

C L I N I C A L M A N A G E M E N T

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Martorell Hypertensive Ischemic Leg Ulcer: An Underdiagnosed Entity[©]



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PURPOSE:

To enhance the learner's competence with knowledge of care for patients with Martorell hypertensive ischemic leg ulcers.

TARGET AUDIENCE:

This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.

OBJECTIVES:

After participating in this educational activity, the participant should be better able to:

1. Demonstrate knowledge of the pathogenesis of Martorell hypertensive ischemic leg ulcers (HYTILU) and differentiation of this ulcer from other causes of painful leg ulcers.
2. Apply current treatment recommendations for Martorell HYTILU to patient case scenarios.

ABSTRACT

Martorell hypertensive ischemic leg ulcer represents rapidly progressive and extremely painful ulcers that are frequently underdiagnosed. These occur most commonly on the lateral-dorsal calf and are associated with hypertension and diabetes. This article will synthesize a review of the literature for the accurate diagnosis and treatment of this painful debilitating condition.

KEYWORDS: leg ulcers, Martorell hypertensive ischemic leg ulcers

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INTRODUCTION

Chronic wounds are a major healthcare problem and represent the highest diagnostic group direct medical cost for dermatological disease. A 2004 report from the American Academy of Dermatology¹ reported that wounds were the most financially costly of all skin diseases.

The differential diagnosis of leg ulcers covers a wide range of diagnoses, posing a difficult diagnostic challenge. In a retrospective chart review study of 950 patients with wounds who attended a regional wound clinic in Toronto, Ontario, Canada, 526 patients had leg ulcers with different etiologies, including venous leg ulcers, lymphedema, peripheral vascular disease, trauma, cancer, pyoderma gangrenosum (PG), vasculitis, and other causes. The majority of leg ulcers (75%) were due to vascular etiologies.² Although venous leg ulcers are the most common etiology for leg ulcers, the differential diagnoses are vast. The clinical presentation, the underlying etiology, and pathological manifestations of the ulcers are the major clues to determine the underlying disease. The lack of healing in 4 to 12 weeks, despite adequate treatment, should alert clinicians for further workup regarding unsuspected diagnosis.³ Arterial leg ulcers have a characteristic punched-out appearance and often occur on the anterior shin, dorsum of foot, or over a bony prominence. Pyoderma gangrenosum typically starts as a papule or pustule and rapidly enlarges and ulcerates. The evolving ulcer has a bluish raised and rolled margin with an undermining edge and cribriform base. Vasculitic lesions are often multiple, pruritic, and necrotic, whereas the malignant lesions are slow expanding and commonly painless. The sickle cell ulcers are clinically similar to venous leg ulcers with extreme pain due to microvascular occlusion. Calciphylaxis typically presents as painful, red, violaceous, and mottled indurated plaques in a livedo reticularis-like pattern. These lesions may rapidly break down into painful ulcers and necrosis. Martorell ulcer is a

painful black eschar with necrotic base that presents commonly on the laterodorsal aspect of the leg (Table 1).

Martorell hypertensive ischemic leg ulcer (HYTILU) is a less common and potentially underdiagnosed cause of leg ulcers. It is characterized by localized subcutaneous arteriosclerosis⁴ and needs to be distinguished from other causes of leg ulcers. Patients with a Martorell ulcer characteristically have hypertension and are usually on antihypertensive medications. Clinically, they present with very painful wounds on the lateral-dorsal aspect of the calf or in the Achilles tendon region with bilateral involvement in 50% of cases.⁴ Early diagnosis of this ulcer is important to avoid unnecessary pain, suffering, and treatment measures and to guide appropriate therapy. Skin grafting for this type of ulcer is a relatively new treatment approach noted in the literature. Skin grafts most effectively alleviate the otherwise often intractable pain from the ongoing and spreading skin infarction. Alternatively, after checking the perfusion, some clinicians perform extensive curettage under local anesthesia in the clinic setting. In cases with extensive necrosis, the use of intravenous sodium thiosulfate should be considered.

