PERPLEXING PURPLE PAPULES OF THE PANNUS: AN INTERESTING CASE AND REVIEW

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• No relevant disclosures
OBJECTIVES

• Case presentation
• Clinical features
• Diagnosis
• Prognosis
• Treatment
CASE REPORT

- 50 year old morbidly obese female with a progressively enlarging, painful growth on the left lower abdomen
- Started as a small red “bump” 2 years ago, now with rapid growth over the last 2 months
- Initially told this was a “cyst” then later “calcified fat”
- Past Medical History: Obesity, limb- girdle muscular dystrophy, ventilator dependent respiratory failure with tracheostomy, diabetes mellitus, hypertension. No History of malignancy or radiation
- Past Family History: brain cancer (father)
EXAMINATION REVEALED

AN EXPANDING ERYTHEMATOUS-VIOlACEOUS INDURATED, EDEMATOUS PLAQUE
CLOSER INSPECTION

30-40 CM VIOLACEOUS PLAQUE WRAPPING AROUND THE BACK
CLOSER INSPECTION

ULCERATED, FUNGATING, NODULES
IMMUNOHISTOCHEMICAL STAINS

- Strong and diffusely positive for CD31 and D2-40
- Positive for Ki67
- Negative for HHV-8
KI67
CONCLUSION

• Consistent with Angiosarcoma
ADDITIONAL WORKUP

- Abdominal CT scan showed no evidence of metastatic disease.
- PET scan revealed multifocal hypermetabolic lesions in the lower abdominal wall consistent with malignancy. A hypermetabolic left cervical level III lymph node concerning for metastatic disease.
- Evaluated by surgical oncology and determined an inappropriate surgical candidate given extensiveness of the resection with her significant comorbidities.
- Scheduled to follow up with medical oncology to discuss further staging and systemic chemotherapy.
- Subsequently developed a pulmonary embolism further complicated by septic shock and an acute MI.
- Patient expired within 2 months of diagnosis.
WHY IS ANGIOSARCOMA IMPORTANT?

- Angiosarcoma is one of the most aggressive cancers and has a dismal prognosis
- Rare cancer, 0.1% of adult malignancies
- Variable clinical presentation leads to delay in diagnosis
CLINICAL PRESENTATION

• Angiosarcoma can arise in any soft-tissue structure or viscera
• The most common form of angiosarcoma is cutaneous angiosarcoma affecting the face and scalp of the elderly

<table>
<thead>
<tr>
<th>Location</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck</td>
<td>144 (27.0%)</td>
</tr>
<tr>
<td>Breast</td>
<td>105 (19.7%)</td>
</tr>
<tr>
<td>Extremities</td>
<td>82 (15.3%)</td>
</tr>
<tr>
<td>Trunk</td>
<td>51 (9.5%)</td>
</tr>
<tr>
<td>Liver</td>
<td>32 (6.0%)</td>
</tr>
<tr>
<td>Heart</td>
<td>25 (4.7%)</td>
</tr>
<tr>
<td>Bone</td>
<td>19 (3.6%)</td>
</tr>
<tr>
<td>Spleen</td>
<td>14 (2.6%)</td>
</tr>
<tr>
<td>Other or unknown</td>
<td>62 (11.6%)</td>
</tr>
</tbody>
</table>

Table 1: Distribution of angiosarcoma with pooled data from 534 patients

Young et al. Lancet Oncol 2010;11:983-91
CLINICAL PRESENTATION

• Can initially resemble a “spreading bruise” or a purplish-red papule
• Advanced lesions are violaceous, elevated nodules that bleed easily and may be on a background of brawny, non-pitting edema
• Untreated angiosarcomas grow 20 cm or larger
• Median size ranges from 3-6 cm
• The most common presenting symptom is pain or discomfort
WHO GETS CUTANEOUS ANGIOSARCOMAS

- Tumors arising on the scalp and face of elderly patients (Caucasian males)
- Tumors arising in skin previously exposed to ionizing irradiation
- Tumors arising on the extremities in areas of chronic lymphedema
  - Iatrogenic – post surgery
  - Noniatrogenic – Congenital lymphedema, postfilarial infection
STEWART-TREVES SYNDROME

- Chronic lymphedema of any origin in association with the development of angiosarcoma
- More than 90% of all cases are a result of postmastectomy lymphedema
- Rare condition with approximately 400 cases reported in the world literature
Cutaneous Angiosarcoma Complicating Morbid Obesity

Muhammad Azam, MD; M. Hossein Saboorian, MD; Samuel Bieligk, MD; Todd Smith, MD; Kyle Molberg, MD

- Herein, we report a case of cutaneous angiosarcoma in a 35-year-old, morbidly obese woman. The tumor arose in the most dependent portion of the lower abdominal panniculus and showed typical changes of chronic lymphedema. The patient underwent a radical resection of her lower abdominal wall panniculus, which showed a multicentric, high-grade angiosarcoma with bilateral superficial inguinal lymph node metastases. Histologically, conventional vasoformative areas were admixed with poorly differentiated sheets of spindle and epithelioid cells. Factor VIII was focally positive (membranous), whereas CD31 showed no positivity.

