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Necrotic lower extremities ulcers caused by calciphylaxis in chronic renal failure patient

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ABSTRACT

Introduction: Lower extremity ulcers often create diagnostic challenges and influence patient morbidity and mortality. The most common causes are venous insufficiency, arterial insufficiency, and neuropathic. Ulcers associated with systemic condition often face diagnostic and therapeutic challenge. We report a necrotic lower extremity ulcer caused by calciphylaxis in a patient with chronic renal failure.

Case: We reported a 48-year-old Javanese woman, complained of painful lower extremities ulcers since 1.5 months ago. The patient had a history of renal failure and hypertension, undergone routine hemodialysis since 13 years ago, and used Continuous Ambulatory Peritoneal Dialysis (CAPD) since one year ago. Dermatology status on dorsum pedis sinister as well as cruris dexter and sinister showed multiple ulcers on livid skin covered by black eschar, accompanied by tenderness. Laboratory results showed anemia (Hb 7.6), hypoalbuminemia (2.7), increased serum urea level (170.4 mg/dl), increased serum creatinine (11.23 mg/dl), increased calcium (10.4 mg/dl), high inorganic phosphorus (8.5 mg/dl) and high parathyroid hormone (2,164). BOF examination showed abdominal calcification, while radiographic examination on cruris dexter et sinister showed soft tissue calcification and osteoporosis. Histopathology result supported the presence of calciphylaxis. The patient was diagnosed with stage V chronic renal failure, hypertension, and calciphylaxis caused by secondary hyperparathyroidism. She was managed by low calcium and phosphate diet, lanthanum, paracetamol, folic acid, adalat oros, captopril and wound debridement.

Conclusion: Calciphylaxis is rare phenomenon of cutaneous necrosis associated with end-stage renal disease. Control of end-stage renal disease may be an important factor for treatment of calciphylaxis and patient with calciphylaxis usually had a poor prognosis.

Keywords: necrotic lower extremity ulcer, chronic renal failure, calciphylaxis

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INTRODUCTION

Lower extremity ulcers often create diagnostic challenges and influence patient morbidity and mortality.[1] The most common causes of lower extremity ulcer are venous insufficiency, arterial insufficiency, and neuropathy.[1,2] Ulcers associated with systemic condition often face diagnostic and therapeutic challenge.[1] Other causes of lower extremity ulcers include lymphedema, infection, trauma, vasculitis, calciphylaxis, drug-induced, malignancy, autoimmune disease, and pyoderma gangrenosum.[3] In this article, we report a necrotic lower extremity ulcer caused by calciphylaxis in a patient with chronic renal failure.

CASE

A 48-year-old Javanese woman complained of painful ulcers on her lower extremities since 1.5 months ago. The wounds started with violaceus rashes that progressed into black color and become wider. The patient had a history of renal failure and hypertension since 13 years ago and used Continuous Ambulatory Peritoneal Dialysis (CAPD) since one year ago. She was given medications containing adalat oros, captopril, CaCO3 and folic acid. History of trauma, fever, and diabetes mellitus was denied. Physical examination showed consciousness level of compos mentis, moderate nutritional status, blood pressure 140/90 mmHg, temperature 37°C, respiratory rate 20×/minutes, and heart rate 80×/minutes. Dermatology status on dorsum pedis sinister as well as cruris dexter and sinister showed multiple ulcers on livid skin covered by black eschar, accompanied by tenderness (Figure 1, 2).

Laboratory results showed anemia (Hb 7.6), hypoalbuminemia (2.7), increased cholesterol level (244.0 mg/dL), high triglyceride (153.0 mg/dL), increased serum urea (170.4 mg/dl), increased serum creatinine (11.23 mg/dl), high calcium (10.4 mg/dl), high inorganic phosphorus (8.5 mg/dl) and high parathyroid hormone (2,164). Radiographic examination revealed cardiomegaly, aortic atherosclerosis, and congestive pulmonum. Electrocardiographic examination suggested Left Ventricle Hypertrophy (LVH), while echocardiographic result showed LVH, mild mitral regurgitation and diastolic disorder. BOF examination showed abdominal calcification. Also, radiographic