The assessment and treatment of painful ulcers on the lateral-dorsal surface of the lower leg are a challenging scenario. Correct diagnosis and treatment of the cause are the main steps in the wound management. It is important to include Martorell HYTILU in the differential diagnoses of these painful ulcers that also include PG, calciphylaxis, sickle cell, vasculitis, and vasculopathies (Table 1). A proper "deep" wound biopsy (elliptical biopsy, 5 × 0.5, including all skin levels down to fascia) across the ulcer edge and necrosis confirms the diagnosis and helps to rule out other etiologies. In a study by Hafner et al⁴ on 31 patients, 52% of diagnosed Martorell ulcers were referred with a suspected diagnosis of PG. Martorell ulcers are associated with hypertension in all of the patients, and 58% had a diagnosis of diabetes mellitus. In this study by Hafner et al,⁴ a uniform histopathology appearance of subcutaneous arteriosclerosis with thickened arteriole walls at the cost of a narrowed lumen was documented. In approximately 70% of histologies, the involved subcutaneous arterioles also showed a highly characteristic form of medial calcification.⁴

Obliterating lesions of small vessels have been reported in HYTILU.⁵ Although associated with hypertension, a high prevalence of hypertension and low incidence of Martorell ulcer suggest that hypertension alone is not the cause of this small vessel obliteration. Early recognition and diagnosis of this leg ulcer are important to avoid unnecessary suffering and to guide the approach to therapy. HYTILU will be more commonly recognized with the appreciation of its existence and introduction of a set of criteria to facilitate their diagnosis.

Table 1.**COMMON DIFFERENTIAL DIAGNOSES FOR MARTORELL HYPERTENSIVE ISCHEMIC LEG ULCER**

Cause	Common Location	Clinical Characteristics	Pain	Association	Tests
Venous	Medial malleolus Lateral malleolus/ lower gaiter area	Shallow, granulation tissue base Serpiginous margin Woody fibrosis Venous varicosities Pitting edema Hyperpigmentation	+	Varicose veins Previous surgery Deep vein thrombosis Obesity Multiple pregnancy	Venous Doppler to demonstrate incompetent valves; superficial, perforator, or deep Occasionally venous disease is due to clots or occluded vessels
Arterial	Anterior shin or trauma/infection location	Punched-out, fibrous base Deep ulcer	+++	Smoking Coronary artery disease	Arterial Doppler Angiography Computed tomography angiography Magnetic resonance angiography
Martorell	Lateral-dorsal of shin	Shallow, necrotic Rapidly enlarging Deep necrosis Palpable pulses	++++	Hypertension Diabetes	Often normal ankle-brachial index unless coexisting arterial disease Deep wedge biopsy to identify small vessel changes and skin necrosis
Pyoderma gangrenosum	Any location	Rapidly enlarging Rolled (metal gray) border that evolves into a central ulcer	+++	Inflammatory bowel disease Rheumatoid arthritis Myeloproliferative disorders 50% idiopathic	Diagnosis of exclusion: clinical picture/ associations with a skin biopsy to rule out other disorders (eg, infections, vasculitis)
Vasculitis	Often distal with often symmetrical lesions	Palpable purpuric lesions Fixed urticarial/blisters Necrosis, ulceration Usually bilateral	++	Hepatitis C/other infections Connective tissue disorders, drugs, malignancy 50% other organ involvement; common to involve joints, liver/kidney (eg, Henoch-Schlein purpura)	Biopsy for regular histology and immunofluorescence C-ANCA P-ANCA

