

Single Case

Calciophylaxis Presenting with Various Symptoms: A Case Report

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Keywords

Calciophylaxis · Calcification · Hyperparathyroidism · Hemodialysis

Abstract

Calciophylaxis causes ischemia in multiple organs and skin ulcers owing to progressive calcification in small and medial arteries. It has a poor prognosis and often occurs in patients with hyperparathyroidism associated with end-stage renal failure and those undergoing hemodialysis. Here, we present a case of calciophylaxis associated with a wide range of symptoms, including lower thigh skin ulcers, a rectovaginal fistula, and femoral neck fracture. The patient underwent multiple treatments. However, she eventually died of cardiac failure.

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Case Report

The patient was a 52-year-old woman. She started hemodialysis in 2005 for chronic renal failure, and she experienced symptoms associated with hyperparathyroidism complications in 2013. Her other medical history included diabetes since 2000, diabetic gangrene in the second toe of the right foot in 2012, and cardiac infarction in 2013. She visited our department for an initial examination in June 2015, with the chief complaint of intense pain and purpura in both lower thighs. Subsequently, the purpura spots rapidly formed ulcers, and she was hospitalized urgently. Clearly demarcated ulcers with yellow gangrenous tissue

were observed on her right ankle and several areas of her left leg. Blood tests at the time of hospitalization showed elevated levels of intact parathyroid hormone (1,250 pg/mL), calcium (10.4 mg/dL), and phosphate (6.4 mg/dL), along with hyperparathyroidism. Her white blood cell count was 13,200/ μ L and C-reactive protein level was 12.77 mg/dL, indicating inflammation. She was negative for autoantibodies associated with collagen disease and angitis.

Computed tomography of the legs showed extensive calcification from the external iliac artery to the artery of the extremities (Fig. 1). However, her ankle-brachial index indicated that blood flow was maintained relatively well (right, 1.13; left, 0.94).

Skin biopsy of the periphery of the ulcers showed calcification of the intima media of the small arteries in the dermis, and extensive inflammatory cell infiltration was observed in the periphery. Therefore, she was diagnosed with calciphylaxis (Fig. 2).

After hospitalization, debridement and negative pressure wound therapy was performed for the ulcers, and following therapy, healthy granulation tissue formed. Additionally, cinacalcet was administered to reduce her blood serum calcium and phosphate levels.

One month after hospitalization, she complained of acute pain in the left hip during rest. A radiograph revealed fracture of the left femoral neck and thinning of the cortical bone. Based on the findings, she was diagnosed with pathological fracture due to hyperparathyroidism. Treatment was planned with the orthopedics team. Emergency surgery was not performed, considering her general condition, the presence of intractable ulcers in the surgical field, and the possibility of the development of new ulcers because of skin resection. We selected preservation therapy.

In the second month after onset, new ulcers formed in the right groin and vagina (Fig. 3). The vaginal ulcer formed a rectovaginal fistula within several days. Melena was observed persistently, and this was treated conservatively with pressure. The ulcer in the groin was infected owing to stool contamination, and a subcutaneous gas pattern was observed in the abdomen. On the same day, the abdomen was opened above the fascia, and antibiotic administration was started. Her melena and abdominal infection improved. However, 1 month later, the patient died of cardiac failure.

Discussion

In 1961, Selye et al. [1] reported the first case of calciphylaxis (phenomenon of acute ectopic calcification on the skin and the whole body). Calciphylaxis occurs mainly in end-stage renal failure patients undergoing hemodialysis, and the main symptoms are intense pain and refractory skin ulcers [2]. This disease is refractory and has a very poor prognosis [3–5]. It occurs in 1–4% of end-stage renal failure patients, frequently manifesting on the torso and limbs [6]. It is characterized by calcification of the tunica media of the small and medial arteries in the dermis and subcutaneous fat tissues, and necrosis of tissues due to blockage of the lumen. Histological observations are very effective for diagnosing calciphylaxis [1, 7]. The present patient was diagnosed with calciphylaxis based on biopsy assessment conducted at the time of hospitalization.

Metabolism disorders of calcium and phosphate, decline in vitamin D₃ production, hyperparathyroidism, intake of warfarin or prednisolone, low albumin, and external injuries are known causal factors of calciphylaxis. In the present patient, hyperparathyroidism from long-term dialysis and resulting abnormal metabolism of calcium and phosphate are believed to have provoked this condition.

