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*Case report*

# Calciphylaxis in A Patient with Chronic Renal Failure: Report of A Libyan Patient and Review of the Literature

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**A B S T R A C T**

Calciphylaxis is a rare, life-threatening disorder characterized by systemic arteriolar calcification, tissue ischemia, and painful ulceration, most commonly affecting patients with end-stage renal disease and secondary hyperparathyroidism. We report the first documented case of calciphylaxis in Libya: a 54-year-old man with chronic renal failure on long-term hemodialysis, who developed large painful ulcers on both calves. Laboratory findings revealed markedly elevated parathyroid hormone levels, while histopathology confirmed epidermal necrosis, vascular calcification, and ischemic fat necrosis. The patient responded to local wound care, systemic antibiotics, and debridement. This case highlights the importance of considering calciphylaxis in the differential diagnosis of chronic renal failure patients presenting with painful leg ulcers. Prompt recognition and aggressive management of mineral metabolism are essential to improve outcomes and reduce mortality associated with this devastating condition.

## Introduction

Calciphylaxis or Calcific Uremic Arteriolopathy (CUA) is a rare, life-threatening disorder characterized by progressive vascular calcification and ischemic tissue loss in patients with chronic renal failure [1-6]. Subcutaneous skin nodules with ulcerating plaques and extensive tissue necrosis with vascular calcification characterize this process, leading to death by sepsis in 60% of patients [9,13]. It is a painful complication of end-stage renal disease and secondary hyperparathyroidism. Calcification most commonly affects the skin and soft tissue of the lower extremities, resulting in excruciatingly painful skin ulcers. Female gender, hyperphosphatemia, high alkaline phosphatase, and low serum albumin are risk factors for calciphylaxis [12,14]. Rare cases of calciphylaxis not associated with chronic renal failure have been reported with breast cancer, hyperparathyroidism, and alcoholic cirrhosis [6,11].

Patients infected with the human immunodeficiency virus (HIV) are predisposed to renal failure and thus may develop this serious complication [4,19]. Widespread calcification may develop in patients with HIV infection and renal failure, and, in some cases, calcium and phosphorus levels may be normal [4]. In one study, they investigated the extent of skin ischemia in patients with calciphylaxis by means of transcutaneous oxygen tension (TCPO) measurement, a noninvasive test that accurately assesses skin oxygenation. They found that TCPO levels are abnormally low in patients with calciphylaxis, indicating that severe and diffuse skin ischemia exists, even in areas free of skin lesions [2,3].

The skin biopsy specimens showed a broad necrosis of the epidermis and thrombosed dermal vessels with focal calcium deposits within the wall. In addition, increased serum calcium-phosphate product is a commonly reported laboratory finding in calciphylaxis described in the literature. Thus, we diagnosed calciphylaxis on the basis of clinical, biochemical, and histopathological criteria.

## *Case Report*

We hereby report this 54-year-old Libyan man, who presented with six months duration of two painful, large ulcers covered with thick crust over both calves, which started as a small nodule, which gradually increased in size and then ulcerated. Patient has been a known case of chronic renal failure since 1993, on dialysis. The patient had a kidney transplant for the right kidney in 1995 in Iraq. Patient restarted on hemodialysis because of organ rejection, which was removed in 2005. Patient is on dialysis 3 times per week. On investigation / WBC 5.4 x $10^3$, Hb 14 g/dL, platelets 199 x$10^3$. Liver function test is normal (GPT 27 U/L, total bilirubin 0.4 mg%, Alkaline phosphatase 205 U/L). FBS 65 mg/dL. Urea 181 mg (↑), creatinine 6.4mg (↑), serum calcium 9.8 mg (normal), serum magnesium 2.8mg (normal). Parathyroid hormone 1256 pg/mL (↑↑) (NR 15-65). Viral screen (HCV-positive and HIV-negative). Histopathology examination showed a broad necrosis of the epidermis associated with calcification of the small blood vessels, with ischaemic fat necrosis and mixed inflammatory infiltrate. The histological feature is consistent with the diagnosis of calciphylaxis. The patient did well on local dressing, systemic antibiotics, and debridement. Calciphylaxis should be


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considered in the differential diagnosis of any patient with chronic renal failure and a painful leg ulcer. To the best of our knowledge, this is the first reported case of calciphylaxis in Tripoli.