Continues

Table 1.**COMMON DIFFERENTIAL DIAGNOSES FOR MARTORELL HYPERTENSIVE ISCHEMIC LEG ULCER, CONTINUED**

Cause	Common Location	Clinical Characteristics	Pain	Association	Tests
Sickle cell	Medial malleolus	May have central necrosis and scarring with frequent coexisting venous disease or infections	++++	Sickle cell anemia Pulmonary hypertension	Sickle prep Hb electrophoresis
Malignant	Any location	Slow expanding Crusted for squamous cell carcinoma Rolled border and telangiectasia for basal cell carcinoma Pigmented lesion with asymmetry, irregular border, color variability (black, blue, red, white) for melanoma	+	Photodamage Previous osteomyelitis Previous radiotherapy edge of a graft or other area of chronic inflammation	Diagnostic biopsy, >1 biopsy may be necessary to ascertain a diagnosis
Calciphylaxis	Any location	Livedo reticularis-like pattern peripherally that evolves into central necrosis bilateral symmetric	+++	Chronic renal failure and renal impairment or on dialysis Secondary hyperparathyroidism	Biopsy
Vasculopathy	Lower leg	Livedo reticularis of the vascular supply leading to local areas of atrophy and necrosis	++	Abnormal circulating proteins: anticoagulant, cryoglobulins, cold agglutinins	Biopsy Appropriate serum factors

After reading this article, clinicians will be better able to assess the pathogenesis of Martorell HYTILUs, differentiate Martorell ulcer from other causes of painful leg ulcers, and evaluate the current treatment for Martorell HYTILUs.

Information for this review was gathered from textbooks; PubMed, EMBASE, and MEDLINE literature searches; and expert opinion. The PubMed, EMBASE, and MEDLINE searches were performed using a variety of combined search words including “Martorell ulcer,” “hypertensive ischemic leg ulcer,” or “angiodermite nécrotique.” Relevant articles are cited in the text where appropriate.

CLINICAL PRESENTATION

The 1985 study by Duncan and Faris⁶ demonstrated that patients with HYTILU have a normal ankle brachial index but have small and medium blood vessel changes. There is an in-

creased local vascular resistance, and the vasoconstriction may influence localization of the ulcers. HYTILUs are extremely painful, necrotic, and rapidly spreading on the lateral-dorsal aspect of the leg (Figure 1).^{4,7} The pain is usually disproportionate with different characteristics than typical arterial ulcers. Patients often are heavily dependent on painkillers, including narcotics such as morphine, for years.⁸ The pain is not exacerbated with exercise, limb elevation, or other typical activities that aggravate arterial ischemic leg ulcers.⁹

Martorell HYTILU was originally described in females, aged 50 to 70 years, with a history of hypertension.^{7,10} However, in a recent epidemiological prospective cohort study of 59 patients with HYTILU,¹¹ the mean age of patients was 74.5 years. Moreover, newer studies cannot confirm a female preponderance.⁴ In addition to the patient with metabolic syndrome that includes hypertension and diabetes, nonobese subjects with long-standing

Figure 1.
TYPICAL CLINICAL ASPECT OF MARTORELL
HYPERTENSIVE ISCHEMIC LEG ULCER



well-controlled hypertension have developed Martorell HYTILU. A plausible explanation for the rather late occurrence of Martorell HYTILU would be that these patients have escaped the typical macrovascular events of long-standing hypertension because their blood pressure may have been well controlled. Thus, Martorell HYTILU may be understood as a very late complication in well-controlled hypertension. In a recent study,¹⁰ the wound duration before the diagnosis was 11.1 weeks, and the mean wound surface area 19 cm.^{3,11} The vast majority of patients (94.4%) had hypertension, and 39.7% had associated diabetes mellitus. The lower-extremity pulses were present in 91.5% of patients, indicating less involvement of the large arterial vessels.

