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## Case Report

# Heinz-Lippmann disease as an underrecognized cause of chronic venous insufficiency-associated cutaneous ulcers: Clinical and imaging findings

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### ARTICLE INFO

#### Article history:

Received 3 June 2020

Revised 17 June 2020

Accepted 18 June 2020

#### Keywords:

Heterotopic ossification

Ulcer

Skin

Venous insufficiency

Magnetic resonance imaging (MRI)

Computed tomography (CT)

### ABSTRACT

Venous insufficiency is a frequent cause of consultation in primary care settings. Heterotopic ossification, consisting of an abnormal formation of true bone in extraskeletal soft tissues, is an underrecognized complication of chronic venous insufficiency that may cause torpid ulcers. We report a case of 78-year-old woman, with a long-standing history of venous insufficiency and tibial fracture, showing a non-healing ulcer associated with subcutaneous calcifications of the left lower extremity. Gold standard of imaging diagnosis are both plain radiographs and computed tomography but also magnetic resonance imaging could be useful for assessing the characteristics of the pathology. We describe a case of Heinz-Lippmann disease, diagnosed by using both computed tomography and magnetic resonance imaging.

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## Introduction

Heterotopic ossification (HO) is an underrecognized complication of chronic venous insufficiency that may cause torpid ulcers.

We describe a case of Heinz-Lippmann disease localized in left lower extremity, diagnosed by using both computed tomography (CT) and magnetic resonance imaging (MRI).

The features are here in described.

## Case report

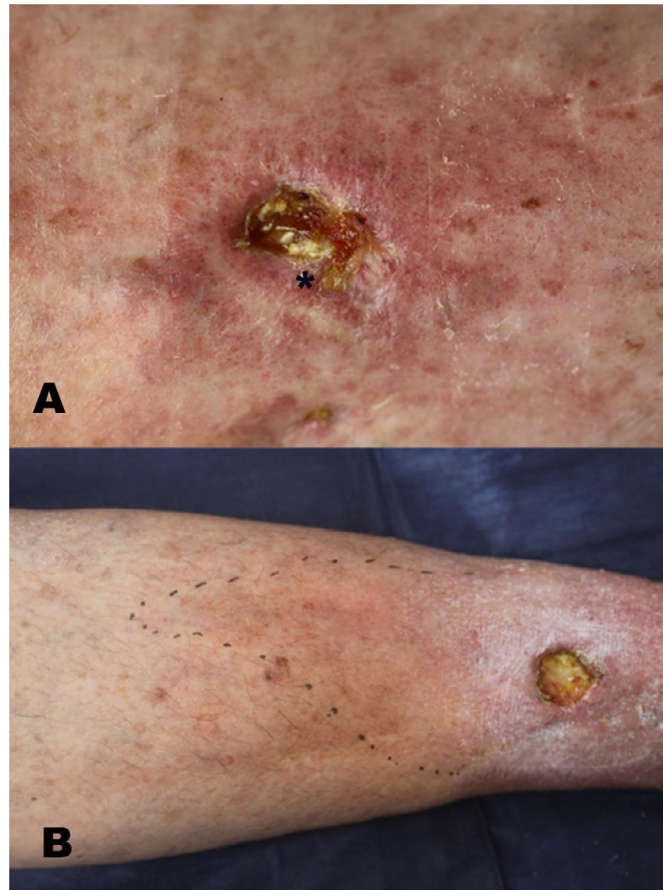
A 78-year-old woman with a long-standing history of venous insufficiency and tibial fracture (8 years earlier) presented to our institution with a nonhealing ulcer of the left lower extremity. She had undergone varicectomy several years before in the same leg with no other relevant medical co-morbidities. She did not take calcium supplements. Physical examination revealed a full-thickness ulcer measuring 2 × 1.8 cm

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<https://doi.org/10.1016/j.radcr.2020.06.035>

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**Fig. 1 – (A) Chronic superficial ulcer, with a size of about 2.5 cm, showing calcium extrusion (black asterisk); (B) Skin marked area of palpable woody subcutaneous tissue.**

involving the distal one-third of the left leg (Fig. 1A). The skin surrounding the ulcer showed signs of atrophy, hypopigmentation and erythema consistent with *atrophie blanche*. An extrusion of calcified material could also be observed. A petrous plaque extending proximally over the pretibial area and measuring 10 × 8 cm could be noted on palpation in a subsequent follow-up (Fig. 1B).

