

A Wound That Won't Heal

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Patient Overview

59-year-old female with a history of hypertension, coronary artery disease, atrial fibrillation on Warfarin, COPD.

Initial Symptoms:

PCP- Dark, painless, plaque-like lesions on legs evolving into painful non-healing chronic ulcerating wounds. Treated for multiple rounds of cellulitis. Being treated over a course of 3-4 months by PCP in neighboring state

4 months later: Patient admitted to ED at OSH for her ulcerating skin wounds that are now painful with redness, numbness and tingling on bilateral lower extremities.

Labs and imaging

Test	Value	Range	Units
ESR	96	0-20	mm/hr
CRP	6.3	<1.0	mg/L
WBC	9.7	3.5-11.0	k/uL
Platelet	295	150-450	k/uL
Hgb	10	12.4-15.2	g/dL
Na	132	135-145	mmol/L
Albumin	2.1	3.5-5.0	g/dL
Alk Phos	75	38-126	u/L
AST	53	14-36	u/L
ALT	37	0-34	U/L
K	3.9	3.5-5.0	mmol/L
Cr	0.53	0.7-1.1	m/dL
Ca	8.4	8.4-10.5	mol/L

Test	Value	Range	Units
C3	141	88-165	mg/dL
SSA/SSB	Negative		
Cryoglobulins	Negative		
ANCA	Negative		
ANA	Negative		
Infectious Work-up	Negative		
Urine	Negative protein and no RBC		
Chest Xray	5/13/2023 – No abnormality's		



Imaging from OSH

A) CT femur Left with Contrast

- 1. Subcutaneous edema of the LEFT thigh region with no high suspicion findings for necrotizing fasciitis.
- 2. Advanced osteoarthropathy of the LEFT hip.

B) CT Angiogram Abdomen Pelvis Without and With Contrast

- 1. **No vascular abnormalities** are seen to explain mesenteric ischemia
- 2. Inflammatory changes involving the right colon have improved
- 3. Peripheral vascular disease, particularly involving the infrarenal aorta, and the common iliac arteries. The left common iliac artery is occluded **with reconstitution** at the level of the external iliac artery
- 4. Soft tissue defects are seen in both thighs, and lateral to the left hip

Imaging from OSH (cont.)

C) CT Angiogram LE Bilateral W contrast

1. **Diffuse atherosclerotic disease** in the visualized aorta and major arterial vessels of the lower extremities, as detailed above. No lower extremity vessel thrombosis. Some of the arterial vessels in the right calf are poorly visualized distally potentially related to peripheral vascular disease. Please see discussion above.
2. **Prominent soft tissue ulceration/defects in the bilateral thighs**, left more prominent than right, but without evidence of subcutaneous abscess or fluid collection.
3. **Extensive superficial soft tissue edema** throughout the pelvis and bilateral lower extremities. This may represent sequela of anasarca and/or cellulitis



Initial Differentials?

- Infection
- Malignancy
- Vasculitis
- Other Inflammatory process
- Drug reaction



Superficial Biopsy

- Superficial and deep suppurative inflammation predominantly around blood vessels and fat septa
- Epidermal necrosis is noted
- No calcifications seen
- The presence of suppurative inflammation helps rule out warfarin induced skin necrosis

“Overall, the clinical and histologic features are most concerning for a diagnosis of cutaneous polyarteritis nodosa (cPAN)”

Treatment

- Debridement + Cyclophosphamide 150 mg and prednisone 20 mg daily on discharge

Worsening Symptoms

- Patient readmitted to OSH 3 months later then transferred to our hospital
- On arrival s/p 1g Solu-Medrol x2 days for concern of worsening cPAN by previous facility



Physical Exam

General appearance: Oriented to time and place. Patient unwilling to perform any exams

Skin exam: Multiple back eschar lesion with open wounds and exposed subcutaneous tissue on B/L L/E of various sizes

Hair and scalp exam: hair exam is normal without alopecia or scalp lesions

Musculoskeletal exam: Grossly intact active U/L movements

Chest: Unlabored breathing. Unable to further perform exam

CVS exam: Unable to perform

Abdominal exam: No abnormality on visual inspection

Neurological exam: Oriented to self. No focal deficits. Answering questions appropriately



