Calciphylaxis is a rare, life-threatening condition of widespread metastatic calcification most commonly seen in the setting of end-stage renal disease. The etiology of calciphylaxis is not well described, though there are several hypotheses. Cutaneous lesions are characteristically found on the abdomen, buttocks, or thighs as reticulated, painful, purple plaques that often undergo ulceration and may serve as a portal of entry for potentially life-threatening infectious agents. Histology reveals medial calcification with intimal proliferation involving small vessels in the subcutaneous fat, associated with a lymphohistiocytic infiltrate of the affected lobules. Treatment, including phosphate binders and parathyroidectomy, is not universally effective. We present one case of calciphylaxis and discuss the clinical features, pathophysiology, histology, and treatment of the condition.

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Calciphylaxis is a condition of progressive calcification of small and medium-sized blood vessels leading to necrosis of the skin and internal organs. Although the condition is rare and the prognosis is often poor, it is important to recognize calciphylaxis because early treatment may prevent the progression of the disease.

**Case Report**

A 28-year-old Hispanic woman with a history of chronic renal insufficiency secondary to congenital
hypoplastic kidneys presented with tender lesions on her shins. She had never received treatment for her renal disease.

On examination, there were reticulated, purpuric, tender, necrotic, ulcerated plaques symmetrically distributed on both shins. Bilateral lower extremity edema and erythema surrounded the necrotic plaques (Figure 1). The thighs, abdomen, and buttocks were unaffected.

Initial laboratory values revealed a significant elevation of blood urea nitrogen measuring 137 mg/dl (normal range, 8 to 24 mg/dl) and creatinine of 12.2 mg/dl (normal range, 0.5 to 1.5 mg/dl). Serum calcium was 8.5 mg/dl (normal range, 8.6 to 10.6 mg/dl), serum phosphorus was 19.7 mg/dl (normal range, 2.5 to 4.8 mg/dl) giving a calcium-phosphate product of 167. The intact parathyroid hormone level was 2089 pg/ml (normal range, 13 to 65 pg/ml).

A punch biopsy showed calcium deposition within the walls of the subcutaneous vessels with necrosis of the overlying dermis and epidermis. There was a lymphohistiocytic inflammatory cell infiltrate within the dermis and the fat. These findings were consistent with calciphylaxis.

**Discussion**

Calciphylaxis, also called calcifying panniculitis and calcific uremic arteriolopathy, is a rare, life-threatening condition of widespread metastatic calcification leading to vascular compromise and subsequent ischemia and necrosis of the skin and other organs. The condition most commonly affects people who have end-stage renal disease requiring dialysis. It is commonly seen in the setting of secondary hyperparathyroidism. Most of the patients described in the literature are female, and there is a significant association with diabetes mellitus. Though more commonly associated with hyperparathyroidism and an elevated calcium-phosphate product, calciphylaxis can occur in other clinical settings such as metastatic breast cancer and low turnover uremic bone disease associated with a relatively low intact parathyroid hormone level and calcium phosphate product.

The etiology of calciphylaxis is unclear. One theory considers calciphylaxis as a condition of induced hypersensitivity and is based on the experimental studies on rats performed by Selye in 1962. Calciphylaxis was induced by first exposing the rats to a sensitizing agent (such as parathyroid hormone, dihydrotestosterone, or vitamin D), followed by exposure to a challenging agent (such as egg albumin, metallic salts, or corticosteroids). In humans, the sensitizing agents may be an elevated parathyroid hormone level or an elevated calcium and phosphate product (>70). Challenging agents may include albumin and other blood products, glucocorticoids, immunosuppressants, or local trauma. A different theory considers that there is underlying vascular damage within the small vessels, perhaps related to the cause of the renal failure, and that this predisposes patients to metastatic calcification in the setting of an elevated parathyroid hormone level with an elevated calcium and phosphate product. There has also been speculation that a protein C functional deficiency may play a role in the pathogenesis of cutaneous necrosis seen with calciphylaxis by producing a hypercoagulable state, but this is not seen uniformly. A recently published case-control study by Zacharias et al suggests that calcium carbonate ingestion is a strong risk factor for the development of calciphylaxis.

Calciphylaxis presents as painful, purple subcutaneous nodules and plaques, most often located on the abdomen, buttocks, or thighs. The plaques are often reticulated, leading to a livedo reticularis pattern. Extensive necrosis of the overlying skin typically occurs and may lead to the development of gangrenous areas. Dry gangrene of affected digits without systemic sepsis is often left to autoamputate, as this preserves finger length for better function.

The histology of lesions of calciphylaxis shows medial calcification with intimal proliferation of the small vessels within the subcutaneous fat. A lymphohistiocytic inflammatory infiltrate may be seen in the affected lobules. In later disease, fat necrosis is present as well as necrosis of the overlying epidermis.

The treatment of calciphylaxis is difficult. Precipitating agents should be removed when possible and a low-phosphate diet initiated in the case of hyperphosphatemia. Phosphate binders such as aluminum hydroxide gel may be instituted. As mentioned previously, calcium salts have been found to contribute to the development of calciphylaxis by some investigators and may not be the optimal phosphate binder to use in the setting of chronic renal failure. Thorough skin care of the affected areas with debridement of necrotic tissue must be performed in an attempt to prevent septicemia. Systemic antibiotics should be given when appropriate. The benefit of total or subtotal parathyroidectomy in the management of calciphylaxis is not firmly established. In a study by Hafner et al of 104 cases of calciphylaxis associated with renal disease, there was a significant survival benefit of parathyroidectomy. This more aggressive approach may be required in cases of extensive skin necrosis not responsive to more conservative therapies. The mortality rate associated with calciphylaxis is high and the usual cause of death is overwhelming sepsis.
REFERENCES