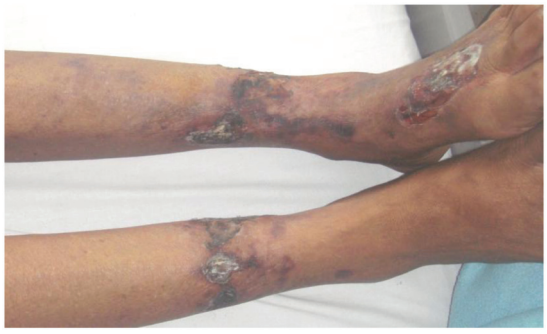

Figure 1 Dermatological status at dorsum pedis sinister, cruris dexter et sinister showed multiple ulcers on livid skin covered by black eschar

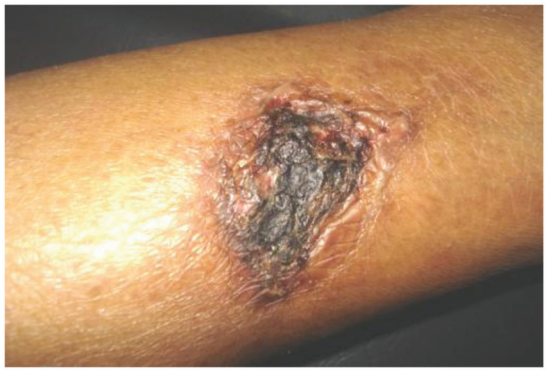

Figure 2 Close up shot of the patient's ulcer

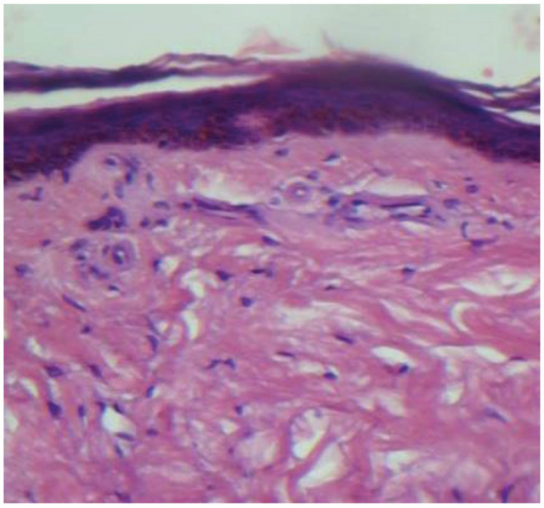

Figure 3 Histopathological examination of the superficial dermis showed arterial blood vessels with thickened walls containing a hyaline concentric/hyaline arteriolosclerosis

examination on cruris dexter et sinister showed soft tissue calcification and osteoporosis.

Histopathology examination of the superficial dermis showed the appearance of arterial blood vessels with thickened walls containing a hyaline concentric/hyaline arteriolosclerosis (Figure 3). In the subcutaneous fat tissue of the interlobular septum, the medium size vessels contain sub intestinal basophilic calcification materials/sub-intimal calcifications (Figure 4). Conclusions of histopathology result supported calciphylaxis.

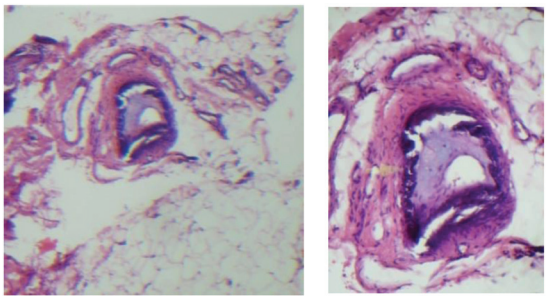

Figure 4 Calcification on subintima blood vessels

The patient was diagnosed with stage V chronic renal failure, hypertension, and calciphylaxis caused by secondary hyperparathyroidism. She was managed by low calcium and phosphate diet, lanthanum, paracetamol, folic acid, adalat oros, captopril and wound debridement.

DISCUSSION

Calciphylaxis or Calcific Uremic Arteriolopathy (CUA) is a rare phenomenon of cutaneous necrosis that typically occurs in association with end-stage renal disease.[4,5] The incidence of calciphylaxis was estimated as high as 5% of dialysis-dependent patients. Data from Partners Research Patient Data Registry reported increasing incidence rates from 3.7 per-10,000 dialysis patients (before 2007) to 5.7 per-10,000 patients (after 2007).[5]

Calciphylaxis lesions presented as tender, indurated subcutaneous plaques with overlying livedo racemosa that progress to nonhealing, stellate-shaped ulcers covered by black eschar.[5,6] The skin lesions usually begin as painful nodules or violaceous mottling similar to livedo reticularis, or as painful panniculitis.[7,8] Areas of involvement include adipose-rich areas of the trunk, including breasts, abdominal pannus, flanks, lower back, buttocks and lower extremities.[5,6] Patient usually complained of pain caused by skin ulceration and necrosis.[5] Risk factors for calciphylaxis include diabetes mellitus,[5,9] obesity,[5,9] female sex,[5,9] liver disease,[5] and Caucasian race.[9]

