



## Case Report

# Calciphylaxis Secondary to End Stage Renal Disease

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### Abstract

Calciphylaxis is a debilitating condition with sometimes fatal implications if not diagnosed in a timely manner. We describe a case of an 85-year-old patient with ESRD on peritoneal dialysis who presented with severe progressive calciphylaxis wounds on both lower extremities.

**Keywords:** Calciphylaxis; End-Stage Renal Disease; Lower Extremity Myopathy; Case Report

### Introduction

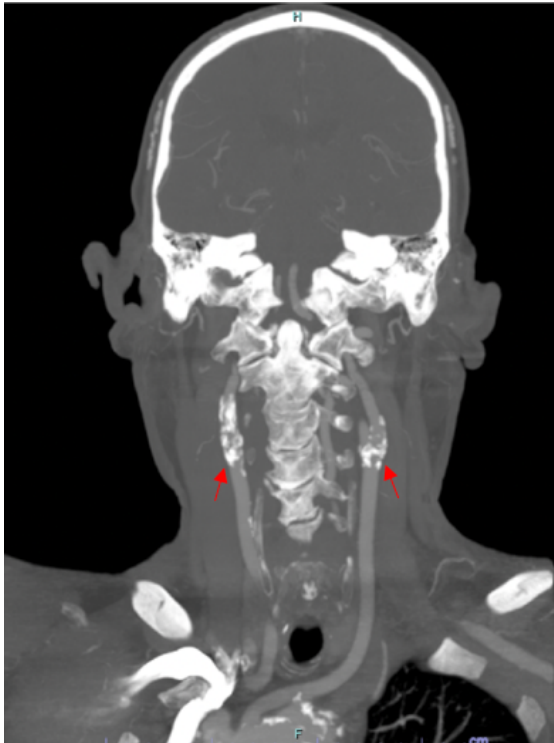
Calciphylaxis, or calcific uremic arteriolopathy, is a rare and debilitating medical condition predominantly seen in patients with end stage renal disease on dialysis. It is characterized by calcification of small and medium-sized blood vessels, leading to skin necrosis and ulcers. The annual incidence of this disease is 35 cases per 10,000 in the United States. Calciphylaxis can be difficult to identify as it is uncommon and has a complex pathogenesis. Hence, before the mortality rate can be decreased, improved understanding and awareness of this illness is required. Prompt and extensive medical intervention is needed to enhance patient's prognosis and quality of life.

### Case Presentation

An 85-year-old male with a past medical history of end stage renal disease on peritoneal dialysis, prostate cancer status post prostatectomy, esophageal cancer status post resection and radiation, permanent atrial fibrillation on apixaban, wet macular

degeneration of eye, hypertension, hyperlipidemia, left inguinal hernia status post resection, and idiopathic peripheral neuropathy presented to the emergency room with chief complain of severe bilateral lower extremity pain, fatigue and the inability to stand. The lower extremity pain had been present for years but had acutely worsened a week prior to presentation [1,2].

One month prior to arrival, patient had an admission for acute painless left eye vision loss, without temporal tenderness or jaw claudication. ESR noted to be elevated at 67 and CRP elevated at 14.5. CT brain done on admission showed no acute pathology. CTA head and neck with bilateral calcified plaques in carotids without significant stenosis, seen in Figure 1. MRI brain showed right parietal and Right CR foci stroke. Neurology was consulted and patient started on Aspirin and statin. Given the consequence of complete blindness, Vascular Surgery team was consulted, and temporal artery biopsy was performed to rule out possible temporal arteritis. Temporal artery biopsy showed severe arteriosclerosis with calcifications. Ophthalmology was consulted and patient received three days of 1g IV solumedrol. Patient was discharged on prednisone 60mg, Aspirin 81mg and Lipitor 40mg with instructions to taper the dose [3,4].