The physical examination of a Martorell ulcer typically reveals a black eschar with a necrotic base and purplish-red edges.⁴ It may initially present as a painful red blister that becomes blue and finally ulcerated.^{5,8} Ulceration often is preceded by a livedo reticularis or net-like appearance of the vasculature, pigmentation, and “shin spots.” The necrotic area is often progressive, and satellite lesions may occur within the livedo reticularis zone of involvement. The typical location in more than 90% of cases is the lateral-dorsal lower leg and the Achilles tendon area.^{4,7} Medial and anterior locations also occur.⁴ Local skin ischemia and infarction cause very strong and almost intractable pain, independent from the position or activity of the leg.⁶ These extremely painful ulcers commonly disturb the sleep, a fact that helps in differentiation from venous leg ulcers.

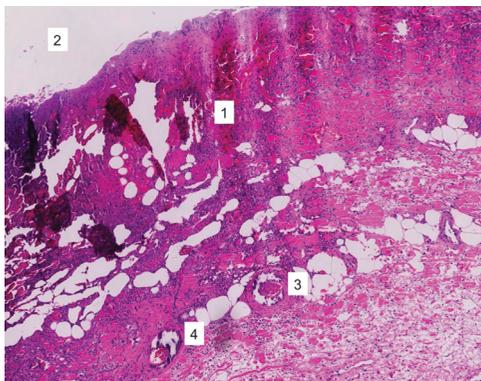
Pyoderma gangrenosum is a differential diagnosis for Martorell ulcer because of clinical similarity—a painful ulcer with a progressive violaceous border.¹² Confounding Martorell HYTILU with PG may have detrimental consequences for the patient because treatment is diametrically different. Debridement and surgical management are the key in the management of Martorell ulcer, whereas it is contraindicated in PG. Pyoderma gan-

grenosum is a neutrophilic disorder, and debridement can provoke pathergy phenomenon and worsening of the ulcer.¹² On the other hand, misdiagnosing an inflammatory type of skin ulcer, including PG, that is treated with systemic immunosuppression exposes the patients with Martorell ulcer to the risk of sepsis.⁴ In a study by Hafner et al,⁴ the 4 types of painful ulcers related to ischemic subcutaneous arteriolosclerosis: (1) Martorell HYTILU, (2) calciphylaxis with distal skin necrosis in chronic renal insufficiency, (3) nonuremic calciphylaxis in morbid obesity with proximal skin necrosis (eutrophication: body water enriched with nutrients or anorganic substances leading to calcification), and (4) calciphylaxis with proximal skin necrosis, were compared with PG on pathophysiological features.^{3,4} Martorell HYTILU and nonuremic calciphylaxis with morbid obesity are both associated with coexisting hypertension. Moreover, patients with nonuremic calciphylaxis and morbid obesity frequently have diabetes.^{10,13} In both Martorell HYTILU (distal skin necrosis) and nonuremic calciphylaxis and morbid obesity (proximal skin necrosis), ischemic subcutaneous arteriolosclerosis represents the common hallmark of these conditions. Calciphylaxis in its distal and more critical proximal form demonstrates clinical and histological features close to those in Martorell HYTILU; however, it is by definition associated with chronic renal failure or a history of a kidney transplant. By comparison, PG commonly occurs in different settings, including patients with inflammatory bowel disease, hematoproliferative disorders, or rheumatoid arthritis, with smoking being a risk factor (RF).¹⁴ Approximately 50% of persons with PG are idiopathic with no apparent association.¹⁵ Pyoderma gangrenosum shows a more superficial type of skin necrosis lacking subcutaneous ischemic arteriolosclerosis and responds to immunosuppression.

DIAGNOSIS

The diagnosis of HYTILU is based on the typical history and clinical presentation and confirmed by obtaining a large elliptical biopsy specimen (5 × 0.5 cm) down to the fascia, starting from healthy skin at the wound border and extending into the necrotic area. The specimen should be left intact and embedded for histological examination with a longitudinal orientation.⁴ Oftentimes, biopsies are made too superficial, such as a punch biopsy from the wound base, and may thus miss the typical histologic elements of Martorell HYTILU, particularly subcutaneous occlusive arteriolosclerosis. In contrast, in superficial biopsy samples from the wound base, necrotic dermis with sheets of neutrophil granulocytes may be found, “confirming” the erroneously supposed diagnosis of PG. In fact, in a Martorell ulcer series, 50% of Martorell ulcers were diagnosed as PG, and 20% were misdiagnosed as necrotizing vasculitis.⁴

