Nonhealing venous ulcer in a patient with dystrophic soft tissue calcification

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ABSTRACT

Venous leg ulcers (VLUs) are lesions of the skin found in regions of venous hypertension. VLUs that fail to heal can become chronic, especially because of calcified deposits in the bed of the ulcer. The unclear mechanism behind the cause of calcification poses a challenge when approaching diagnosis and management. In the present report, we discuss the case of a 58-year-old woman who had presented with a chronic VLU that was resistant to healing despite numerous interventions. During a 3-year period, a multidisciplinary team was involved to provide medical and surgical care. Eventually, she was found to have dystrophic calcification of the VLU. (J Vasc Surg Cases Innov Tech 2022;8:164-6.)

Keywords: Calcification; Leg ulcer; Venous ulcer

Venous leg ulcers (VLUs) are usually found in regions of venous hypertension, which can be secondary to vein insufficiency and/or vein occlusion of the lower extremities.[1] VLUs and chronic nonhealing wounds can significantly affect patients' quality of life and overall health. In the United States, the overall prevalence of venous ulcers has been 1%, with the prevalence increasing to 3% for those aged >65 years.[2] The overall incidence is greater in women than in men. The common risk factors associated with the development of VLUs include age, family history, connective tissue laxity, prior trauma to the lower limbs, physical inactivity, smoking, and cardiovascular disease.[3]

Venous ulcers that fail to heal can become chronic, which are more challenging to manage. Chronic VLUs have the potential to persist after standard treatment, especially because of dystrophic calcification deposits in the bed of the ulcer. Dystrophic calcification is known to arise after trauma, burns, and inflammatory or neoplastic disease.[4] The exact mechanism of dystrophic calcification development remains unknown. It has been estimated that ~10% of patients with chronic venous insufficiency will have subcutaneous calcification.[5] When calcification deposits are present within an ulcer, wound healing will fail because of the physical barrier calcification presents. Also, these crystals can cause a foreign body reaction and inflammatory response, which further prevents healing.[4] Calcified tissue in a VLU bed is challenging to identify and will often be misdiagnosed as fibrotic tissue.[4]

Dystrophic calcification in ulcers is a more serious chronic condition that is often overlooked and underdiagnosed. The unclear mechanism behind the cause of calcification has posed a challenge when approaching the diagnosis and managing dystrophic calcification in a chronic ulcer. In the present report, we have described a case of VLU with dystrophic calcification. The patient provided written informed consent for the report of her case details.

CASE REPORT

A 58-year-old woman had presented to the vascular surgery team with an 18-month left anterior tibial nonhealing VLU. Her medical history was significant for breast cancer after lumpectomy, type 2 diabetes, hypertension, and morbid obesity. She had undergone vein ablation and vein removal in the past. She had a history of acute renal failure that had resolved. Her most recent renal function, liver function, calcium, and phosphorus test results were normal. She had been treated previously with collagen and foam dressings with no improvement. On physical examination, the left anterior tibial ulcer measured 1.4 × 1.6 × 0.1 cm with pink viable granulation tissue, a small amount of serosanguineous drainage, no erythema, and no tenderness in the peri-wound area. She had good peripheral pulses with bilateral lower extremity edema. A left venous ultrasound scan was conducted, and multiple varicosities of unknown origin were present in the mid-calf at the site of the ulcer with some noncompressible varicose veins. The diagnosis at presentation was a venous stasis ulcer. She was treated with an Unna boot.

Two months later, she presented because of skin color changes with two new ulcers on the right calf, one anterolateral

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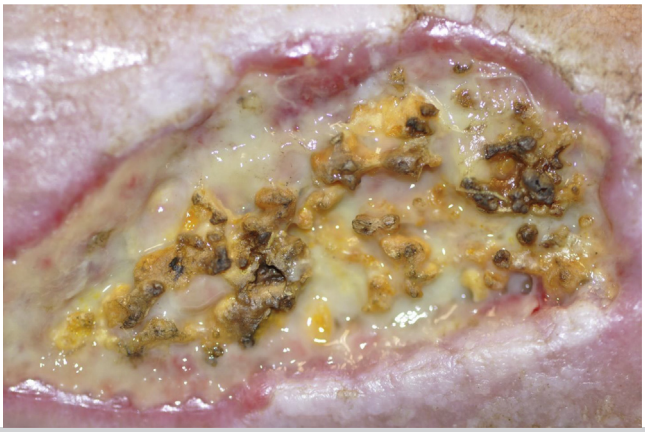

Fig 1. Photograph of a chronic venous ulcer with dystrophic calcification of the left leg.

and one medial. Venous ultrasound showed inflammatory changes at the sites of the right leg ulcers with vein perforators (1.8 mm in diameter) that had originated from the posterior tibial vein that fed into the region of the ulcers. The left leg ultrasound showed multiple varicosities in the mid-calf at the site of the ulcer and segments of thrombosed superficial varicosities with an absent greater saphenous vein.