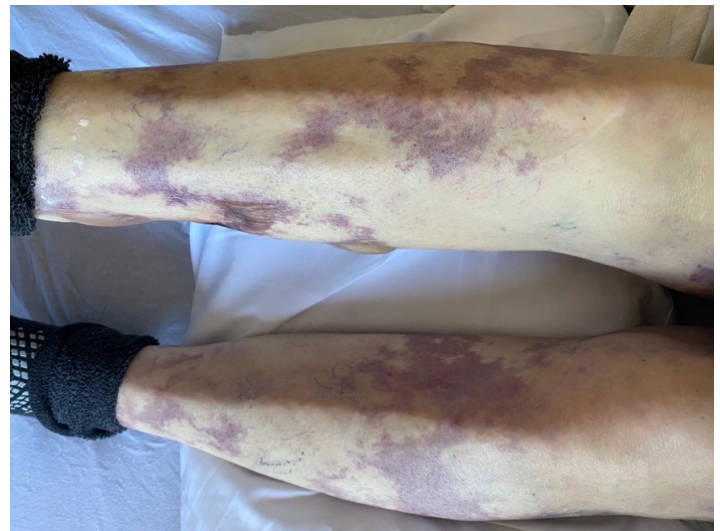
**Figure 1:** CTA Head and Neck with bilateral calcified plaques (red arrows) in carotids without significant stenosis from prior admission.

Six days prior to arrival at hospital, patient had a follow up visit with neurology for prior admission. At that time, no skin lesions, ecchymosis, cyanosis were noted. On neurological exam, patient was awake, alert, oriented, following commands. Cranial nerves were intact, 5/5 motor strength in all extremities with intact tone, no drift noted. Sensation was intact in all extremities. Normally patient is able to walk, and carry out activities of daily living however few days prior to presentation at hospital patient was unable to stand, and started requiring assistance. Upon examination in the Emergency room, patient had complaints of worsening bilateral leg weakness and soreness causing difficulty walking over the past week. Patient had full range of motion in all extremities, no skin lesions noted on exam, diffuse tenderness over bilateral lower extremities. On exam, bilateral lower extremity weakness noted 2/5. CTA was notable for substenotic peripheral vascular disease (PVD). Ultrasound of the lower extremities was negative for DVT [5,6].

## Methods

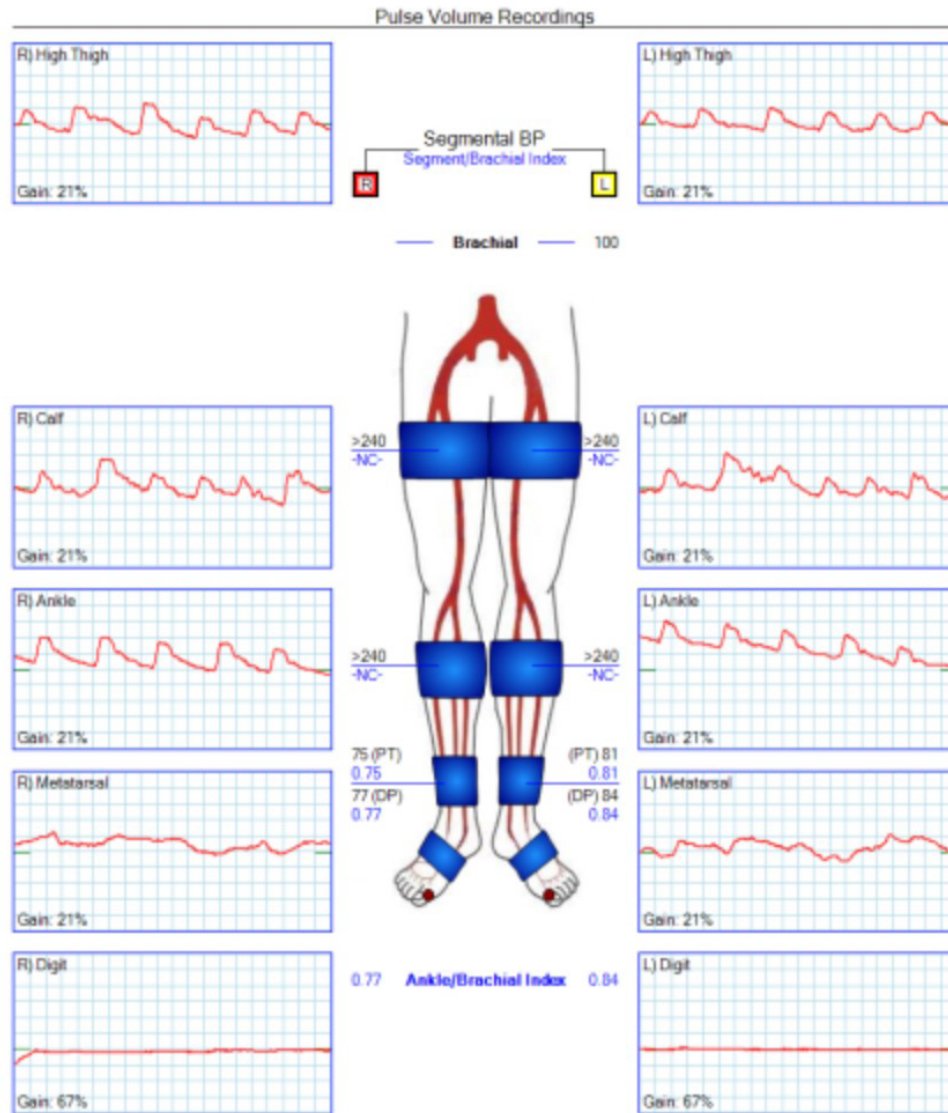
Initial differential diagnoses included PVD, glucose induced myopathy given recent high doses of subsequent prolonged steroids use, statin induced myopathy, and vasculitis. On admission, statin was discontinued. Several hours later, patient was noted to have upper extremity strength 5/5 and lower extremity strength of 0/5 due to pain and sensation changes. Patient also had decreased sensation and increased pain to touch in lower extremity. Nephrology, cardiology, neurology, endocrinology, vascular surgery and wound care services were consulted.

