Case Report: Calciphylaxis in the End Stage Renal Disease Patient

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Introduction

- Calciphylaxis, or calcific uremic arteriolopathy, is a rare disorder characterized by the calcification of arterioles leading to ischemia and the development of cutaneous necrotic ulcers[1]
- Lesions typically occur on the proximal lower extremities, buttocks, and trunk[1,2]
- In those on hemodialysis, the incidence rate has been estimated to be 5.7/10,000[3]
- Risk factors include chronic kidney disease, long-term hemodialysis, female sex, obesity, hyperparathyroidism, and warfarin use[1,2]
- Diagnosis can be clinical and/or confirmed with skin biopsy[2,4]
- Treatment should be multimodal[2,4] and often involves mitigating attributing factors, wound care, treating secondary infections, hemodialysis optimization, pain control and interventions such as sodium thiosulfate and cinacalcet[2,5]
- Even with treatment, prognosis is poor[4] with a 1-year mortality of 40%-70%[5,6]
- The leading cause of death for these patients is sepsis due to secondary infections[1]

Table 1. Differential Diagnosis

Calciphylaxis/calcific uremic arteriolopathy
Diabetic ulcer
Warfarin-associated skin necrosis
Peripheral artery disease
Purpura fulminans
Necrotizing fasciitis
Cholesterol embolization
Antiphospholipid antibody syndrome

Case Description

History

- 40-year-old African American female
- Patient initially admitted and treated for pneumonia and later complained of painful, non-healing wounds on bilateral proximal lower extremities
- ROS: Endorsed fatigue and bilateral leg pain; No fever/chills, night sweats, chest pain, dyspnea, GI complaints
- Medical History: DMII, end stage renal disease, chronic hemodialysis (>10 years), class 2 obesity
- Surgical History: parathyroidectomy (2016), aortic and mitral valve replacement
- Medications: warfarin 5 mg daily, gabapentin 300 mg TID, methylprednisolone 4mg, metoprolol Succinate 50 mg daily, pantoprazole 40 mg BID, rosuvastatin 10 mg daily
- Allergies: Iodine
- Family History: mother, type 2 diabetes and obesity
- Social History: Periods healthcare coverage gaps. Never a smoker. No alcohol or illicit drug use

Table 1 includes differential diagnosis

Physical Exam

- Vital Signs:
  - BP: 114/68 mmHg
  - Pulse: 112 bpm
  - Temp: 37.5 °C
  - Resp: 18
  - SpO2: 95% room air
- General: Ill-appearing, obese
- Cardiovascular: Murmur most pronounced at left parasternal area
- Integument:
  - Bilateral medial thigh wounds, necrosis and eschar noted (Figures 1 & 2)
  - Ulcer with areas of necrosis on left buttocks
- Remainder of physical exam was within normal limits

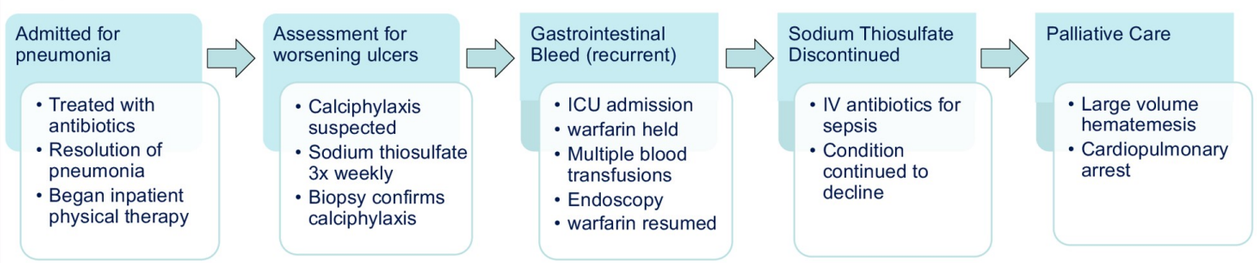
Diagnostic Results

- Routine CBC and chemistries remarkable for leukocytosis, anemia, thrombocytosis, and renal labs consistent with end stage renal disease
- Punch biopsy of left buttocks showed one calcified vessel at junction between dermis and subcutaneous fat. Findings consistent with calciphylaxis
- Blood culture revealed no growth
- Upper endoscopy showed large pedunculated gastric polyp and ulceration

Fig 1. Right medial thigh 3 weeks after clinical diagnosis

Fig 2. Right medial thigh 7 weeks after clinical diagnosis

Fig 3. Hospital Course



Case Outcome

- Figure 3 shows hospital course
- Patient received wound care and began sodium thiosulfate therapy 3x/week during dialysis once calciphylaxis suspected
- Wounds on lower extremities and buttocks continued to progress and new wounds developed on trunk
- Cinacalcet added to medication regimen
- Patient transitioned to enoxaparin 0.8 mg/kg SQ daily and factor Xa levels were monitored after third recurrence of GIB
- Patient developed sepsis likely secondary to wounds and treated with IV antibiotics
- Condition not responsive to treatment and sodium thiosulfate discontinued after 8 weeks
- Patient transitioned to palliative care and later went into cardiopulmonary arrest following large volume hematemesis.

Discussion

- There was a high index of suspicion for calciphylaxis given the multiple risk factors of this patient
- As seen in this patient, ulcerated wounds at time of diagnosis is associated with poor outcomes[7]
- While avoiding or discontinuing warfarin is optimal,[4,5] discontinuation may not be feasible in all patients as seen in this patient (poor renal function, history of cardiac valve replacement)
- Sodium thiosulfate may benefit some patients however, it is generally ineffective in later stages of the disease[7]
- While sepsis is the most common cause of mortality in calciphyaxis[1], this patient ultimately succumbed to a massive gastrointestinal bleed (GIB)
- This patient's recurrent GIB may have been related to her calciphylaxis diagnosis, as gastrointestinal involvement has been reported in the literature[8,9]

Conclusion

- Calciphylaxis is a serious condition with high mortality rates
- While it is thought to be rare, it should be considered in high-risk patients
- Diagnosis can be made clinically and can be confirmed with biopsy
- Management consists of early recognition, addressing risk factors, trialing sodium thiosulfate, and preventing/treating secondary infections

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