Evening Specialty Conference  
Dermatopathology  
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 Disclosure of Relevant Financial Relationships  
Dr. George Jour declares he has no conflict(s) of interest to disclose.

Clinical History

- 35 year old female, with history invasive ductal carcinoma.
- She presented to the dermatology clinics in 2016 for persistent small crusted papules on the inferior aspect of her sternum.
- Physical examination showed raised, mildly erythematous, non-painful crusted papules measuring 4 to 5mm, no pustules. There is no palpable lymphadenopathy.
DIAGNOSIS
Lymphangioma-Like Atypical Vascular Lesion

Atypical Vascular Lesion
• Female predominance - median age of 59 years (range, 36-90 years).
• Small erythematous-violaceous papules or nodules to large plaques with discoloration.
• Various anatomic location depending on the previous radiation site.
• Most frequently encountered on the breast.

Atypical Vascular Lesion
• Poorly circumscribed.
• The endothelial lining shows mild nuclear atypia.
• Multilayering, and projection of the stroma in the vessel lumens is constantly absent.
• Dissection of dermal collagen by the vascular channels can be seen but is not typical.
• Usually no subcutaneous tissue involvement

Differential diagnosis
**Lymphangioma Circumscriptum**
- Rare, dermal based lesion.
- Presents most often in infancy, but may arise at any age and shows an equal sex distribution.
- It has a propensity for the limbs.
- Limited to the superficial dermis and shows numerous dilated lymphatic channels which often have fairly thick walls that can extend in the overlying epidermis.

**Acquired Progressive Lymphangioma**
- Frequent extension in the deep dermis and superficial subcutis.
- Dermal collagen dissection and slit like vessels can be seen mostly in the deep dermis and subcutaneous tissue.
- Benign lesion with very low risk of recurrence.

**Secondary Angiosarcoma**
- Poorly circumscribed lesions in superficial to mid dermis and subcutis.
- Complex anastomosing and focally dilated vascular spaces.
- Prominent hyperchromatic endothelial cells.
- Areas with a dissecting growth pattern within dermal collagen.

**Secondary Angiosarcoma**
- Solid areas and severe nuclear atypia with mitotic figures in the high grade lesions.
- Multilayering and increased mitotic activity in high grade AS.
- High grade tumors show solid tumor growth with numerous atypical pleomorphic and spindle cells with areas of necrosis associated with blood lakes.

**Morphological Features that Differentiate Between AVL and Angiosarcoma.**
Molecular Features that Differentiate AVL From Secondary Angiosarcoma (SAS)

- High levels of amplification in the 8q24 locus (c-MYC) in 100% of SAS, but in none of the AVL.
- Co-amplification of FLT4 (encoding VEGFR3) was identified in 25% of secondary AS but in none of AVL’s or other AS.
- MYC protein expression identified by WB.

C-MYC and FLT4 Protein Expression in AVL and SAS

- High-level c-MYC amplification and c-MYC protein overexpression in 54 to 77% of SAS.
- Diffuse strong cytoplasmic FLT4 and FLT4 amplification by FISH in 18% SAS cases.

C-MYC and FLT4 amplification in AVL and SAS

- Concordance between c-MYC amplification (FISH) and protein expression (IHC) is 100% in AVL, PAS, and SAS.
- Strong FLT4 immunoreactivity correlated with FLT4 amplification.
- FLT4 IHC may be used to screen for patients with FLT4 amplification who might benefit from targeted therapy.

Treatment and Prognosis

- While it is clear that AVL are not equivalent to angiosarcoma, growing evidence supports that these lesions may progress to angiosarcoma in some patients, as reported in some studies.
- As such, many authors recommend excision of the lesion with margins depending on clinical judgment and the lesion encountered.