On hospital day 2, the patient developed diffuse tenderness over the entirety of his bilateral lower extremities with ecchymosis over distal legs, as seen in Figure 2.



**Figure 2:** Bilateral Shins with violaceous patches with surrounding retiform purpura

Patient exhibited 2/5 bilateral lower extremity motor strength with diminished sensation and bilateral lower extremity weakness. Lab results were significant for WBC 16.2, hypocalcemia 7.4, elevated BUN 94, creatinine 9.24, EGFR 5.1, hyperphosphatemia 10.5, PTH 832.3. US Venous Doppler bilateral lower extremity was negative for deep vein thrombosis. Computed Tomography Angiography (CTA) Aorta/Ileal/Femoral showed stable 4.8 cm ascending thoracic aneurysm and diffuse atherosclerotic changes, but no critical stenosis [7-9].



**Figure 3:** Illustrates the ABI's (Ankle brachial Index), PVR waveforms and segmental pressures. PVR waveforms are moderately abnormal at bilateral thighs, calves and metatarsals. Waveforms are mildly abnormal at ankles bilaterally. Waveforms are non-pulsatile at the great toes bilaterally. Segmental pressures on bilateral high thighs and below knee are noncompressible (NC). This illustrates that segmental pressures are unremarkable.

Right			Left		
Brachial		Index	Brachial		Index
High Thigh	>240	NC	High Thigh	>240	NC
Calf	>240	NC	Calf	>240	NC
Ankle (PT)	75	0.75	Ankle (PT)	81	0.81
Ankle (DP)	77	0.77	Ankle (DP)	84	0.84

**Table 1:** Illustrates ABI. Right ABI shows dorsalis pedis 0.77 and posterior tibialis 0.75. Left ABI's show DP 0.84 and PT 0.81. This indicates significant disease bilaterally. In table form, segmental pressures on bilateral high thighs and calf are noncompressible, indicating segmental pressures are unremarkable. ABI interpretations: >1.40 = noncompressible, 1.00-1.40 = normal, 0.91-0.99 = borderline, < 0.90 = abnormal

On hospital day 4, patient's bilateral lower extremities worsened with new ulceration scar formation due to suspected calciphylaxis.



