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Characteristics of atypical postradiation vascular proliferation: A retrospective review of 193 patients

To the Editor: Atypical postradiation vascular proliferations (APRVPs) can be difficult to distinguish from cutaneous angiosarcoma.[1,2] Angiosarcomas are associated with *MYC* amplification and Ki-67 expression, whereas APRVPs are not.[3,4] However, the potential for angiosarcomatous transformation of APRVP remains unclear. We conducted a large, multi-institutional review to examine individuals with APRVP, determine the rate and timing of angiosarcoma diagnosis after APRVP diagnosis, and compare outcomes of APRVP after excision vs active surveillance.

The study included patients with histopathologic atypical postradiation vascular proliferation diagnoses from January 1, 1988, to December 8, 2018, at Brigham and Women's Hospital, Dana Farber Cancer Institute, and Massachusetts General Hospital. Patients with concurrent (diagnosed on the same day) or prior histopathology showing cutaneous angiosarcoma and those without radiation exposure were excluded. Records of included patients were reviewed, and percentages were reported with the denominators excluding missing cases.

There were 193 patients (98% women) who met inclusion criteria, with mean age of 61.3 years at APRVP diagnosis (Table I); of these, 88% had primary breast malignancies. The median time to APRVP onset was 6 years postradiation. Follow-up was available for 100 patients (median, 3.2 years). Radiation-associated complications occurred in 42 patients (42%), 21 of whom had lymphedema (Table I). The primary cancer recurred in 25% of patients, with 92% (23 of 25) experiencing recurrence before APRVP onset.

Table I. Demographic and clinical features of patients diagnosed with atypical postradiation vascular proliferations (*APRVPs*)*

Variables	Patients with APRVP (N = 193)
Demographic features	
Age at APRVP diagnosis, mean (95% CI), y	61.3 (59.5-63.0)
Female sex	190 (98.4)
Race/ethnicity	(n = 189)
White	178 (94.2)
Hispanic	4 (2.1)
Asian	4 (2.1)
Black	3 (1.6)
Smoking status	(n = 82)
Current	4 (4.9)
Former	39 (47.6)
Never	39 (47.6)
Clinical features	
Mutation	(n = 15)
BRCA1	2 (13.3)
BRCA2	2 (13.3)
Variant of unknown significance	5 (33.3)
No found mutations	6 (40.0)
Primary cancers	(n = 163)
Breast	143 (87.7)
Lymphoma	4 (2.5)
Lung	2 (1.2)
Vulvar cancer	2 (1.2)
Anal squamous cell cancer	2 (1.2)
Merkel cell carcinoma	2 (1.2)
Melanoma	2 (1.2)
Leiomyosarcoma	1 (0.6)
Synovial sarcoma	1 (0.6)
Angiosarcoma	1 (0.6)
Liposarcoma	1 (0.6)
Desmoid tumor	1 (0.6)
Mucoepidermoid cancer	1 (0.6)
Radiation characteristics	
Radiation dosage, median (range), Gy (n = 15)	50.4 (45-64)
Time from radiation to disease, median (range)† (n = 127)	6 (1-40)
Complications of radiation	(n = 100)
Lymphedema	21 (21)
Cardiopulmonary restrictive disease	3 (3)
Thyroid dysfunction	1 (1)
Chronic dermatitis	9 (9)
Infection	4 (4)
Delayed wound healing	3 (3)
Chronic pain from lymphadenopathy	1 (1)
Treatment	(n = 91)
Excision	43 (47.3)
Monitor	48 (52.7)