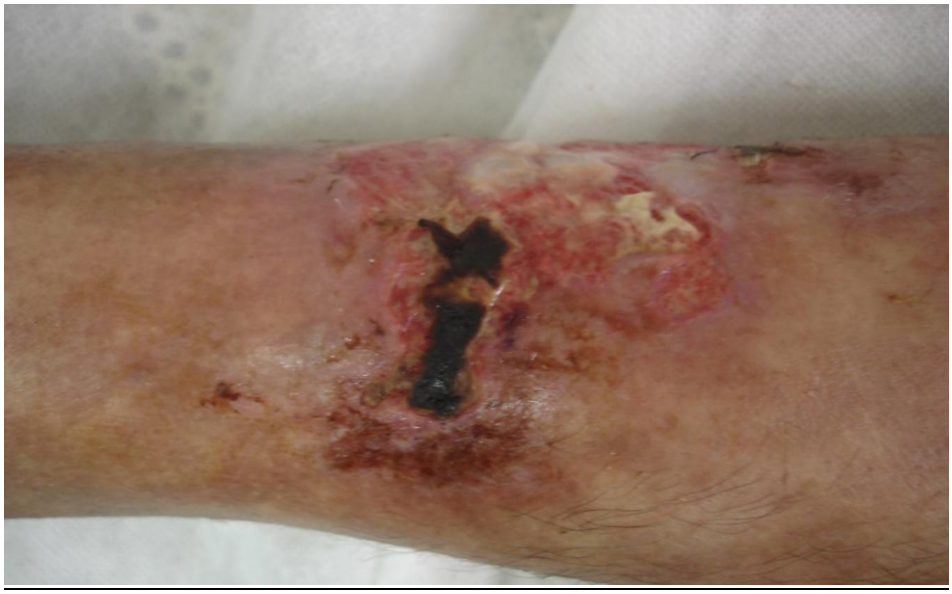

***Figure 1. Painful large ulcers covered with thick crust***

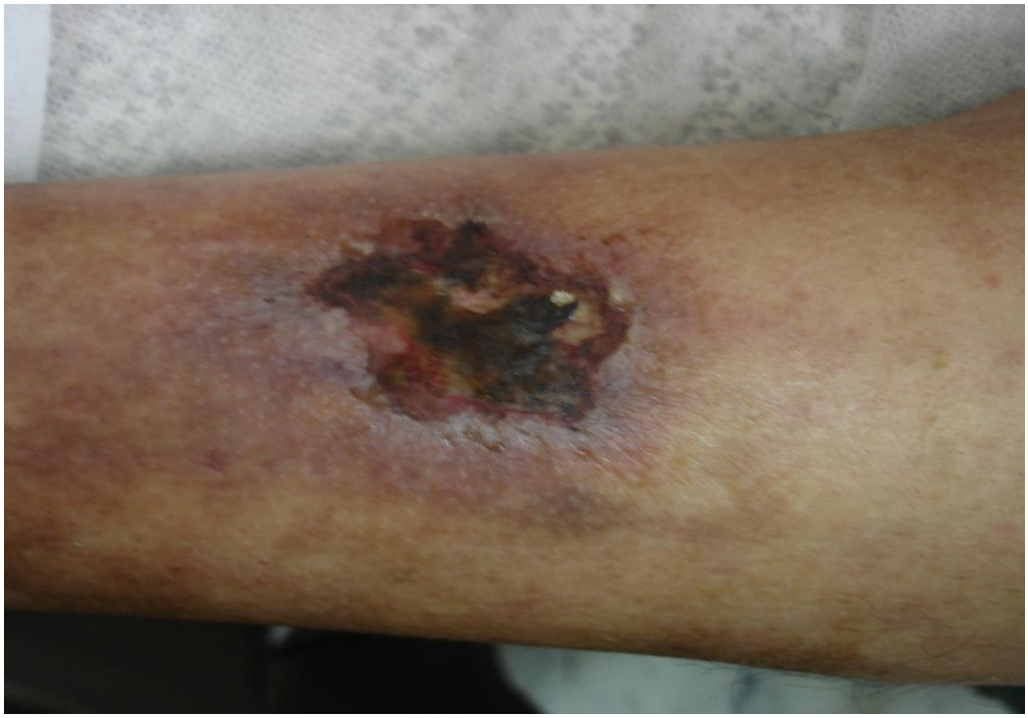

***Figure 2._ Calciphylaxis. Skin ulceration associated with calcification of the arteries in a patient with chronic renal failure and secondary hyperparathyroidism***


