Complicated Case of Relapsed Cutaneous Angiosarcoma of the Proximal Right Lower Extremity

Deanna Sgambato PA-S, Magdalena Lukaszewicz MHS, PA-C
Quinnipiac University Physician Assistant Program

Introduction

- Cutaneous angiosarcoma is an aggressive, rare malignancy arising from the vascular epithelium[1]
- Incidence of sarcomas overall is 7.1 per 100,000 persons with cutaneous angiosarcoma making up 1% of all sarcomas[1,2]
- For patients with no cancer history, 83% of cutaneous angiosarcomas occur in the head and neck/scalp, whereas 51% of cases occur on the trunk for patients with previous cancer diagnoses[3]
- Risk factors include past radiation exposure, chronic lymphedema, and exposure to foreign bodies such as Dacron and other graft materials[4,5]
- Cancers requiring radiation treatment may increase risk for cutaneous angiosarcoma development with breast cancer being the most common[3]
- The phenomenon of cutaneous angiosarcoma in areas affected by chronic lymphedema was first observed and described by Stewart and Treves in 1948 with postmastectomy patients[6]
- Stewart-Treves Syndrome is still described today as cutaneous angiosarcoma arising from tissues that have been chronically lymphedematous[7]
- MYC gene amplification has been found in many patients with radiation-associated cutaneous angiosarcoma as well as other angiosarcomas[8]
- Figure 1 depicts the prognostic staging of soft tissue sarcomas that is used for cutaneous angiosarcoma

Figure 1. Prognostic Staging of Soft Tissue Sarcoma[13]

T category	N	M	G	Stage
T1	N0	M0	G1, GX	IA
T2, T3, T4	N0	M0	G1, GX	IB
T1	N0	M0	G2, G3	II
T2	N0	M0	G2, G3	IIIA
T3, T4	N0	M0	G2, G3	IIIB
Any T	N1	M0	Any G	IV
Any T	Any N	M1	Any G	IV

**Scoring of histologic grade refers to total differentiation, mitotic count and necrosis

T = Primary tumor;
T0 for no tumor
T1 for ≤ 5*cm*
T2 for > 5, but ≤10 cm
T3 for > 10, but ≤15 cm
T4 for > 15 *cm*
N = Regional lymph nodes
N0= none, N1 = present
M = Distant Metastasis
M0= None, M1 = present
G = Histologic Grade
GX= Cannot be assessed
G1= Score of 2 or 3
G2= Score of 4 or 5
G3= Score of 6, 7, or 8

Differential Diagnosis

- Metastases from other primary cancer
- Cutaneous Angiosarcoma
- Stewart-Treves Syndrome
- Cellulitis
- Kaposi Sarcoma

Case Description

History

CC: "I feel weak"
HPI:
- 59 year-old, white female who initially presented to the emergency department for "low blood counts" and returned to skilled nursing facility (SNF) after being vitally stable for 24 hour
- Went back to SNF and readmitted to emergency department within 8 hours of first admission with new onset weakness and hypotension
- Had 9/10 pain and bleeding in right lower extremity

PMH
- Chronic lymphedema of right lower extremity, relapsed cutaneous angiosarcoma, type 2 diabetes mellitus, chronic obstructive pulmonary disease, Barrett's esophagus, hypertension, obstructive sleep apnea, gastroesophageal reflux disease, depression, deep vein thrombosis

PSurgHx
- Right above-the-knee amputation in 2020 after cutaneous angiosarcoma diagnosis in distal right lower extremity

Allergies
- No known drug allergies

FHx
- Leukemia and colon cancer in unknown family members at early ages
- No history of sarcomas or breast cancer

SHx
- Tobacco: quit 17 years ago, approximate 20 pack-year history
- No current ETOH or recreational drug use

Home Medications
- bupropion 150mg twice daily
- ferrous sulfate 325mg twice daily
- pantoprazole 40mg once daily
- pregabalin 150mg twice daily
- tizanidine 4mg once daily
- sennosides 2 tabs once daily
- sucralfate 1g twice daily
- rosuvastatin 10mg once daily
- omega-3 once daily
- folic acid 0.4mg once daily
- multivitamin once daily
- For angiosarcoma: **pazopanib and paclitaxel**

As Needed Medications
- acetaminophen 650mg
- calcium carbonate1000mg
- metoclopramide 10mg
- hydromorphone 2mg
- ondansetron 4mg
- fluticasone spray
- ipratropium-albuterol 3mL nebulizer

ROS: (+) fatigue, generalized weakness

Physical Exam

Vital Signs:
- BP: **94/57 mmHg** HR: 84 bpm
- RR: 18 breaths per minute
- SpO2: 97% Temp: **100.0**°F
- Wt: 134 kg BMI: **49.31 kg/m²**

General: No acute distress noted, appeared to be uncomfortable and in pain on exam

Skin: Elevated, red, asymmetric, ulcerated, circumferential lesion and yellow-colored, rough, elevated patches noted to the proximal right lower extremity with sanguineous drainage; no pallor noted