Labs

Component	Result	Ref Range
WBC	7.2	4.0 - 10.5 K/uL
RBC	2.86 (L)	4.1 - 5.1 M/uL
Hemoglobin	8.8 (L)	12.0 - 16.0 g/dL
Hematocrit	28.4 (L)	36 - 46 %
Platelets	150	130 - 400 K/uL
Sodium	138	136 - 148 MMOL/L
Potassium	4.9	3.5 - 5.2 MMOL/L
AST	25	15 - 37 U/L
ALT	90 (H)	10 - 49 U/L
Alkaline Phosphatase	158 (H)	46 - 116 U/L
Total Bilirubin	1.4 (H)	0.3 - 1.2 MG/DL
Creatinine	0.68	0.55 - 1.02 MG/DL

Component	Result	Ref Range
BUN	24 (H)	7 - 23 MG/DL
eGFR	>90	>60 ml/min/1.73m2
Hepatitis B Core Ab, Total	Nonreactive	Nonreactive
Hep A Total AB	Nonreactive	NON-REACTIVE
Hepatitis B Surface Ag Screen	Nonreactive	Nonreactive
Hep B Post Vac Quant	<10.00	MIU/ML
Hepatitis C Ab Screen	Nonreactive	Nonreactive
Cardiolipin Antibody (IgG)	<2.0	<20.0 GPL
Cardiolipin Antibody (IgM)	<2.0	<20.0 MPL
Cardiolipin Antibody (IgA)	<2.0	<20.0 APL



Cultures

- OSH cultures revealing:
 - LLE Wound – 1) Pan-sensitive *Proteus Penneri* & 2) MDR *Pseudomonas aeruginosa* (Resistant to imipenem, levofloxacin, meropenem, and piperacillin-tazobactam)
 - Blood: Pan-sensitive *Pseudomonas fluorescen*
- Treatment with Ceftolozane-tazobactam in addition to debridement



What does this change?

Repeat Full-Thickness Biopsy

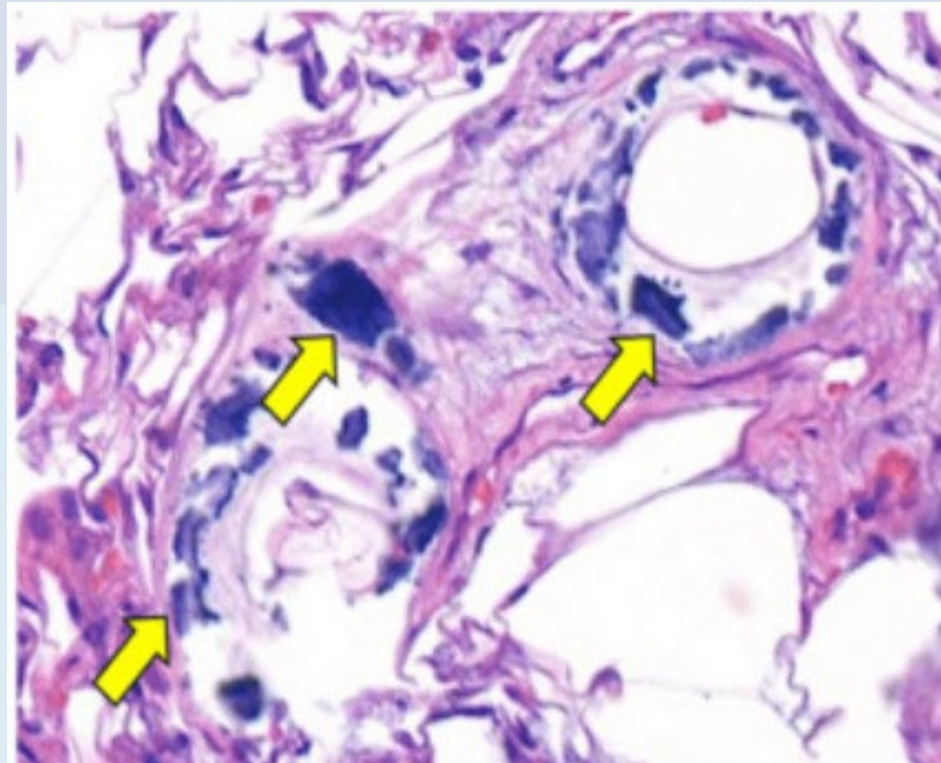
- Ulcerated skin with underlying subcutaneous adipose tissue showing **stippled microcalcification of capillaries, extravascular microcalcifications as well as calcification of medium to larger sized vessel walls**

