Recurrence Risk Following Resection of Cutaneous Angiosarcoma is Associated with Primary Site of Disease

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Background: Cutaneous angiosarcoma (CAS) is a rare, aggressive sarcoma of vascular origin that occurs in the skin with a poor prognosis and is associated with 5-year survival rates between 10 and 50%. The primary modality of treatment has been and remains radical surgical resection, though neoadjuvant taxane-based chemotherapy is often used for advanced cases that would require complex reconstruction. CAS is often subdivided into primary or secondary CAS with the latter often associated with a history of radiation treatment (RT) at the primary site or chronic lymphedema (Stewart-Treves Syndrome). The purpose of this study was to evaluate the risk of recurrence relative to primary tumor location, comparing primary CAS in the breast to those that arise in a non-breast location.

Methods: This is a single-institution retrospective review of patients treated for CAS from November 1998 – November 2017. Demographics, primary tumor characteristics, treatment, and outcomes were analyzed.

Results: A total of 107 patients were analyzed (median age 70 years and 53% female). Of these, 38 (36%) presented with a history of RT to the primary site with a median time from RT to diagnosis of 8 years (range 3-50 years). Median tumor size was 3 cm (range 0.2-38 cm). 74% of tumors were high grade, 8% intermediate grade, and 18% low grade. (Table 1)

Median follow-up was 31 months (range 0-208 months). 99 patients (92%) underwent surgery as primary treatment, 1 (1%) received RT alone, 2 (2%) received chemotherapy alone, and 5 (5%) received chemotherapy and RT without surgery. Of patients undergoing resection, 83% underwent resection up to or including deep investing fascia. 18 (17%) patients received preoperative chemotherapy and 9 (9%) received preoperative RT. 27% of patients received adjuvant chemotherapy and 51% received adjuvant RT. Of those that received preoperative chemotherapy, more (87% vs 72%) were considered high grade at diagnosis and more (53% vs 34%) had tumor size greater than or equal to 5 cm compared to those not receiving preoperative chemotherapy. 59 (55%) patients experienced recurrence, 68% of which occurred locally with a median time to recurrence of 10.5 months.

Two distinct presentation groups were identified based on primary tumor location: breast, n = 36, and non-breast, n = 71. Of these groups, there was a strong positive trend toward improved outcomes in breast primary vs. non-breast with no recurrence experienced in 49% and 22%, respectively ($p = 0.25$). Interestingly, this trend was not present in likelihood of second recurrence. On MV analysis, only lack of preoperative chemotherapy correlated with improved OS ($p = 0.03$).

Discussion: In this large single institution retrospective review, CAS carries an overall high risk of recurrence. The inferior outcomes in those patients with preoperative chemotherapy is likely due to higher grade and larger size of disease at presentation. While there was no definitive

tumor or patient factor identified that predicted lack of recurrence, there is a strong trend toward improved outcome for CAS which arises within the breast vs non-breast primary tumor.

Table 1. Clinicopathologic Characteristics, Treatment, and Outcomes in Cutaneous Angiosarcoma		
Clinicopathologic characteristics		
History of radiation to tumor site	62 (57%)	
History of lymphedema at tumor site	7 (7%)	
Tumor location • Breast • Head/neck • Extremity • Trunk	 36 (34%) 56 (52%) 14 (13%) 1 (1%)	
Tumor depth of invasion • Dermis • Subcutaneous tissue • Fascia/muscle/cartilage/bone	 25% (25) 49% (49) 26% (26)	
Median tumor size (cm)	3 (0.2-38)	
Tumor grade • Low • Intermediate • High	 17 (18%) 7 (9%) 69 (74%)	
Treatment		
Pre-operative treatment • Radiation • Chemotherapy	 9 (9%) 18 (17%)	
Depth of resection • Subcutaneous tissue • Fascia • Muscle/cartilage/bone	 8 (7%) 26 (24%) 56 (52%)	
Final margin status • Positive • Negative	 21 (21%) 77 (79%)	
Adjuvant treatment • Radiation • Chemotherapy	 52 (51%) 28 (27%)	
Outcomes		
Median RFS (years)	2.1 (1.4-4.5)	
Median RFS by location (years) • Breast • Non-breast	 2.2 (1.7 – NE) 1.6 (1.4 – 4.5)	p = 0.25
Median RFS by tumor depth (years) • Dermis • Subcutaneous tissue • Fascia/muscle/bone/cartilage	 4.1 (1.4 – NE) 1.4 (0.6 – 4.7) 2.1 (0.9 – NE)	p = 0.22

Median RFS by pre-operative chemotherapy (years) • Yes • No	 1.2 (0.8 – 4.1) 2.5 (1.5 – 4.7)	 p = 0.03
Median RFS by depth of resection (years) • Subcutaneous tissue • Fascia • Muscle/bone/cartilage	 1 (0.5 – 8.2) 2.1 (0.8 – NE) 2.5 (1.7 – 4.7)	 p = 0.49
RFS: Recurrence free survival *NE*: not estimable		