Patient Report

Calciphylaxis due to poor compliance in a child with end stage renal disease: A case report

DEMET TOPRAK, ZELAL BIRCAN AND AYSE SEVIM GOKALP

1Department of Pediatrics, and 2Division of Pediatric Nephrology, Kocaeli University Faculty of Medicine, Kocaeli, Turkey

Key words calciphylaxis, end stage renal failure, childhood.

Calciphylaxis (calcific uremic arteriolopathy) is a vasculopathy that is often defined in patients due to renal failure, however, some patients with calciphylaxis do not show secondary or tertiary hyperparathyroidism. It results from mural calcification of arteries and arterioles in the deep dermis and subcutaneous adipose tissue, leading to vessel occlusion. The resulting ischemia may be so severe that infarction of the downstream tissue may develop, the most affected sites being the skin and subcutaneous adipose tissue. The regions of the body with thicker subcutaneous adipose tissue such as the breast, abdomen, thighs and buttocks may be more frequently affected. The accepted concept is that reduced glomerular filtration rate, even in the early stages of end-stage renal disease (ESRD), results in diminished renal phosphorus excretion and an increase in serum phosphorus concentration. The retained inorganic phosphorus combines with plasma calcium and the calcium × phosphate product with CaHPO4 concentration rise. This leads to the stimulation of parathyroid hormone secretion and secondary hyperparathyroidism as well as the resorption of calcium and phosphorus from bone with resulting osteodystrophy and metastatic calcification.

Cutaneous metastatic calcification was reported as long ago as 100 years. The lesions are quite characteristic, starting as areas of painful purple discoloration in the extremities that are plaque-like or nodular. They usually progress to necrotizing gangrenous areas and ulcerations. Some reports describe actual gangrene and self-amputation of digits or extremities.

In this case report, we present an 8-year-old girl who experienced cutaneous and widespread visceral calcifications due to poor compliance of her parents to the treatment of chronic renal failure.

Case report

An 8-year-old white girl, presented to our outpatient clinic with widespread necrotic skin ulcers, which were 2–3 cm in diameter and mainly on her cheeks, extremities and buttocks, and purple non-ulcerating hard plaques, which were 7–10 cm in diameter and appeared 10 months before admission to the Pediatric Nephrology Unit in Kocaeli University (Fig. 1). Her skin was indurated and painful to touch. She was previously diagnosed with chronic renal failure due to vesicoureteral reflux at the age of 4. Peritoneal dialysis was initiated when she was 5 years old and dialyzed with PD4 Dianeal with a low calcium content (1.25 mmol/Lt). She received conservative management including oral calcitriol and calcium acetate in another pediatric nephrology unit, in addition to ongoing continuous peritoneal dialysis. Her family was not compliant to the therapy and she stopped taking oral medications for 2 years. She was 15 kg (< 3rd percentile) in weight and 97 cm (< 3rd percentile) in height. Her laboratory was notable with the following findings: serum intact PTH 489.4 pg/mL, calcium 9.4 mg/dL, phosphorus 10.3 mg/dL, ALP 675 IU/Lt, urea 168 mg/dL, creatinine 5.05 mg/dL, total protein 6.2 g/dL, albumin 2.7 g/dL, total cholesterol 154 mg/dL, and triglycerides 341 mg/dL. The calcium × phosphate product was 96.8. The high serum intact PTH value was verified for a second time, while the normal range was between 9 and 65 pg/mL for the assay. Because of the poor compliance of her family, the serum calcium, phosphorus and PTH values over the last 2 years were unknown. Direct roentgenograms of her extremities and buttocks revealed marked diffuse soft tissue calcification (Fig. 2) and the 3rd digit of her left foot was self-amputated. Calcification of the bifurcation of the aorta and splenic artery was evident in the high resolution computed tomography (HRCT) of the abdomen. X-ray and HRCT of the chest showed a diffuse nodular parenchymal calcification of the lungs (Fig. 3), which did not cause any symptoms in the patient. Transthoracic echocardiography revealed dilated cardiomyopathy with no apparent calcification.
of the myocardium, but a thrombus of $3 \times 7$ cm in diameter was observed in the left atrium. Ultrasonography of the thyroid and parathyroid glands was normal. A low-phosphate diet was initiated and an oral phosphate binder (aluminum hydroxide) was prescribed. The skin ulcers were regularly cleaned with topical antiseptic solutions. After 4 weeks of treatment, the serum calcium level was 10.1 mg/dL, phosphorus 4.2 mg/dL and intact PTH 107.8 pg/mL. The calcium \times phosphate product was decreased to 42.4. The skin ulcers were healed with significant scar formation and the indurated lesions softened. Within 2 months, most of the cutaneous lesions disappeared and the necrotic ulcers resolved completely. In contrast, visceral calcifications and the intra-cardiac thrombus persisted. Parathyroidectomy was not required and the calcium \times phosphate product was regulated with calcium containing phosphate binders. The patient suddenly died during her sleep at home at the 3rd month of her follow up, possibly because of an embolic complication.