Because of worsening symptoms on the right leg, she underwent foam sclerotherapy of the right large veins around and within the depth of the ulcer. Compression therapy with Unna boots was continued on both legs. During the subsequent few months, the patient was treated conservatively using compression therapy of different types (Unna boots, two-layer dressings, four-layer dressings, short stretch compression), in addition to horse-chestnut seed extract, pentoxifylline, and an antimicrobial dressing.

At 1 year after her presentation to our service, she presented with an increased size of the left leg ulcer to 3 × 4 × 0.2 cm (from its last measurement of 2.2 × 1.9 × 0.1 cm) and a moderate amount of serous exudate (Fig 1). The right leg ulcers had healed. Venous ultrasound showed significant reflux (>10 seconds) in the saphenofemoral junction, with reflux in one of the perforators (1848 ms) with a 5.8 mm diameter; the remainder of the greater saphenous vein had been previously stripped. The small saphenous vein showed no evidence of significant reflux, with a diameter of 2.5 to 3.3 mm. The deep venous system showed no evidence of thrombosis nor did it have any significant reflux. In addition to conservative therapy, she was offered more foam sclerotherapy, but her insurance declined coverage despite many appeals. One month later, she had developed acute osteomyelitis of the left leg, revealed by a nuclear scan study. She was treated with antibiotics using vancomycin and cefepime. Excisional debridement of the skin and subcutaneous tissue of the ulcerated area with bone biopsy were performed. Pathologic examination showed calcified subcutaneous tissue in the ulcerated area, with no evidence of osteomyelitis in the bone biopsy. Parathyroid hormone, calcium, and phosphate tests were ordered, with normal results.

Four weeks later, improvement was seen, with a decrease in the ulcer size, which had worsened after a few more months. She returned to surgery for excision of the calcified subcutaneous tissue and debridement (Fig 2). During surgery, an underlying layer of calcium was found extending beyond the ulcerated area. The clinical timeline of the ulcer since her presentation at our center is shown in Fig 3.

DISCUSSION

Venous ulcers result from increased venous pressure following the development of reflux and/or obstruction for a prolonged period. This increased venous pressure and inflammation within the venous circulation, vein wall, and valves causes shear stress that results in the activation of adhesion molecules, endothelial cells, and leukocytes, in addition to multiple cytokines, growth factors, and matrix metalloproteinases.[6,7] Extravasation of inflammatory cells and molecules into the interstitial tissue causes inflammation and oxidative stress in the affected region.[6,7] The continual presence of inflammatory cells with poor oxygenation leads to tissue necrosis and interferes with wound healing. Inflammation, in conjunction with issues with blood inflow and/or outflow, nerve damage, high venous pressure, neoplastic changes, and/or infection, impairs wound healing.[8]

Chronic VLUs can fail to heal despite standard treatments. One of the causes for the failure to heal is the presence of dystrophic calcified deposits in the bed of the ulcer. The exact mechanism of dystrophic calcification development remains unknown. It is thought to be related to apoptotic cells failing to regulate intracellular calcium and precipitation of calcium phosphate crystals, which accumulate in the wound.[9,10] Unlike the elevated serum levels seen in metastatic calcification, the serum levels of calcium and phosphate will be normal in the presence of dystrophic calcification. Additionally, other internal organs will not be affected because the calcification will typically be centered at the wound and ulcer area, which supports the dystrophic, rather than the metastatic, calcification diagnosis.[4] The presence of calcified deposits in the wound and ulcer bed interferes with healing. In addition to providing a physical barrier that interferes with healing, the presence of calcified crystals will lead to a foreign body reaction and inflammatory response. The presence of necrotic tissue and changes in collagen, elastin, proteoglycans, or other cellular components cause calcific precipitation, which further interferes with healing.[4] The lack of understanding of the mechanism underlying tissue calcification has posed a challenge to managing chronic ulcers and wounds with calcification.