Figure 2.
**HISTOLOGIC HALLMARKS OF MARTORELL
HYPERTENSIVE ISCHEMIC LEG ULCER**



Skin infarction (1) leading to leg ulceration (2) caused by subcutaneous arteriosclerosis (3,4). Hypertensive arterioles show thickening of the vessel wall to the cost of the lumen (3), thrombosis (3) and in 70% of histology slides also medial calcification (4).

The hypertensive ischemic ulcer histology typically demonstrates necrosis or necrobiosis (death of cells within the tissue) of all 3 skin layers (epidermis, dermis, and subcutis). The histopathologic hallmark is the presence of arteriosclerotic arterioles with a thickened vessel wall associated with a narrow vessel lumen. These vascular changes are most consistently identified in the subcutaneous fat layer. In 70% of the histology slides, some arterioles also show a striking medial calcinosis that is often associated with hyperplasia of the intima (Figures 2 and 3).⁴

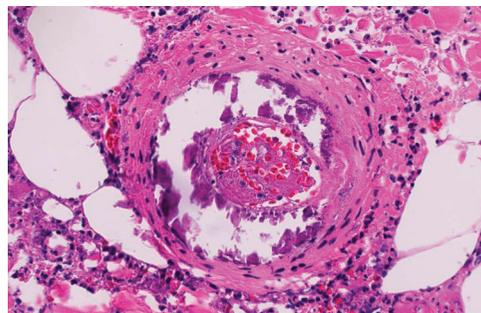
Patients with HYTILU have the same cardiovascular RFs as those with peripheral arterial disease or those with coronary heart disease, but hypertension (in 100%) and diabetes (approximately 60%) are the leading RFs in HYTILU patients. Therefore, it is not surprising that approximately 50% have peripheral arterial disease of the legs at the same time. Vascular assessment is required at the start of any leg ulcer management plan, and patients with relevant large vessel arterial occlusions need consideration of revascularization procedures.^{4,8} Although a palpable pulse generally indicates a foot arterial pressure of 80 mm Hg or higher, the presence of a pulse may not always exclude a coexisting arterial compromise that may benefit from treatment. Although a foot pulse might be palpable, the nonhealing wound may be situated in a different angiosome (an area of skin that has a blood supply from a branch of an artery) that requires revascularization to facilitate ulcer healing (angiosome model).^{16,17}

MANAGEMENT

Surgery is the most rapid and effective treatment for medium (>3-cm diameter) or large (>6-cm diameter) Martorell HYTILU.^{4,18} Necrotic skin is completely removed, leaving a surgical wound that normally extends to the fascia and a macroscopically healthy-looking wound border. Split-skin graft can follow immediately after necrosectomy (removal of the dead tissue) during the first surgery or be postponed after wound conditioning with optimized local wound management as outlined in the wound bed preparation paradigm.¹⁹ This may include local negative-pressure treatment in selective cases.^{4,8}

Pain reduction is of paramount importance and frequently noted on the first postoperative day. It is remarkable that some patients no longer require pain medication after a couple of days (even patients previously requiring narcotic agents including morphine and related substances). The medical management of wound-associated pain is based on the management of both nociceptive or stimulus-dependent (gnawing, throbbing, aching) and neuropathic or spontaneous pain (burning, stabbing, shooting). Nociceptive pain is treated with the World Health Organization's pain ladder medications including aspirin, nonsteroidal anti-inflammatory drugs, and short- and long-acting narcotics.¹⁷ The neuropathic pain is treated with tricyclics, primarily second generation (nortriptyline, desipramine), gabapentin, pregabalin, or other antiepileptic agents. The impact of chronic persistent pain can be devastating and affect the patient's quality of life significantly. Pain control is a key factor in the wound bed preparation paradigm. Following that guideline, clinicians are obliged to provide adequate pain control for patients by using an