**Discussion**

In this case of calciphylaxis (calcific uremic arteriolopathy), metastatic calcifications occurred due to the high calcium \times phosphate product (96.8), and improved with lowering of the serum phosphorus level. Metastatic calcinosis of the dermis, attributed to calcification of arteries and arterioles, is extremely rare.\(^4\) Although calciphylaxis is usually defined in older patients, there are only a few children reported in the literature having developed metastatic calcinosis during life.\(^5\)

---

**Fig. 1** (a) Necrotic ulcers located on the buttocks of the patient. (b) Ulcers located on the cheek of the patient that have partially healed.

**Fig. 2** Direct roentgenograms of the buttocks revealing marked diffuse soft tissue calcification.
A case-control study has been reported by Ahmed et al. to define demographic, clinical and biochemical risk factors for the development of calcific uremic arteriolopathy (CUA). They have reported a significant association between CUA and white people and the female gender. The reasons for racial and gender difference in disease occurrence, as has been observed in our case report, have not been explained in previous reports.

Although medial calcification of larger arteries in chronic renal failure is relatively common, calcification of the cutaneous vascular system is a rare finding in skin biopsy specimens. The cutaneous lesions of calcific uremic arteriolopathy (calciphylaxis) usually consist of tender subcutaneous nodules and reticulated, ecchymotic, necrotic plaques and ulcers in a livedoid pattern predominantly on the buttocks and extremities. In addition, gangrene and self-amputation of the fingers and toes may be observed as seen in our patient. The ulcerations in patients with this cutaneous necrosis syndrome are painful, debilitating and often lethal when complicated with sepsis. The diagnosis of calciphylaxis is difficult. By the time the clinical lesions are apparent, it is usually too late to reverse the vasculopathy and improve the morbidity and mortality of this syndrome. Within weeks of the diagnosis, significant infectious morbidity occurs and within months, death is common and often due to sepsis or even visceral organ involvement by the vasculopathy.

The number of cases with long-term survival or even reports of patients whose skin lesions healed completely are limited. An essential part of the treatment of patients with calciphylaxis is supportive, and a vigorous systemic treatment should be carried out. Electrolyte levels and body fluid disturbances should be corrected. Infection and sepsis must be kept under control, since they are often the cause of death. Skin lesions must be kept clean, dressed and debrided when necessary, and antibiotics need to be used generously based on microbiological studies. Specific treatment of calciphylaxis primarily involves the elimination of the cause. It is strongly recommended that any time cutaneous necrosis or pulmonary calcification is noted in a patient with chronic renal failure, a total parathyroidectomy should be carried out. In patients with a high serum calcium × phosphate product or a high serum phosphate level, the hyperphosphatemia must be corrected by a low-phosphate diet and phosphate binding agents. Although usage of aluminum-containing phosphate binders cannot be approved, it was prescribed for a short period because of the economic difficulties in obtaining calcium-free phosphate binders for our patient. When the serum phosphorus level of our patient decreased to normal values, calcium-containing phosphate binders were started instead. Our patient responded well to phosphate chelation, and total parathyroidectomy was not required. The rapid decline in serum intact PTH and calcium × phosphate product is addressing the poor compliance of the patient. Treatment of our case supports the hypothesis that a high calcium × phosphate product is one of the most important components of this syndrome.

Non-visceral deposits usually consist of hydroxyapatite crystals, whereas visceral and skeletal-muscle deposits are amorphous or microcrystalline compounds composed of calcium, phosphate and magnesium. While hydroxyapatite crystals and thus, non-visceral calcifications can be reduced...
by decreasing serum phosphate, visceral calcifications may persist. Cutaneous calcinosis was treated with the reduction of serum calcium × phosphate product in our patient, though visceral calcifications remained unchanged as expected.

The outcome of patients with calciphylaxis is reported generally to be poor because of complications. In our case, it is obvious that the etiology of calciphylaxis was lack of proper therapy due to poor compliance of the parents. This is a case of fulminant metastatic calcinosis and cutaneous necrosis without tertiary hyperparathyroidism, and also the first case of cutaneous necrosis who responded rapidly to lowering of the serum phosphate and calcium × phosphate product together with aggressive wound care.

References


