

## The Painful Killer; Calciphylaxis: Let No Disease Pull You Down So Low So As You Quit In Despair

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### Case history

The patient is 72 years old Caucasian male with end-stage renal disease on hemodialysis, type-2 diabetes mellitus, obstructive sleep apnea with respiratory insufficiency, calcific aortic stenosis and congestive heart failure. He developed ulcers in the upper thighs, and lower abdomen with violations skin around the ulcers. The skin ulcers progress to webbing non-healing wounds that necessitate multiple debridement. Tissue diagnoses and the clinical picture are consistent with Calciphylaxis (CPX) or calcific uremic arteriopathy (CUA). The patient was evaluated for Tran-aortic valve replacement (TAVR) but because he had wound infection the procedure was postponed until he is cleared of infection. In the course of the hospital stay he developed septicemia with low blood pressure requiring vasopressor support in the intensive care unit. Despite multiple efforts the patient surrendered to his disease after multiple attempts to revive him.

### Discussion

Calciphylaxis (CPX) or calcific uremic arteriopathy (CUA) is a shocking disease that usually claims the life of the enduring patient. The disease is renowned by having relentless course in many patients that ends in painful demise of the victim. The mortality reaches as high as 70% if the disease is not controlled [1]. It is characterized by calcification of the small vessels of the skin and subcutaneous tissue jeopardizing the blood supply and ends in ischemic changes and non-healing ulcers with attendant risks of secondary infection, septicemia, and death of the sufferer [2-4].

It is observed more frequently in patients with end-stage kidney disease especially those on dialysis with a prevalence of 4.1% [5].

Nobody knows why the disease strikes some patients and spares others who have the same characteristics. Many attempts at explaining the pathogenesis of the disease which remains speculative, ranges from chronic renal failure, hyperparathyroidism, and high phosphate diet acting as a trigger resulting in high calcium-phosphate product with resultant precipitation of the calcium-phosphate crystals in the media and internal elastic lamina of the small arteries of the skin and subcutaneous tissues [6-9]. The speculation of disease pathogenesis went so far as to include intravenous iron dextran, albumin infusion, low serum albumin, immunosuppression, trauma to the subcutaneous tissue, and deficiency of protein C and S causing hypercoagulability and subsequent thrombosis of the small vessels [10-16]. Diabetes and obesity have been established as risk factors for CPX [7, 8, 17-19]. These triggering factors are not consistently present in each patients with CPX, throwing some doubt to the effect of these factors as sensitizers in some patients for the occurrence of the disease.

Treatment to target these triggers are not always associated with gratifying results, making one wonder that our knowledge of the disease is still very primitive to help these unfortunate targets. Because our efforts have been directed toward these triggers, akin to chasing the dog's tail, which may be misguided to say the least.

The disease is characterized by deep and superficial ulcers of the skin and subcutaneous tissues that have predilection to the abdomen and upper thighs especially in obese patients. Limb ischemia with digital gangrenes and auto-amputations, and involvement of the internal organs like trachea, aortic calcification and stenosis, and ocular calcification have been reported [20].



We tried to link the disease to chronic kidney disease-bone mineral metabolism (CKD-BMD) with treatment of hyperparathyroidism including even parathyroidectomy, the use of cinacalcet [21-23] targeting calcium and phosphorus abnormalities, the use of sodium thiosulfate [24-29], extensive wound debridement and the use of hyperbaric oxygen chambers [30-32] to no avail.

Calciphylaxis have been reported in patients with no chronic kidney disease [2, 33, 34], casting doubt on the connection of CKD to the disease process. The implications of warfarin, glucocorticoids, and auto-immune disease in the pathogenesis of CPX implies that may be more than one mechanism would have been involved in the disease process [2, 33]. The facts that should fascinate us are why some patients resolve their ulcers and do better while others failed to show improvement. Are we dealing with the same disease process or are we missing some things that characterize those who showed unfavorable prognosis. If this is the case we should strive to know the characteristics of advantageous prognostic factors and target them.

As nephrologists, many of us had the opportunities or adversity to manage these patients with mixed feeling of optimism and despair. Knowing that there is only very little you can provide to these unfortunate casualties. That many of these patients succumb to their disease in pain and agony, and that our determination have little to no impact on this appalling malady. Hyperbaric oxygen as a second-line therapy for refractory CPX wounds have been advocated. However, hyperbaric oxygen is costly and not widely available for all patients [30-32]. If this type of treatment proved to be worth providing to these patients, one wonder if randomized controlled trial of this modality should be carried out to resolve the issue of its efficacy once and for all. We owe it to our patients to do whatever we can to help them overcome this peril and to let no disease pull us down so low so as we quit in despair.

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