Calcification within the ulcer and wound bed can be suspected by palpation of the ulcer bed and surrounding tissue. Noninvasive diagnostic methods such as ultrasound and computed tomography have been

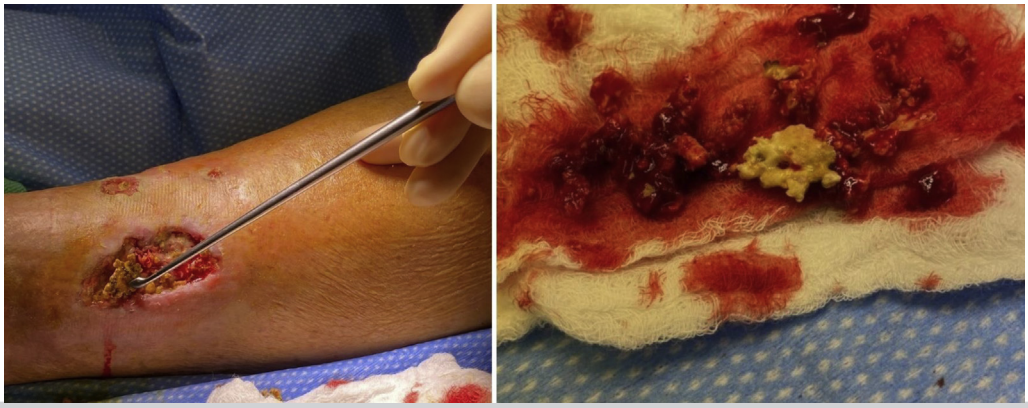

Fig 2. Excision of the calcified subcutaneous tissue and debridement of the ulcer.

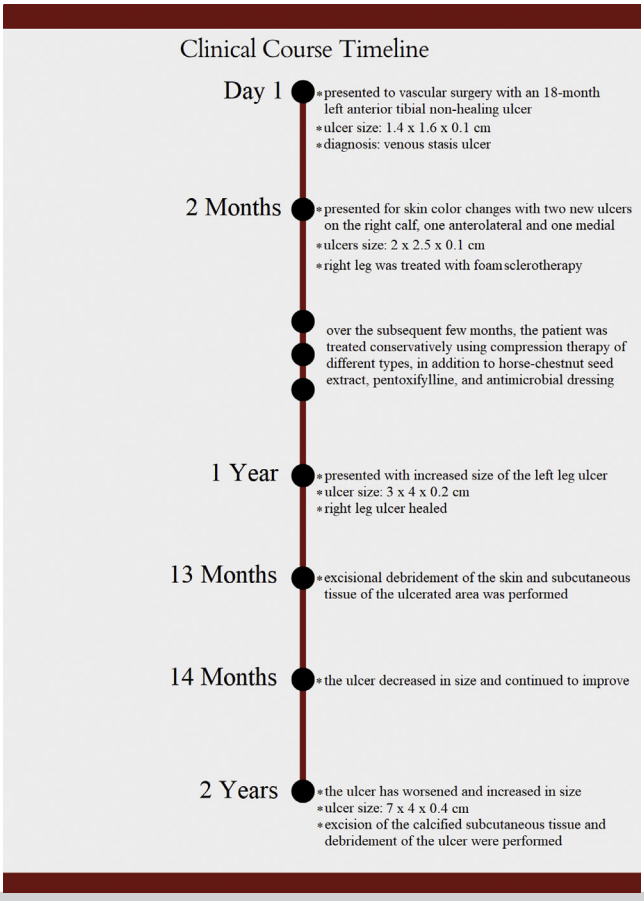

Fig 3. Clinical course timeline of the ulcer since presentation.

recommended for viewing calcification in subcutaneous tissue.[4] The presence of calcium particles in the base of the ulcer should raise the suspicion of subcutaneous tissue calcification.

Nonhealing ulcers with calcification pose a challenge to treatment because limited literature is available to support treatment recommendations. An initial conservative approach is a hydrogel dressing for moisturizing the wound and facilitating autolytic debridement or breakdown of damaged tissue in the wound site using the body's natural enzyme defense system.[4,11] Physical removal of the calcifications is another recommended treatment approach; however, removal can be severely painful and must be conducted according to patient tolerance. If patients cannot tolerate mechanical removal, surgical treatment with calcification removal could be necessary.[4] Similar to advanced nonhealing ulcers, calcified VLUs can also be treated by complete surgical excision of the ulcer and its bed with coverage of the area via split-skin grafting. However, the potential for calcification and ulcer recurrence still exists.[4,12]

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