HEENT: PERRLA, no conjunctival pallor
CV: Regular rate and rhythm
Pulm: No accessory muscle use noted, lungs clear to auscultation
GI: Soft, non-tender abdomen; no abdominal bruits noted; no hepatosplenomegaly
MSK: Decreased ROM of right hip; strength testing deferred secondary to pain; right above-the-knee amputation noted
Neuro: A&Ox3
Psych: Depressed mood with congruent affect

Diagnostic Studies

- MRI of right lower extremity: cutaneous angiosarcoma diagnosis without evidence of osteomyelitis
- Abdominal CT scan identified hepatic mass
- PT: 19.1 seconds
- Sodium: 131 mmol/L at beginning of hospitalization, then decreased 128 mmol/L during hospital course
- Urine cx: (+) *Klebsiella*
- Cleared for chemotherapy with echocardiogram
- Next generation sequencing panel: (+) MYC gene amplification

Figure 3. Hemoglobin and Hematocrit During Hospital Stay

	Day 1	2 units of blood given	Day 2	Day 3	8 hr later	8 hr later
Hgb (g/dl)	7.3		9.5	7.6	8.4	8.5
Hct	23.5		30.4	24.1	26.3	26.5

Treatment/Outcome

- Rapid decline after hospitalization as described in Figure 2 with hypotension, sepsis, and findings similar to Figures 4 and 5
- Hypotension managed with IV midodrine 75mg twice daily as well as norepinephrine and vasopressin during rapid responses
- Sepsis treated with IV vancomycin 20mg every 12 hours and IV levofloxacin 750mg every 24 hours
- Multidisciplinary consults obtained to aid in complex care

- **Conclusion of vascular surgery consult:**
- Proposed possible diffuse embolization for palliation and to improve blood volume along with the application of proper wound care
- Hold rivaroxaban to decrease bleed from leg

- **Oncological care:**
- Chemotherapy restarted on hospital day 3 sigh with doxorubicin and paclitaxel
- Determined that hepatic mass would not impact treatment modality

- After 11 days in hospital complicated with septic shock, patient was made comfort measures only and died in hospital

Figure 2. Hospital Course

Days 1-2
- Initial visit to ED for 24 hour observation
- Second emergency department visit with BP of 94/57
- Was provided 2 units of blood and stabilized before being admitted
- Started IV vancomycin for possible superimposed cellulitis of cutaneous angiosarcoma

Day 3
- Rapid response called for hypotension with systolic BP of 66 – believed to be septic shock
- Admitted to the ICU
- Chemotherapy treatment for angiosarcoma restarted
- Held anticoagulation due to active bleed in RLE

Day 4
- Hepatic mass identified through imaging, not previously seen
- Right ureter stent placed due to UTI with AKI and calculus
- Remained in the ICU

Days 5-9
- Levofloxacin and vancomycin provided throughout for UTI and possible cellulitis of RLE
- Blood transfusions provided as Hct and Hgb decreased
- Rapid response called again for hypotension

Days 10-11
- Patient became comfort measures only and died on hospital day 11, secondary to septic shock

Discussion

- Local recurrence of cutaneous angiosarcoma is approximately 57% with ulceration and bleeding at affected sites occurring frequently[1,9]
- Five-year survival rate of cutaneous angiosarcoma is 12-33%, which is lower than other angiosarcomas[1]
- Surgical treatment is typically indicated for cutaneous angiosarcoma followed by radiotherapy[1]
- For cases that are ineligible or refractory to surgical resection, chemotherapies can be used[10]
- Doxorubicin, paclitaxel, and cisplatin-based chemotherapies have shown success in some with cutaneous angiosarcoma[10,11]
- Palliative embolization was suggested in this case, which could be used in a variety of cancers to mitigate negative outcomes with refractory, uncontrolled bleeds[12]

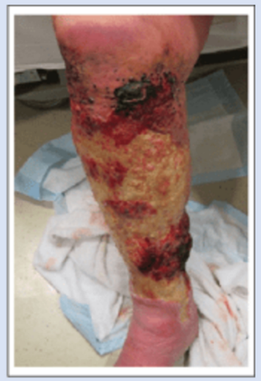

Figure 4. Example of a cutaneous angiosarcoma of the leg[14]

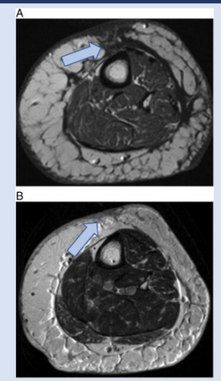

Figure 5: Example of T1 and T2-weighted MRI images of cutaneous angiosarcoma of the leg[15]

Conclusion

- Cutaneous angiosarcoma should remain on the differential diagnosis and be investigated in patients with non-healing lesions and a history of irradiation or chronic lymphedema
- Recurrence is common, so it is imperative to follow-up every 3 to 6 months in patients with a history of cutaneous angiosarcoma
- More research is needed to continue to improve treatments and patient outcomes as there is currently no standard guideline to treatment for cutaneous angiosarcomas

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