Our patient exhibited calciphylaxis with a vaginal ulcer and rectovaginal fistula formation. Our search of the literature revealed no previous case involving complications of a vaginal ulcer and rectovaginal fistula. Generally, possible treatments for a rectovaginal fistula include rectovaginal closure surgery, colostomy, and conservative therapy. Although we considered surgery for the rectovaginal fistula, we opted not to perform surgery because of the possibility of the development of new ulcers at the laparotomy site and intestinal resection site. A conservative approach led to the cessation of melena and the disappearance of infection. Locally, the patient progressed favorably. Rivera et al. [8] performed a colectomy in a patient with calciphylaxis, but could not close the laparotomy site after surgery. The authors reported that the patient died from septicemia. Necrosis of the penis owing to calciphylaxis has been reported to respond more favorably to conservative treatment than to surgery [9, 10]. A surgical approach for calciphylaxis can stimulate the sympathetic nerves and may cause the formation of new ulcers [6]. Therefore, surgery may worsen the calciphylaxis prognosis, suggesting that surgical treatment should be selected with caution after careful consideration of the risks to the patient's condition and general risks.

Currently, treatment for calciphylaxis involves whole-body management, including prevention of infection, correction of the abnormal metabolism of calcium and phosphate, and local management of ulcers by debridement [1]. In recent years, treatment with sodium thio-sulfate has been gaining attention [11–13]. In the present case, blood serum calcium and phosphate levels were normalized by administering cinacalcet after hospitalization. Cinacalcet acts directly on the calcium receptors in the parathyroid cells and inhibits parathyroid hormone without elevating blood serum calcium levels. It also lowers blood serum phosphate levels. Previous reports have mentioned improvement in calciphylaxis with the administration of cinacalcet [14]. However, in the present case, new ulcers formed after the correction of blood serum calcium and phosphate levels with cinacalcet. This rapid progression may have been prevented if the administration had been started in the early stages of the disease.

This patient was diagnosed with calciphylaxis based on ulcers on both thighs, which was followed by complications of femoral neck fracture, groin ulcers, and a rectovaginal fistula. The patient ultimately died of cardiac failure. Calciphylaxis causes refractory ulcers and various complications throughout the body. Dermatologists are often involved in the treatment of this disease, and they should be well acquainted with the pathology of calciphylaxis and its symptoms in order to offer appropriate treatment from an early stage.

Ethics Statement

Informed consent for publishing this case report was obtained from the patient.

Disclosure Statement

The authors declare no conflicts of interest.

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Fig. 1. a, b Black necrotic eschar on bilateral lower extremities. c Radiograph of legs showed extensive calcification of the lower extremity arteries.

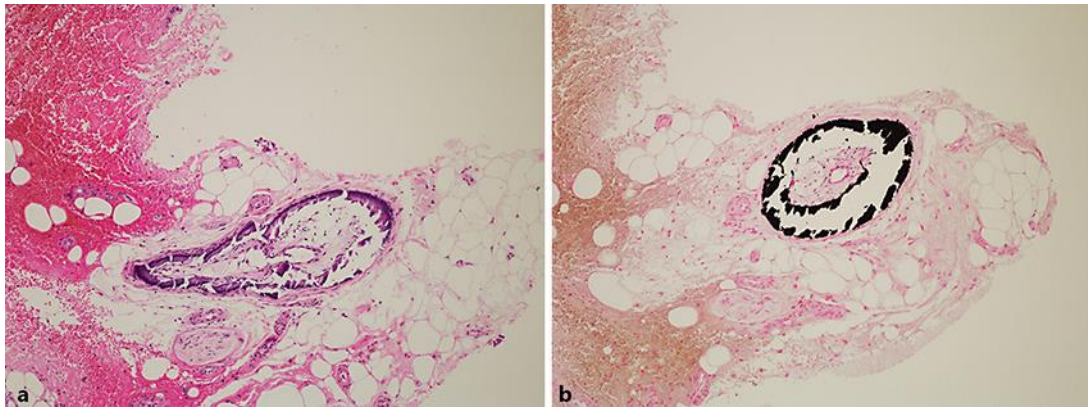


Fig. 2. Microscopic findings of vascular lesions of calciphylaxis. **a** H-E staining showed calcification of the intima media of the small arteries in the dermis, and extensive inflammatory cell infiltration was observed in the periphery. **b** Von Kossa staining showed the accumulation of calcium in the vessel. $\times 100$.



Fig. 3. In the second month after onset, new ulcers formed on the right groin and vagina.