A case of angiosarcoma of abdominal wall panniculus associated with chronic lymphedema due to morbid obesity.

REPORT OF A CASE

Clinical Findings

A 35-year-old, morbidly obese woman weighing 407 lb presented with multiple skin nodules in the periumbilical region with focal ulceraions. The surrounding skin was thick and brawny with the typical change of peau d’orange. There was no clinical history of radiation, and family history was unremarkable.
• Few case reports of angiosarcoma of the abdominal wall panniculus associated with chronic lymphedema due to morbid obesity

• This patient was virtually confined to her bed as a result of limb-girdle muscular dystrophy and ventilator dependent respiratory failure

• Morbid obesity combined with immobility is probably sufficient to cause chronic lymphatic engorgement in the abdominal wall
PATHOGENESIS

• Mechanisms between chronic lymphedema and angiosarcoma are unknown
• Questionable role for a systemic carcinogenic factor
• Possible relationship between defective immune surveillance with loss of normal control of endothelial proliferation
  • The blockage of afferent lymphatic drainage results in impaired antigen presentation and the edematous area becomes an “immune privileged site” allowing tumors to develop
DIFFERENTIAL DIAGNOSIS

- Hemangioma
- Kaposi Sarcoma
- Melanoma
- Squamous Cell Carcinoma
- Few case reports mimicking rosacea or eczema
- Rare case reports mimicking eyelid edema, solid non-pitting facial edema, and scarring alopecia
STAINING PATTERN

• Angiosarcomas express endothelial markers
  • CD34
  • CD31
  • Vascular endothelial growth factor
  • Von Willebrand factor
  • Ulex europaeus agglutinin 1
STAGING

- Staged using the International Union Against Cancer and American Joint Committee on Cancer system (UICC/AJCC)
- Based on TNM system
- Since angiosarcomas are high-grade tumors, histological grading is not part of the staging
- CT imaging and PET scan are useful to detect metastases
- Value of sentinel-lymph-node biopsy is unknown

Panel 3: TNM staging for soft-tissue sarcomas, including angiosarcoma

<table>
<thead>
<tr>
<th>T</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No primary tumour found</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour ≤5 cm diameter</td>
</tr>
<tr>
<td></td>
<td>T1a: superficial; T1b: deep</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour &gt;5 cm diameter</td>
</tr>
<tr>
<td></td>
<td>T2a: superficial; T2b: deep</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph-node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph-node involvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mx</td>
<td>Cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>
METASTATIC DISEASE

- 20-45% of patients have metastatic disease at presentation
- Angiosarcomas spread hematogenously
- The lungs are the most common site of metastases
- Other common sites include: liver, bone, soft-tissue and lymph nodes
PROGNOSIS

- Overall 5 year survival ranges from 10-35%
- Median survival of 7 months
- AGE < 50, localized tumor stage, size < 5 cm, and anatomical site are all good prognostic factors
PROGNOSIS

**Table 3**

Relative survival of the most common anatomical sites for angiosarcomas of the skin

<table>
<thead>
<tr>
<th>Anatomical site</th>
<th>No. of patients</th>
<th>5-y survival</th>
<th>10-y survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp and neck</td>
<td>135</td>
<td>33.6%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Other/unspecified parts of face</td>
<td>59</td>
<td>65.5%</td>
<td>48.8%</td>
</tr>
<tr>
<td>Trunk</td>
<td>19</td>
<td>75.3%</td>
<td>75.3%</td>
</tr>
<tr>
<td>Lower limb/hip</td>
<td>15</td>
<td>63.5%</td>
<td>51.0%</td>
</tr>
</tbody>
</table>

**FIG. 3** OS for cutaneous angiosarcoma by maximum tumor size

J. Albores-Saavedra et al. / Ann Diagn Pathol 2011

TREATMENT

• Current treatment options are limited due to lack of randomized trials

• Surgery with complete resection and wide margins is the treatment of choice

• Adjuvant radiotherapy with large doses and wide treatment fields is recommended due to the high risk of recurrence
  • This is usually avoided in cases of radiation-induced angiosarcomas
TREATMENT

- Chemotherapy is used for advanced regional or metastatic disease
  - Doxorubicin and/or paclitaxel
  - Role for bevacizumab as a tumor stabilizer
TAKE HOME POINTS

• Angiosarcoma is an uncommon, aggressive neoplasm of the endothelium
• Prognosis is extremely poor, most long-term survivors received early radical ablative surgery
• With the continuing epidemic of obesity, the incidence of obesity-related angiosarcoma will likely increase
• It is critical that patients are carefully examined so that cutaneous neoplasms can be diagnosed at a stage where they can be treated effectively
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