A diagnosis of HO in the setting of chronic venous insufficiency was made. The patient was treated with conservative medical measures such as compression stockings no surgical debridement was performed due to the extensive area of calcification. She was referred for endocrine review and oral vitamin D was prescribed. No signs of cellulitis or other complications have developed during a 3-year follow-up period.

Ankle brachial index was within normal range. A skin biopsy showed focal osseous metaplasia of the dermis with calcium extrusion and without signs of vasculitis or thrombotic occlusion (Fig. 2). *Candida albicans* was cultured from the wound. Laboratory studies were normal for renal function, calcium and phosphorus, connective tissue and thrombophilia screening. Parathyroid hormone was moderately increased at 80 pg/mL and Vitamin D was slightly decreased at 11.28 ng/mL.

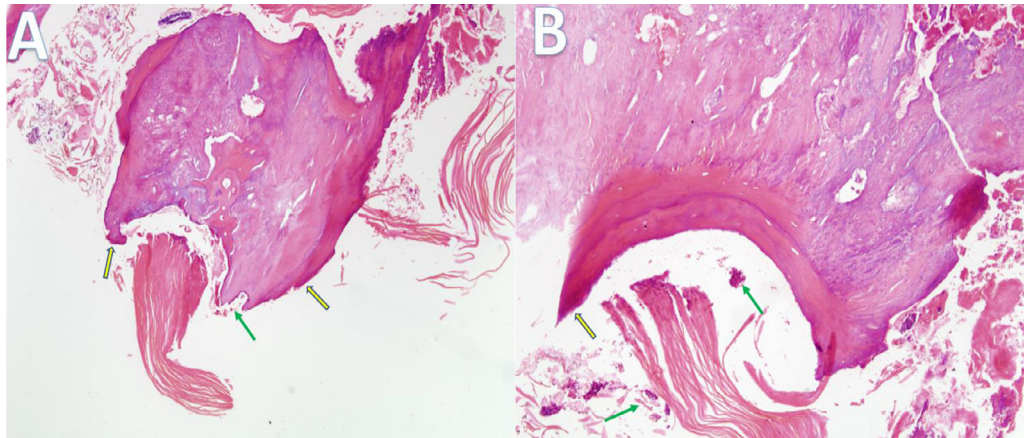
CT (Fig. 3) and MRI (Fig 4) showed a consolidated chronic fracture in the middle third of the left tibia associated with a moderate periosteal reaction of the tibial bone. In addition, an

anterior deep periosteal skin ulcer, which deepened in the deep tissue involving the distal one-third of the left leg, was observed.

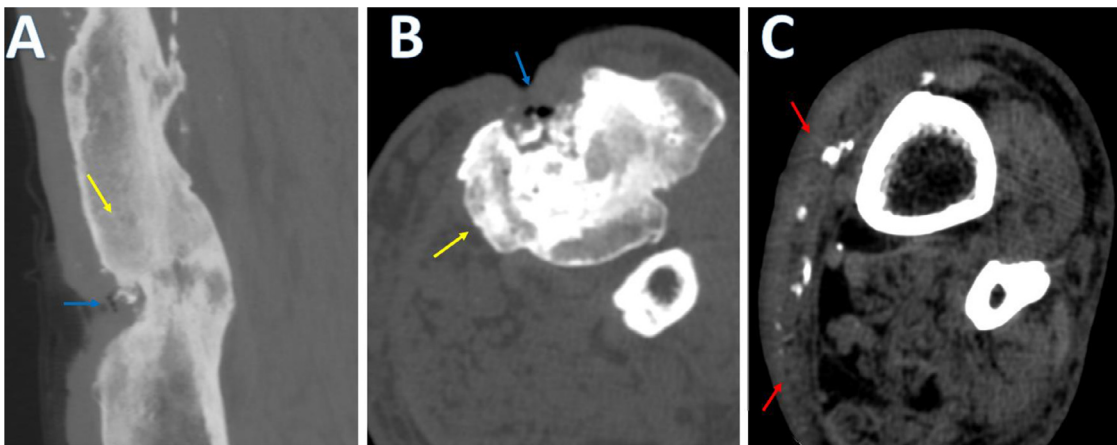
It was also observed diffuse superficial venous ectasia and microcalcifications involving tibial dermal tissues, caudally to the fracture, compatible with of Hertz-Lippmann's disease.