Figure 3.
**CLOSE VIEW TO SUBCUTANEOUS ARTERIOLE WITH
HISTOLOGIC HALLMARKS OF MARTORELL
HYPERTENSIVE ISCHEMIC LEG ULCER**



This subcutaneous arteriole shows an increased wall-to-lumen ration (thick wall to the cost of a narrow lumen), medial calcification, intimal hyperplasia, and a partly recanalized thrombosis.

appropriate modality until the patient is ready for surgical treatment. Blood pressure control, smoking cessation, and compression therapy (when associated with coexisting venous disease) are part of the general management of Martorell HYTILU.^{10,19}

All wounds are colonized with bacteria. They pass through the spectrum of contamination, colonization, superficial critical colonization, and deep and surrounding tissue infection. Wound healing requires an appropriate bacterial balance. The number and nature of the pathogens, as well as host resistance, determine the risk of infection. Infection is more prevalent in chronic wounds with decreased blood supply and needs to be addressed in the wound management strategy.¹⁷ Wounds with increased bacterial burden may respond to topical antimicrobials, and deep infection usually requires the use of systemic antibacterial agents.¹⁷

Dagregorio and Guillet¹⁸ reported the results of surgical treatment followed by immediate mesh grafting in 20 patients. In all cases, pain disappeared within 1 week after surgery. In 75% of cases, the ulcer had completely healed upon leaving the hospital after an average postoperative period of 16 days. At the final follow-up, the ulcers of all the remaining 9 patients had completely healed (Table 2).

Hafner et al⁴ reviewed the documents from 330 patients with leg ulcers, 31 with diagnosis of HYTILU based on clinical examination and confirmed by histopathology. In this retrospective study of patients between 1999 and 2007, 52% of the hypertensive ischemic ulcer patients had bilateral involvement. All patients had hypertension, and 58% had diabetes. Subcutaneous stenotic arteriosclerosis was a unique histology finding in all cases. Twenty-eight of 31 patients (94%) underwent 1 or repeated debridement procedures, by surgical excision (larger ulcerations) or a ring curette (smaller or medium wounds), at the bedside or in the operating room. In this series, the majority (85%) received autologous split-thickness grafts. The overall healing rate was reported as 91%.

It is, however, most important that clinicians and patients realize that surgery for HYTILU may be fast-tracked, compared with its natural course, but it may also be time consuming and cumbersome (including skin grafting). After surgery, the split-skin graft often looks completely viable for a week or so before the edges start to become necrotic on an area averaging 1 to 2 cm as a sign of ongoing necrotic process at the excision margins. This has to be discussed with the patient, as well as the fact that multiple split-skin grafting may be necessary. The patient needs to be aware of the natural history of the disease and the potential surgical complications before they give their informed consent for surgery. The dramatically decreased pain level after the first surgical intervention usually prevents patients from being disappointed when future procedures are required.

The role of anticoagulation therapy to enhance the small and medium vessel circulation has been discussed in different studies. It has been hypothesized that vitamin K antagonists, as they are broadly used in oral anticoagulation, also inhibit a vitamin K-dependent calcification-protecting protein.²⁰ Advanced therapies, such as hyperbaric oxygen²¹ and intravenous infusions of prostaglandin E₁,²² have been used with success in a limited number of cases.