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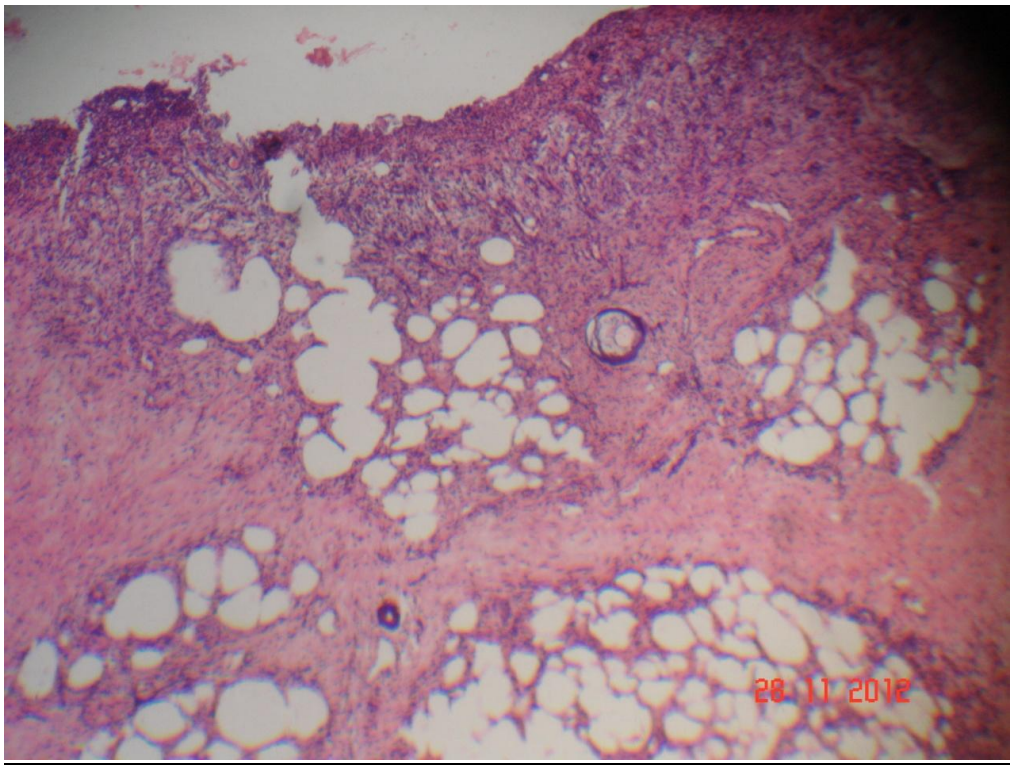


***Figure 3. The histopathology of the calciphylaxis (necrosis of the epidermis, calcification of the small blood vessels with ischaemic fat necrosis and mixed inflammatory infiltrate)***