Next Steps

- Prednisone and cyclophosphamide discontinued
- De-escalated to Cefepime
- Initiated oral Sodium Thiosulfate 25mg Daily



Pathology



Obtained from: Al Yacoub R, Jamalifard F, Ladna M, Walker A. Non-uremic Calciphylaxis With Possible Initial Misdiagnosis as Erythema Multiforme/Toxic Epidermal Necrolysis Successfully Treated as Inpatient. *Cureus*. 2023 Aug 17;15(8):e43618. doi: 10.7759/cureus.43618. PMID: 37719563; PMCID: PMC10504681.

After Thoughts

- Importance of obtaining full thickness biopsy or repeat if clinical picture does not improve
- Misdiagnosis can lead to inappropriate treatments that exacerbate the condition
 - IE; steroids in this case that can worsen calciphylaxis

Conclusion

- Despite aggressive treatment patient passed away due to sepsis/infection

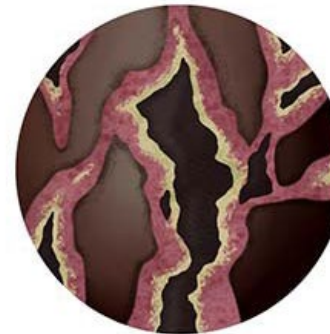




Moderate
*Blistered lesions and
leathery, hard skin*



Mild
*Lesions that have a
next-like appearance*



Severe
*Star-like wounds with
scabs of black, dead skin*

Cleveland Clinic. (2024). *Calciophyaxis Illustration*. Retrieved August 15, 2024, from <https://my.clevelandclinic.org/-/scassets/images/org/health/articles/calciophyaxis-illustration>

Non-Uremic Calciphylaxis

- A rare, life-threatening condition characterized by calcification of small and medium-sized blood vessels in the skin and subcutaneous tissue, leading to tissue necrosis
- Risk factors: Hyperparathyroidism, Hyperphosphatemia, Medications (Warfarin, Vit D, Steroids), Malignancies, Hypercalcemia, DM, Obesity, Liver disease, Protein C and S def.
- Pathophysiology: Vascular calcification -> Thrombosis -> Reduced blood flow -> Tissue Ischemia and Necrosis
- Prognosis: Poor due to secondary infection risk/sepsis



Retrospective Labs

Component	Result	Ref Range
PTH intact	72.6	18.4 - 88 pg/ml
Calcium	8.8	8.5-10.4 mg/dl
Phos	4.1	2.4-5.1 mg/dl
Vit D	37	30-100 ng/ml



Resources

1. Weenig, R. H., Sewell, L. D., Davis, M. D. P., McCarthy, J. T., & Pittelkow, M. R. (2007). "Nephrogenic Fibrosing Dermopathy and Nonuremic Calciphylaxis: Clinicopathologic Comparison in Five Patients." *Journal of the American Academy of Dermatology*, 56(5), 768-783. doi:10.1016/j.jaad.2006.12.021
2. Zhao, H., Li, S., & Zhang, L. (2021). "Nonuremic Calciphylaxis: A Rare but Life-threatening Condition." *The American Journal of Medicine*, 134(6), 786-788. doi:10.1016/j.amjmed.2020.10.030
3. Nigwekar, S. U., Thadhani, R., & Brandenburg, V. M. (2018). "Calciphylaxis." *The New England Journal of Medicine*, 378(18), 1704-1714. doi:10.1056/NEJMr1505292
4. Hoffman, L., & Mather, P. J. (2017). "Non-Uremic Calciphylaxis: Case Report and Review of the Literature." *World Journal of Clinical Cases*, 5(6), 226-233. doi:10.12998/wjcc.v5.i6.226