## Discussion

HO consists of an abnormal formation of true bone and osteoblastic activity within extraskeletal soft tissues. [1] Several conditions, such as musculoskeletal trauma, surgical scars, cutaneous neoplasms, neurologic injury, genetic abnormalities, as well as chronic venous insufficiency may cause HO. Venous insufficiency is a common disease with a prevalence ranging from <1% to 40% in females and from <1% to 17% in males. [2] It may cause cutaneous alterations such as hyperpigmentation, lipodermatosclerosis, and *atrophie blanche*. HO or Heinz-Lippmann disease is an underrecognized complication of chronic venous insufficiency that may cause torpid ulcers. In 1960, Heinz Lippmann and Goldin reported subcutaneous bone formation in 10% of patients with chronic venous insufficiency. [3] It mainly affects postmenopausal women with no disturbance of the calcium or



**Fig. 2 – Representative histologic aspect with hematoxylin-eosin, original magnifications at 8x (A) and 20x (B) of skin biopsy. Dermic tissue containing calcific metaplastic tissue with the underlying fibrous capsule (yellow arrows), surrounded by many small free calcifications extrusions (green arrows). (Color version available online.)**



**Fig. 3 – Computed tomography (CT) scan in sagittal and axial planes of the left leg with bone (A-B) and soft tissue (C) window settings. (A and B) Deep anterior leg skin ulcer is observed (blue arrows) which deepens and erodes the adjacent anterior tibial bone showing diffuse remodeling, sclerosis and periosteal reaction (yellow arrows). (C) Diffuse microcalcifications (red arrows) distributed in the anterior integumentary soft tissues of the tibia. (Color version available online.)**

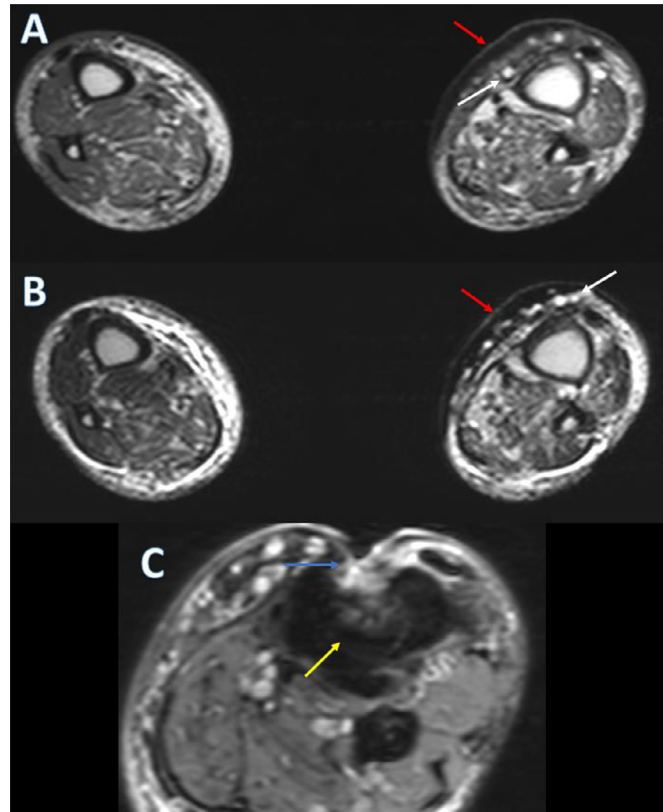
phosphorus metabolism. Thus, altered hormonal activity and *de novo* metaplasia transforming subcutaneous tissue into viable bone in chronic venous insufficiency probably play a role in its development.

Recurrent or nonhealing ulcer is not a typical appearance of HO. Patients presenting with HO typically complain of inflammatory symptoms including pain, swelling, erythema, and warmth along with joint immobility typically appears as a recurrent or nonhealing ulcer. [4] Calcium extrusion may be observed, and large sheets of woody subcutaneous tissue may be palpable and should alert about the presence of a Heinz-Lippmann disease.