Calciphylaxis is a small–vessel vasculopathy characterized by mural calcification, intimal fibrosis, and thrombosis. The vascular injury leads to the development of tissue ischemia, especially necrosis, of the skin, subcutaneous fat, visceral organs and skeletal muscle.[9] Histopathological examination will demonstrate medical calcification and intima

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proliferation of small arteries leading to ischemic epidermal necrosis.[5] Primary lesions appear to be the accumulation of calcium salts in small arterial media and arterioles. Furthermore, the intima is thickened by a loose connective tissue, which narrows the lumen.[7] Calcium appears as fine granules in the dermis and as a large irregular mass in the subcutis. Calcium deposits stain dark blue with hematoxylin and eosin and black with von Kossa stain. Vascular thrombotic occlusion may also be noted. Inflammatory cells, especially neutrophils, may extend into subcutaneous fat that mimics lobular panniculitis.[8]

Necrotic and painful ulcer may occur in other diseases such as Martorell ulcer (hypertensive leg ulcer), vasculitis, and pyoderma gangrenosum.[2,10] Martorell ulcer is an ischemic ulcer that associated with longstanding, uncontrolled hypertension.[2,10] Martorell ulcer defined by a painful ulcer on the anterior-exterior of the lower two-thirds of the leg, often symmetrically in the lower extremities, with presence of systemic elevation of blood pressure, absence of atherosclerotic large artery occlusive disease or venous disease of the lower extremity,[10] with histopathology demonstration of calcification on small vessel walls in some areas, intimal thickening in other areas, and re-canalization.[2]

Vasculitis ulcers usually localized in the lower half of the leg and the foot, with palpable purpura as the most frequent sign. Histopathological feature showed leukocytoclastic vasculitis with predominant neutrophil granulocytes and fibrinoid necrosis of the vessel wall.[11]

Pyoderma gangrenosum (PG) occurred commonly on the lower legs with predilection on pretibial area but can occur on other sites of the body including breast, hand, trunk, head, and neck. PG ulcer starts as a follicular pustule with rapid growth, tissue necrosis, and enlargement of the area. The ulcer borders are typically undermined and violaceous, surrounded by erythema skin with infiltration and edema. Histopathology feature of PG was not specified with leukocytoclastic vasculitis presence in 40% of cases.[12]

Our case fulfilled calciphylaxis criteria since there was history of chronic renal failure and hemodialysis altogether with multiple ulcers covered by black eschar over the skin with livedo reticularis pattern. Laboratory examination found increased calcium level (10.4 mg/dl), high inorganic phosphorus (8.5 mg/dl) and high parathyroid hormone (2,164). BOF examination showed abdominal calcification, radiographic examination on cruris dexter et sinister showed soft tissue calcification, and histopathology result supported the diagnosis of calciphylaxis.

Pathogenesis of calciphylaxis remains unclear. However several theories described deposition of calcium in the intima of the arterioles causing tissue ischemia and necrosis. Elevation of serum phosphate in end-stage renal disease leads to increasing of serum calcium from bone and causes deposition into the arterioles.[13]

The prognosis of calciphylaxis is usually poor, with sepsis and ischemic events as the most common complications.[7,8] Management of patients with calciphylaxis involved the use of non-calcium-containing binders and suppression of phosphor serum level under 6.0 mg/dL. Patient without evidence of hyperparathyroidism, daily (5 or 6 days a week) dialysis with a low calcium dialysate may be beneficial. However, when hyperparathyroidism is present (parathyroid hormone above 600 pg/mL), parathyroidectomy should be performed on an emergent basis. Local wound care, debridement of ulcer, and treatment of sepsis were crucial.[7] Our case showed a good response with low calcium and phosphate diet, lanthanum, paracetamol, folic acid, adalat oros, captopril, and wound debridement, with termination of oral calcium supplement.

CONCLUSION

Calciphylaxis is rare phenomenon of cutaneous necrosis associated with end-stage renal disease. Control of end-stage renal disease may be an important factor for treatment of calciphylaxis, another treatment such as the use of non-calcium-containing binders and suppression of phosphor serum level may be beneficial. Patient with calciphylaxis usually had a poor prognosis.

CONFLICT OF INTEREST

Author has no conflict of interest regarding all aspect of this report.

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