Becaplermin is a recombinant platelet-derived growth factor with some evidence to facilitate wound healing. In a study by Senet et al,²³ the topical becaplermin gel was compared with hydrogel on 64 patients with HYTILU. No statistically significant difference was observed in 12 weeks between the groups on topical becaplermin compared with topical hydrogel. In a case report, where spinal cord stimulation was primarily used as a treatment for ischemic chronic pain, healing of HYTILU was eventually achieved with a proposed device-related stimulation of wound healing.²⁴ The electrical stimulation related to wound healing stimulation would require further controlled studies in a group of patients before it is accepted as a treatment for this disorder (Table 2).²⁴

It has been suggested that, in maintenance wounds (wounds in which clinicians cannot immediately correct the cause because of patient or healthcare system factors), the local wound care should be nontraumatic and gentle.¹⁷ In this case, the patient is waiting for definitive treatment, and the local wound care goals are different. Strategies should include nontraumatic removal of slough but not an aggressive debridement of tissue that may extend the ulcer. In addition, the local wound care should include reduction of bacteria and moisture. Cleansing with saline and/or water may be followed by the use of topical antiseptic (such as povidone iodine or polyhexamethylene biguanide). In this case, the prevention of deep and surrounding infection is more important than tissue toxicity of the antiseptic agents because infection may be limb- or life-threatening.¹⁷ However, it must be stated that Martorell ulcers should only temporarily qualify for the concept of maintenance wounds. Appropriate surgical treatment is associated with up to 100% healing rate in a case series of HYTILU.¹⁸ Hafner et al⁴ suggested that systemic antibiotic therapy was standard during the perioperative period of necrosectomy and skin graft.

It should be emphasized that the majority of clinicians familiar with Martorell HYTILU regard skin graft as the most effective single treatment measure to alleviate the often-excruciating pain these patients suffer.^{4,18} Therefore, it is important to spread the awareness of the diagnosis of Martorell HYTILU among wound specialists around the world and to give these patients rapid access to decisive and effective treatment.

Table 2.**DIFFERENT TREATMENT OPTIONS FOR MARTORELL HYPERTENSIVE ISCHEMIC LEG ULCER**

(SUMMARY OF RELEVANT LITERATURE 1989 TO PRESENT, SEE METHODS FOR SEARCH TERMS)

Author, Year	Treatment	Study Design	Study Population	Results	Conclusion
Senet et al, ²³ 2011	Platelet-derived growth factor BB once daily 1 to 8 weeks	RCT (vs hydrogel dressings)	64	5 of 28 healed with becaplermin 3 of 31 healed with hydrogel	Topical becaplermin gel is not superior to hydrogel in the management of Martorell ulcer
De Andres et al, ²⁴ 2011	Spinal cord stimulator	Case report	1	Pain relief Decrease ulcer size	Increase distribution of blood flow to the ischemic area and/or normalization of the activity in the nervous system
Pacifico et al, ²² 2011	Prostaglandin E(1) Group A antihypertensive versus group B prostaglandin E(1)	2-group study (6 hypertensive; 4 prostaglandin E[1])	10	Wound surface area reduction Pain control	Intravenous infusion of prostaglandin improves peripheral perfusion
Hafner et al, ⁴ 2010	Surgical debridement and split-thickness skin graft	Retrospective case series	31	94% complete healing	Martorell ulcer can easily be confused with pyoderma gangrenosum
Dagregorio and Guillet, ¹⁸ 2006	Mesh split-thickness skin graft	Retrospective case series	20	14 of 20 complete healing in 2 wk after discharge and 100% pain relief	Early mesh grafting of hypertensive leg ulcers is beneficial, because healing is very quick, and the pain will disappear quasi-instantly
Frada et al, ²¹ 1989	HBO	Case report	1	Healed	HBO helped healing of Martorell ulcer in 1 case study and personal experience (R.G.S.)

Abbreviations: HBO, hyperbaric oxygen; RCT, randomized controlled trial.

Conservative therapy may be appropriate in 2 situations, namely, rather small Martorell ulcers (up to 3-cm diameter) and the progressive wound borders in freshly grafted patients, as long as the situation does not deteriorate. In patients who have extension post grafting, a second graft seems more promising in shortcutting the otherwise extremely long conservative treatment period.