Clinical History

- 89 year old gentleman, who was recently seen in the dermatology clinic for a non-healing crusted lesion.
- The patient has history of multiple basal cell carcinoma, squamous cell carcinomas.
- A skin shave biopsy was obtained.
Follow-up and Excision

- The tumor nodule measured 2.42 x 1.55 mm.
- The lesion was mostly centered in the dermis and away from the main scar site.
Squamomelanocytic Tumor: Melanocarcinoma

- Squamomelanocytic tumor (SMT) is rare.
- Admixture of melanocytic and squamous cellular phenotypes.
- In most cases, SMT is composed of an admixture of 2 cell populations including both melanocytic and squamous phenotypes.
- Two clearly well demarcated separate areas or intermingling.

**Presenting Cases**

- Twelve cases have been reported so far; the face is one of the most common site of predilection.
- It shows predilection for sun-damaged skin and older population with a mean age of 67 years old at presentation.
- Mass with infiltrative and bulbous edges.
- Typically, it shows connection to the epidermis from which it arises.
- The tumor cells show large atypical squamous cells with prominent nucleoli and areas of keratin deposition.
- Admixed with this population is a second population of large atypical and frequently pigmented melanocytes.
- Mitotic figures and necrosis are also present.

**Atypical Squamous Cells**

- The atypical squamous cells label diffusely with epithelial markers such as:
  - Pan Keratin, HMWCK (CK5/6).
  - p63 and p40.
- Atypical melanocytes label with:
  - MITF, SOX10, and MelanA.
- Patchy and irregular pattern of staining with HMB45.

**Differential Diagnosis**

- True biphenotypic SMT is extremely rare.
- In these cases, the neoplastic cells show simultaneous expression of both melanocytic and epithelial markers.
Melanocytic Matrical Carcinoma

- Rare; 13 cases described in the literature.
- Male predominance (11/13).
- Elderly patients 48 to 84 years; sun exposed skin.
- Good prognosis; local recurrence in 2/13 reported cases.
- No metastases have been reported.

Melanocytic Matrical Carcinoma

- Matrical carcinoma with intralesional melanocytes
  - Asymmetrical
  - Poorly circumscribed growth pattern
  - Surface ulceration
  - Usually no connection to the epidermis is seen.
- The matrical cells show pleomorphic basaloid nuclei with prominent nucleoli and frequent mitoses.
- Scattered or clustered dendritic melanocytes without significant atypia.

Melanocytic Matrical Carcinoma

- Abrupt keratotic material in the center surrounded by ghost cells.
- Atypical matrical:
  - Immunoreactive with cytokeratin, p63, and b-catenin.
  - Lack immunoreactivity with melan-A and SOX-10.
  - Positive for S100 sometimes.
- Melanocytes:
  - Immunoreactive with Melan A, S100, SOX10.

Melanocytic Matrical Carcinoma

- Most cases (12 of the 15 cases reported in the literature) are dermal based without connection to the overlying epidermis.
Melanocytic Matricoma

- Three cell population
  - Basaloid cells (granular nuclear chromatin with distinct nucleoli).
  - Shadow/ghost cells.
  - Dendritic melanocytes.


Squamomelanocytic tumor

- The matrical and supramatrical cells positivity to pancytokeratin AE1/AE3,34BE12, CAM5.2, CK5/6, p63, CD10 and EMA.
- Staining for Ber-EP4, CK7 and CK 20 is negative.
- Also, membranous cadherin and nuclear and cytoplasmic β-catenin positivity.
- The shadow/ghost cells show positivity to pancytokeratin, AE1/AE3, 34BE12 and CAM5.2.

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Treatment and Prognosis

- SMTs have an unpredictable behavior.
- The rarity of these cases and the lack of consensus concerning their classification impeded reaching clear information about their behavior.
- When follow-up was available (8 of the 12 cases), the overall disease-free survival ranged from 8 months to 9 years (average follow-up time of 20 months).


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Important Information Regarding CME/SAMs

The Online CME/Evaluations/SAMs claim process will only be available on the USCAP website until September 30, 2017.

No claims can be processed after that date!

After September 30, 2017 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.

THANK YOU
In a recent study by Amin et al, the authors studied 11 SMT by Fluorescence in situ hybridization. Their study revealed chromosomal alterations in approximately 55% of the cases. Five cases showed chromosomal gains only in the melanocytic component. One case showed 11q13 gains in both the epithelial and melanocytic components.