occlusions of the inferior vena cava can be successfully recanalized and stented [40–42].

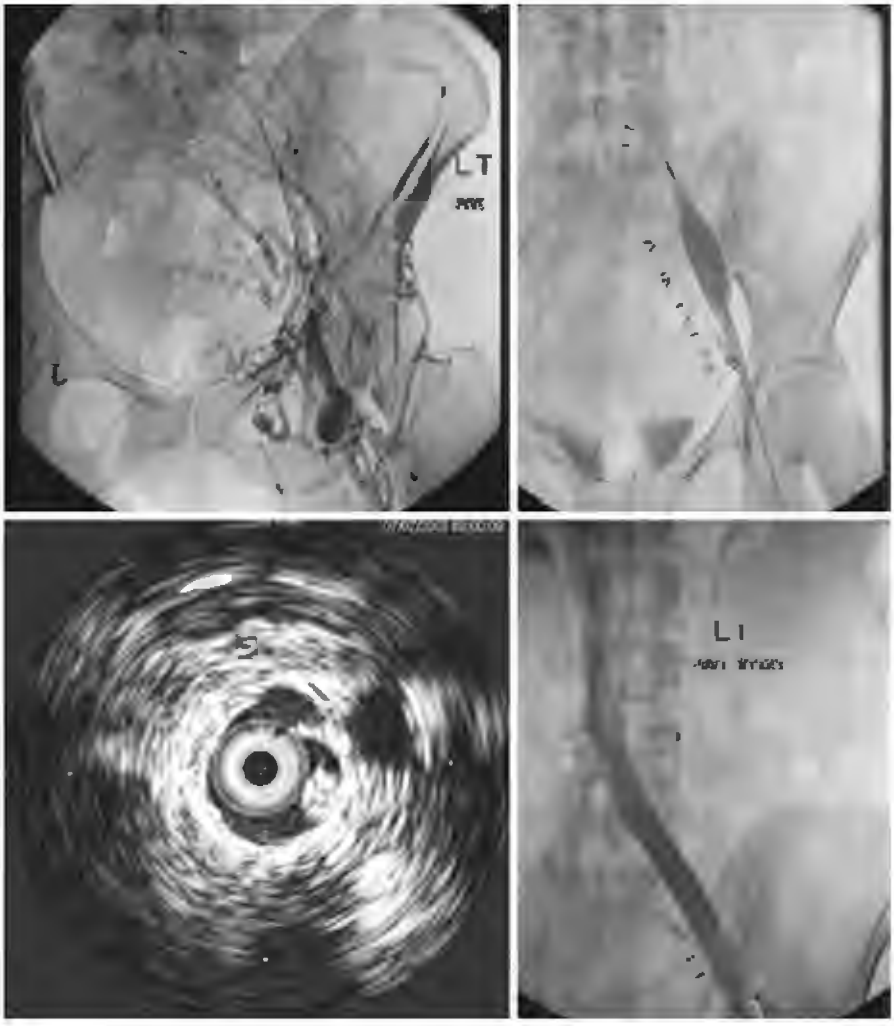

Fig. 51.2 Percutaneous recanalization of occluded iliac vein. Dilation of the recanalized channel and its IVUS appearance prior to stenting are shown [40]

Venous stasis ulcers are generally believed to be the result of reflux, not obstruction. Yet this relatively simple percutaneous outpatient stent technique results in healing of about 60% of venous stasis ulceration [43], even when the associated reflux remains uncorrected. Iliac vein stent placement is currently the first choice in most highly symptomatic patients resistant to compression, whether primary or post-thrombotic in origin. Stent deployment does not preclude later open surgery (reverse, often not the case) such as valve reconstruction or venous bypass if the stent were to fail. It is often combined with percutaneous laser ablation of the saphenous vein when refluxive [44]. Saphenous ablation can be carried out safely, even in the presence of chronic deep venous obstruction (secondary varix) [45].

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