Conservative treatment consists of regular limited debridement, topical anti-infective measures, and the application of nonadherent gauzes, or the potential use of topical negative-

pressure devices. Topical occlusive dressing treatment should be discouraged because this approach can lead to maceration and critical colonization in the setting of compromised wound borders or base (Table 3).

Recently, the use of sodium thiosulfate has been suggested to treat the very extensive proximal forms of nonuremic calciphylaxis in morbid obesity (eutrophication) and of classic calciphylaxis in its proximal form.^{25,26} Sodium thiosulfate is an inorganic salt that dissolves calcium phosphate. It can be intravenously administered or mixed with dialysis fluid for

Table 3.
THERAPEUTIC APPROACH BASED ON WOUND BED PREPARATION PARADIGM

Approach	Management
Treat the cause	Control blood pressure Control associated diabetes Avoid smoking Anticoagulant and vasodilators Control edema by compression therapy Avoid trauma Control obesity
Patient-centered concerns	Pain control Nociceptive pain Neuropathic pain Activities of daily living
Moisture balance	Nontraumatic moisture balance dressings
Debridement	Surgical debridement Removal of necrotic tissue
Infection and inflammation	Antiseptic or other antimicrobial dressings with silver and honey having a topical anti-inflammatory action Treatment of deep and surrounding tissue secondary infection
Edge	Skin graft Hyperbaric oxygen to correct local superficial ischemia Negative-pressure wound therapy

appropriate renal-compromised patients. In congruence with a few cases reported in the literature, the authors confirm that extensive forms of proximal calciphylaxis, in kidney disease or nonuremic associated cases, can benefit from similar surgical approaches to treatment. It may take 10 to 12 weeks after grafting for improvement to become clinically obvious.

CONCLUSIONS

The incidence of Martorell HYTILU is likely increasing and often underdiagnosed in many wound care clinics around the world. It should be suspected when patients with long-standing hypertension or metabolic syndrome, including hypertension and diabetes, develop an extremely painful skin necrosis (black eschar) within a zone of livedo reticularis change to the vasculature, typically at the lateral-dorsal lower leg and over the Achilles tendon.

Martorell HYTILU is the result of long-standing hypertension, with or without diabetes, leading to a highly characteristic form of ischemic subcutaneous arteriolosclerosis (with or without medial calcinosis) that can be regularly detected on an elliptical deep skin biopsy from the border to the center of the zone of necrosis. This condition is part of a whole spectrum of disorders that are characterized by subcutaneous arteriolosclerosis, including calciphylaxis in the context of renal disease. Ischemic hypertensive ulcers can occur together with common peripheral arterial disease (approximately 50% of patients) or as small and medium vessel arteriolosclerosis, without relevant large vessel peripheral arterial disease.

It is critical that Martorell HYTILU is not confused with PG, which shares many of the same clinical initial features, yet different clinical associations. Treatment of these 2 entities is diametrically opposite, and therefore, the distinction is crucial. Martorell HYTILU does not require immunosuppression, but rather appropriate systemic antibiotic therapy and above all a rapid removal of necrotic tissue (necrosectomy) and skin graft as soon as wound bed preparation is optimized.

Further studies are necessary to clarify the classification system and elucidate the potential HYTILU mechanisms. These studies may lead to identification of new therapeutic options capable of successfully treating ischemic hypertensive ulcers. ●

PRACTICE PEARLS

- Martorell HYTILU clinically presents as a painful wound with a necrotic base commonly on the laterodorsal aspect of the calf or Achilles tendon
- Patients with HYTILU characteristically have hypertension and sometimes diabetes
- Unlike arterial leg ulcer, the pain in HYTILU is not exacerbated by exercise and leg elevation
- The diagnosis of HYTILU is based on the typical history and clinical presentation, and is confirmed by a deep elliptical skin biopsy from the wound border extending to the fascia
- Surgery is the most rapid and effective treatment for Martorell HYTILU and a skin graft may follow after necrosectomy.

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