**Figure 4:** Lateral Right thigh with eschar and necrotic ulcers, violaceous patches with surrounding retiform purpura.



**Figure 5:** Medial right leg with central eschar, formations of bullous blisters, and surrounding retiform purpura.

The patient was switched to hemodialysis due to worsening renal function. Pain medications, wound care to lower extremity, sevelamer, calcitriol, phoslo and Sensipar were initiated for treatment. Patient was discharged home on day 5 with close outpatient follow up.

### Conclusion

Clinical awareness and a multidisciplinary approach in patients with ESRD are crucial to timely diagnosis. There is an increased risk of developing calciphylaxis in patients with ESRD, especially when presenting with lower extremity pain, skin necrosis, and ulcers. Proper wound care is crucial to prevent necrotic lesions and limiting infections that further complicate the patient presentation. Further research is needed to better understand calciphylaxis pathogenesis and identify effective treatment strategies.

### Discussion

The exact pathogenesis of calciphylaxis is not fully understood, but it is postulated to involve a combination of factors, including hyperphosphatemia, hypercalcemia, and vitamin D dysregulation. Patients with end stage renal disease are at particular risk as they often have chronic kidney disease mineral and bone disorder (CKD-MBD), which can result in these metabolic abnormalities.

In CKD-MBD, the kidneys cannot effectively excrete phosphate, which leads to hyperphosphatemia. This, in turn, can cause a decrease in serum calcium levels, leading to secondary hyperparathyroidism and bone resorption. The resulting increase in serum calcium levels can lead to soft tissue calcification, including the calcification of blood vessels.

A combination of clinical findings, laboratory testing and histologic examination is essential for diagnosis. Skin biopsy remains a gold standard for diagnosis, with characteristic findings including arteriolar calcification and thrombosis, ischemic necrosis, and inflammation, as witnessed by our patient. Skin lesions

associated with calciphylaxis are quite variable in appearance. Firm calcified subcutaneous lesions, which are tender to touch and patients on dialysis, should raise the possibility of calciphylaxis. Pathological and radiographic findings alone are not diagnostic of calciphylaxis and should be clinically correlated. Other tests, such as serum calcium, phosphate and parathyroid hormone levels can help establish the diagnosis and identify underlying metabolic abnormalities.

Treatment options include pain control, wound care, calcium lowering agents, and hemodialysis. Some literature suggests an increased risk of calciphylaxis with peritoneal dialysis. Medical therapies for calciphylaxis are limited, and there is currently no consensus on the optimal pharmacologic approach. Sodium thiosulfate, a chelating agent that improves outcomes in some patients, is often used as a first line treatment. Other agents, such as bisphosphonates, cinacalcet and systemic corticosteroids, have also been used with varying success. Surgical debridement and hyperbaric oxygen therapy may also be considered in certain cases.

Written patient consent was obtained for this patient prior to sharing images and information. Given weakness, patient was unable to sign consent form however patient guardian signed written consent. Signer's name and relationship to the patient is clearly stated where indicated in the consent form.

**Key Clinical message:** This case discusses the importance of multidisciplinary approach to diagnosing and treating acutely progressive diseases like Calciphylaxis in patients with chronic renal disease to prevent progression and reduce the risk of mortality. Patients with ESRD are at increased risk of developing calciphylaxis, and clinicians should have a high index of suspicion when evaluating patients with chronic renal disease who present with lower extremity pain, skin necrosis, and ulcers.

## Declarations

### Author Contributions

- Krishna Sheth: Conceptualization, Data Curation, Formal analysis, Funding acquisition, Investigation, Writing original draft, Writing reviewing and editing

- Yasmine Hemida: Data Curation, Investigation, Methodology, Project administration, Writing original draft, Writing reviewing and editing
- Czariavna Javed: Conceptualization, Formal Analysis, writing- reviewing and editing
- Ryan Punsalan: Formal analysis, funding acquisition, project administration, supervision, validation, writing-reviewing and editing

**Acknowledgments:** n/a

**Ethics:** Written consent was obtained prior to submission. This case report is written with patient privacy and confidentiality.

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**Conflict of Interest:** N/a

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