Calcinosis cutis can be observed in several diseases. [5] Dystrophic calcification due to local tissue damage may be a complication of cutaneous neoplasms (Pilomatricoma, Trichilemmal cyst) and connective tissue diseases. In scleroderma (CREST syndrome: Calcinosis, Raynaud, esophageal dysfunction, sclerodactyly and telangiectasia) and systemic

lupus erythematosus dystrophic calcification appears in a localized form with a few deposits of calcium. Wide-spread depositions of calcium can develop in patients with late-stage juvenile dermatomyositis. In any case, systemic lupus erythematosus, scleroderma, and dermatomyositis are frequently associated with specific clinical manifestations and laboratory alterations. Inherited disorders may also cause skin calcinosis but these are widespread and appear in flexural (Pseudoxanthoma elasticum) or periarticular areas (Ehlers-Danlos syndrome). Pancreatic panniculitis, which appears on the legs, may also trigger skin calcification. However, episodes of erythematous or subcutaneous nodules that ulcerate and drain are observed.

While no alteration of the calcium and phosphate metabolism can be found in heterotopic calcifications of dystrophic origin, an increase of both parameters is found in patients with metastatic calcification and calciphylaxis. Metastatic calcification is a result of an underlying defect in



**Fig. 4 – MRI of left leg. (A and B) Axial T1 and T2 sequences. Soft tissue calcifications involving tibial dermal tissues show a low signal intensity in T1–T2-weighted sequences (red arrows). It was also observed diffuse superficial venous ectasia (white arrows). C. Axial short tau inversion recovery (STIR) sequence. A deep anterior skin ulcer is also observed (blue arrow) which deepens and erodes the bone showing edema compatible with osteitis (yellow arrow) visible in the STIR sequences. (Color version available online.)**

the calcium and/or phosphate metabolism as observed in patients with hypervitaminosis D or milk alkali syndrome. Unlike Heinz-Lippmann disease, metastatic calcification characteristically manifests as periarticular calcifications. Calciphylaxis is a form of metastatic heterotopic calcification usually observed in patients with chronic renal failure. Calciphylaxis is caused by small vessel vasculopathy and mural calcification. The dermis and subcutaneous fat are involved and extravascular calcification may also appear. Clinical imaging also differs from that seen in Lippmann disease. Patients with calciphylaxis develop painful, violaceous reticulated skin lesions that evolve to skin ulcers on the legs. Although our patient had a mild increase in the parathyroid hormone levels, this was not associated with an increase of the calcium and/or phosphate metabolism, thus ruling out a metastatic calcification or a calciphylaxis.

Radiographically, extensive calcification in the soft tissues can be observed on radiographs as well as on CT in patients with Heinz-Lippmann disease. [6] Both plain radiographs and CT imaging are the standard references for assessing HO maturity, but CT defines the different stages of ossification more accurately than simple radiographs. Amorphous calcification

is poorly defined without recognizable trabecular structure; immature ossification shows poorly defined margins and initial trabecular formation; mature ossification is characterized by a cortical contour with a well-defined spongy bone center. At CT, it can be observed bone formation characterized by cortical and trabecular structure.

At MRI, mature HO presents as typical medullar fat bone that is hyperintense on T1- and T2-weighted images, outlined by a rim of hypointense cortical bone. Amorphous calcification and immature HO can present nonspecific signal intensity and contrast enhancement characteristics. [7]

Pathologically, the ossified tissue consists of mature cancellous bone in plates, sheets, or rings.

Preventive medical management of venous insufficiency before ossification with compression stockings and intermittent extremity elevation may be of help. However, the ossified tissue has to be completely removed surgically to achieve healing of the ulcer. Large resection and subsequent skin grafting may be required [8] but are often ineffective. [9]

In our knowledge, this is the first article that documents a histologically confirmed Heinz-Lippmann disease diagnosed by clinic examination, CT and MRI.

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## Conclusions

An increased awareness regarding HO as a cause of chronic ulcers in some patients with chronic venous insufficiency seems important in order to avoid either misdiagnoses or diagnostic delays. Skin ossification may go unrecognized while simple palpation of the skin around the ulcer searching for rock-hard indurated areas may be sufficient to suspect it. Modern radiological techniques may confirm the diagnosis of Heinz-Lippmann disease and show the associated complications. Therapeutic approaches, including wide surgical debridement and skin grafts are often ineffective.

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