

Calciphylaxis in Primary Hyperparathyroidism: A Case Report & Literature Review

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Introduction

Calciphylaxis, also known as calcific uremic arteriopathy, is a painful, cutaneous, calcific arteriopathy that leads to ischemia and necrosis, most commonly in the extremities. It is frequently associated with cases of secondary and tertiary hyperparathyroidism, and is clinically seen in patients with end-stage renal disease. An underreported cause of calciphylaxis in the literature is primary hyperparathyroidism, where hypersecretion of parathyroid hormone (PTH) by a parathyroid adenoma, carcinoma, or hyperplasia modulates excess calcium reabsorption in the kidneys and resorption of the bone.

Excess calcium results in cutaneous and vascular calcium-phosphate deposits and is pathologically characterized by histological confirmation of epidermal and dermal calcium deposition, including the small and medium vessels of the dermis. Patients with this condition present with painful livedo reticularis-like skin mottling, which progresses to ulceration, necrosis, gangrene, and results in eschar formation. Currently, there are no clear treatment recommendations. Our study identified cases that exist in the literature, and sought to outline commonalities in comorbidities, and survey treatment plans.

Case Report

A 64 yo Caucasian woman, admitted to our hospital with necrotic painful skin lesions on the right lower calf. Biopsy was not performed until 5 months after the diagnosis.

PMH: Dilated cardiomyopathy, CAD, Type II Diabetes, Hypercholesterolemia, HTN, PVD, Stroke, Obesity, CKDIII

FHx: HTN, HLD, DMII

SHx: Denies ETOH, smoking, no illegal drugs

Labs:

- Hb: 12.4, Plt 189
- Na 142, K: 4.5, Bicarb 33, Albumin: 3.6, Glc: 115, BUN: 54, Cr: 2.1, GFR: 32
- PO4: 3.0, Ca 10.6mg/dL, PTH 358 pg/mL
- LFTs normal
- Weight: 145kg, Height: 5'5"
- BMI: 53.1
- Autoimmune serological workup is negative
- Ultrasound doppler ruled out DVT

Biopsy Samples:

- Initial punch bx on 2/14/2020 performed posterior right lower leg showed ulceration and stasis changes with focal thrombotic vasculopathy. However, this may be a poor sample due to the depth of the biopsy.
- Patient developed another wound in left lower extremity, and was seen by the wound care clinic. On 7/3: Punch biopsy on left lateral leg wound. Technique of the biopsy was adequate.
- Description of the biopsy: 0.5 cm scarlike superficial changes w/ granulation tissue and nearby fat necrosis. Pathologic diagnosis of calciphylaxis was made

Management

Management for this patient was wound care. The patient followed up with wound care clinic periodically. Patient was also seen by an otolaryngologist. Due to her medical conditions, she was not a candidate for a parathyroidectomy. Therefore more conservative measures were performed for the patient, which was limited to wound care management due to improvement in wound care alone, and the patient was last followed up in October 2020.

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Results



Image 1. Initial lesion of calciphylaxis patient.



Image 2. Calciphylaxis lesion 5 months after treatment.

Table: Reported Cases of Calciphylaxis in Primary Hyperparathyroidism (See references)

Case #	Demographics	Calcium Level (mg/dL)	Phosphate Level (mg/dL)	PTH level (pg/mL)	Parathyroid Adenoma	Treatment	Outcome
1	71 YO F	19.52	2.69	16.65	Yes	Combo- Prednisolone then Parathyroidectomy	Recovered
2	69 YO F	5.49	5.57	173.7	Yes	Surgery- Parathyroidectomy	Recovered
3	49 YO F	11.2	2.1	82	Yes	Surgery- Parathyroidectomy	Recovered
4	72 YO F	9.06	2.63	NR	Yes	Medical- Magnesium Carbonate	Death- Sepsis
5	56 YO F	10.4	4.3	59	Yes	Combo- Methylprednisolone & Parathyroidectomy	Recovered
6	83 YO F	11.74	3.66	1227	Yes	Medical- Bisphosphonate	Recovered
7	66 YO F	10.4	3.7	216	Yes	Surgery- Subtotal parathyroidectomy	Recovered
8	56 YO F	9.7	8.4	737	Yes	Surgery- Parathyroidectomy	Recovered
9	29 YO F	18.7	4.6	NR	Yes	Surgery- Parathyroidectomy	Death - Organ Failure
10	52 YO F	16	2.13	2,257	Yes	Combo- Bisphosphonate then Parathyroidectomy	Recovered
11	53 YO F	13.1	3.8	295	Yes	Surgery- Parathyroidectomy	Death - Organ Failure, Sepsis
12	76 YO F	11.7	3.2	167	Yes	Surgery- Parathyroidectomy	Recovered
13	63 YO F	13.55	NR	2295	Yes	Surgery- Parathyroidectomy	Recovered
14	58 YO F	9.5	3.4	70	NR	Medical- Prednisone	Not reported
15	53 YO F	7.7	4.5	118.3	Yes	Medical- Sodium Thiosulfate	Death - Organ Failure
16	52 YO F	14.8	1.4	893.3	Yes	Surgery- Parathyroidectomy	Death - Sepsis
17	24 YO F	15.8	4.5	922	Yes	Surgery- Parathyroidectomy	Recovered
18	69 YO M	NR	NR	NR	Yes	Not available- Autopsy	Death - Sepsis
19.1	62 YO F	13.8	3.7	NR	Yes	Surgery- Parathyroidectomy	Recovered
19.2	60 YO F	14.1	1.8	NR	Carcinoma	Surgery- Parathyroidectomy	Death - Sepsis
20	64 YO F	9	4.2	98.3	NR	Medical- Sodium Thiosulfate	Recovered
21	44 YO F	9.6	3.3	164	NR	Medical- Sodium Thiosulfate	Recovered
22	84 YO F	9.3	3.66	236	NR	Medical- Sodium Thiosulfate	Recovered
23	64 YO F	10.6	3.0	358	Yes	Medical - Wound Care	Recovered

Discussion

- Pathophysiology of calciphylaxis remains unknown; however there are different molecular mechanisms that are proposed.
 - Increase in oxidative stress and inflammation, which inhibit the regulation of vascular calcification
 - Increase in the calcium phosphate product increases deposition in the vasculature, resulting in necrosis and ischemic events in the skin and joints, ultimately presenting as sepsis in a patient
 - Proteins involved in regulating vascular calcification are inhibited by a different mechanism that is currently undergoing investigation, namely the Matrix-gla protein, among other proteins.
- Biopsy
 - Calcifications in the small and medium vessels
 - Tunica media calcification
 - Soft tissue calcification
 - Some may show ulcerations and necrosis of the epidermis and dermis
 - Microcalcifications: seen with a special stain such as von Kossa or Alizarin red; not required to make a diagnosis
- Management of Calciphylaxis
 - Wound care
 - Dermatology consultation
 - Sodium thiosulfate, bisphosphonates, calcimimetics
 - Surgical debridement - especially in patients with necrotic lesions
 - Parathyroidectomy is curative

Conclusion

- Patients who have primary hyperparathyroidism and have a skin lesion as seen in our case should have calciphylaxis considered in the differential diagnosis. Without proper treatment, patients are at a high risk of death.
- Biopsy sampling may need to penetrate deeper layers of the skin in order to obtain a proper sample so that the diagnosis of calciphylaxis can be properly made

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