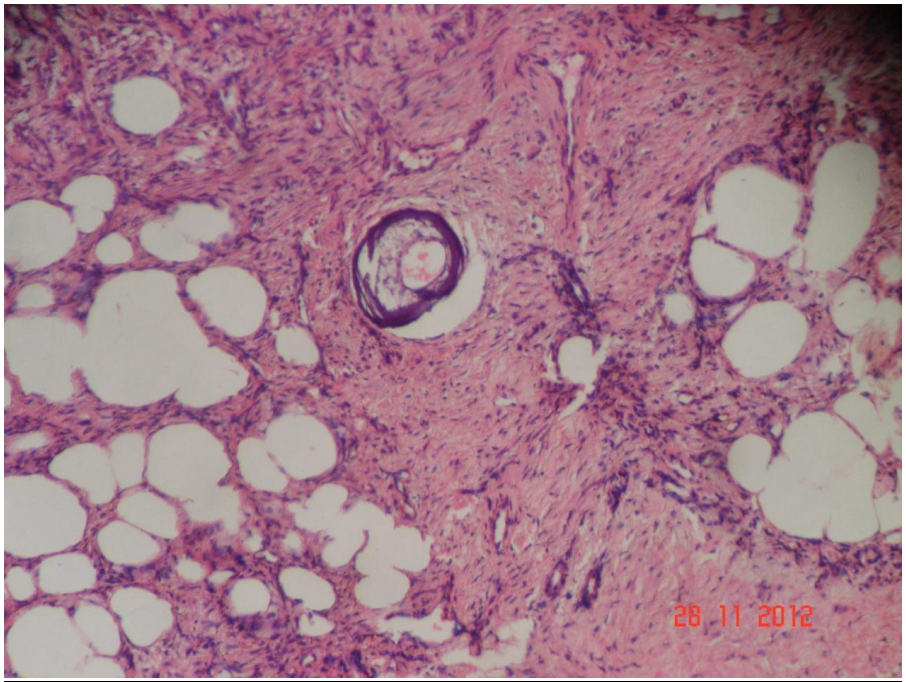


***Figure 4. The histopathology of the calciphylaxis***

## Discussion

Calciphylaxis is a rare, painful, life-threatening problem of cutaneous necrosis and refractory healing in patients with uremia and secondary hyperparathyroidism [17,23,26,29]. Calcification most commonly affects the skin and soft tissue of the lower extremities, resulting in excruciatingly painful skin ulcers. Most cases occur in those with chronic renal failure and secondary hyperparathyroidism. Rare presentation of calciphylaxis in a patient with normal renal function and primary hyperparathyroidism has been reported [28]. Diabetes mellitus and parameters of calcium-phosphate metabolism were not significantly associated with proximal calciphylaxis. These findings suggest that white race, morbid obesity, and poor nutritional status are associated with proximal calciphylaxis in dialysis patients [18]. Histological characteristics of


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calciphylaxis include small-vessel calcifications of skin, subcutaneous tissue, and visceral organs. These vascular changes promote tissue ischemia that often results in tissue necrosis [3,9]. The pathogenesis has been attributed to elevated parathyroid hormone (PTH), abnormalities in calcium and phosphorus metabolism, and acute deposition of calcium in tissues [19,27]. Control of serum phosphorus levels is a central goal in the management of patients with chronic renal failure. Inadequate control of serum phosphorus leads to elevated levels of the calcium-phosphorus product. This plays a pivotal role in vascular calcification, cardiovascular disease, calciphylaxis, and death [25]. Because early treatment (including aggressively lowering the calcium and phosphate levels, parathyroidectomy, and debridement of these necrotic lesions) may improve the outcome, and help to diminish this aggressively destructive process [8,11,19,27]. Parathyroidectomy can be performed with minimal morbidity and is associated with resolution of pain, wound healing, and a significantly longer median survival. Therefore, patients with secondary hyperparathyroidism and signs/symptoms of calciphylaxis should be referred promptly for consideration of parathyroidectomy [15]. Review of the literature revealed 7 other cases of calciphylaxis due to primary hyperparathyroidism and showed that prompt surgical removal of the autonomous parathyroid gland lesion results in clinical recovery of calciphylactic skin lesions [7]. Although parathyroidectomy may have important long-term advantages in patients with calciphylaxis, it does not appear to affect outcome in these advanced cases [5,30]. Parathyroidectomy cannot be recommended routinely in all patients, unless severe hyperparathyroidism mandates intervention [14]. Marked improvement of calciphylaxis has now been reported with the use of intravenous sodium thiosulphate [20,21]. Thus, the intravenous therapy of calciphylaxis with sodium thiosulfate might be a new effective alternative in the treatment of this life-threatening disease [16,20,21]. In some cases, hyperbaric oxygen may be beneficial. Aggressive wound care and debridement to avoid wound infection are very important in the management of this condition. The use of a vacuum-assisted closure device after extensive debridement and prior to skin grafting is very helpful. Total or subtotal parathyroidectomy is very helpful in some cases [22].

## Conclusion

Calciphylaxis is a rare but life-threatening complication of disordered mineral metabolism. Prompt diagnosis, aggressive metabolic control, and consideration of surgical or novel medical therapies can improve survival and quality of life. Continued research into pathogenesis and therapeutic strategies is needed to reduce the burden of this disease.

### *Conflict of Interest*

The authors declare no conflicts of interest related to this work.

### *Ethical Approval*

This study was conducted in accordance with institutional ethical standards and the Declaration of Helsinki. Ethical approval was obtained from the appropriate review board prior to data collection and analysis.

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