Continued

Table I. Cont'd

Variables	Patients with APRVP (N = 193)
Outcome	(n = 100)
Recurrence	20 (20.0)
Stable or better	77 (77)
Angiosarcoma	3 (3)
Time to recurrence, median (range),[‡] d	392 (27-1955)
Time from APRVP to angiosarcoma, median (range), d	229 (54-235)
Died	10/100 (10)
Time to death, median (range), y	2.3 (0.02-8.2)
Follow-up time, median (range), y	3.2 (0-14.8)
Clinical features of APRVP lesions	
Size	(n = 38)
<1 cm	32 (84.2)
1-2 cm	4 (10.5)
>2 cm	2 (5.3)
Primary morphology	(n = 96)
Papule	34 (35.4)
Plaque	21 (21.9)
Patch	17 (17.7)
Nodule	13 (13.5)
Macule	7 (7.3)
Vesicle	4 (4.2)
Secondary features	(n = 96)
Induration	13 (13.5)
Telangiectasia	12 (12.5)
Edema	6 (6.3)
Scaling	4 (4.2)
Pearly/shiny	4 (4.2)
Bruise-like	2 (2.1)
Erosion/ulceration	2 (2.1)
Other features	(n = 96)
On previous scar	8 (8.3)
Infection (cellulitis, abscess)	2 (2.1)
Squamous cell carcinoma	1 (1.0)
Incidental	6 (6.3)
Number of lesions	(n = 81)
Single	55 (67.9)
Multiple	26 (32.1)
Location	(n = 193)
Breast	164 (85.0)
Axilla	8 (4.1)
Groin	5 (2.6)
Back	5 (2.6)
Abdomen	4 (2.1)
Head and neck	2 (1.0)
Arms	2 (1.0)
Legs	2 (1.0)
Buttocks	1 (0.5)
Symptoms	(n = 96)
Pain	6 (6.3)
Pruritus	3 (3.1)
Discharge	5 (5.2)
Serous	2/5 (40)
Yellow	1/5 (20)
Blood	2/5 (40)

CI, Confidence interval.

*Normality assumption was checked for continuous variables, and mean (95% CI) or median (range), depending on the variable distribution, was reported. Categorical variables are reported as the number (%).

[†]If there were multiple malignancies or cancer recurrences, time from initial radiation treatment to APRVP diagnosis was used.

[‡]If there were multiple APRVP recurrences, time to first recurrence was used.

Most APRVPs were single lesions, <1 cm (range, 1mm -9 cm) in size, papule/plaque morphology, and asymptomatic (Table I). Six lesions were found incidentally during breast reconstruction, with no documentation of overlying skin changes.

Angiosarcoma was subsequently diagnosed in 3% (3 of 100) of patients, with a median time of 229 days (range, 54-235 days) from the APRVP diagnosis. These 3 lesions were in women with a primary malignancy of breast cancer. A subsequent APRVP was diagnosed by biopsy sample or clinical appearance in 20% (20 of 100) of patients, with median time of 392 days from the initial APRVP diagnosis. By the end of the study, 10% (10 of 100) of the patients had died, none from angiosarcoma transformation.

The APRVP was excised in 47% (43 of 91) of patients, and 52.7% (48 of 91) underwent active clinical monitoring. This analysis excluded 9 patients because of incomplete documentation. There was no difference in demographic or clinical characteristics or in the incidence rates of recurrence between the excision and monitoring group (Table II).

Our findings suggest that APRVPs are clinically varied and associated with other cancers besides breast cancer. Angiosarcoma was subsequently diagnosed in 3% of our patients, which is lower than previously reported.[5] The short duration between APRVP and the angiosarcoma diagnosis suggests there may be mischaracterization of the initial pathology, concurrent disease processes, or rapid angiosarcoma evolution.

We found no statistically significant difference in outcomes between excision and clinical monitoring. However, results must be interpreted with caution because more clinically worrisome lesions may have been excised, some patients were lost to follow-up, and our follow-up was short. Future investigations correlating histopathology findings with disease and demographic features and examining longer-term

Table II. Comparison of patients with and without APRVP excision*

Variable	Patients with excision (n = 43)	Patients with monitoring (n = 48)	*P* value
Age at APRVP diagnosis, mean (95% CI), y	60.2 (55.8-64.6)	59.2 (55.4-63.0)	.611
Date of APRVP diagnosis, mean (95% CI)	4/18/12 (3/25/04-5/24/18)	12/13/14 (8/28/09- 10/17/18)	.001†
Follow-up time, median (range), d	770 (10-5403)	919 (8-3268)	.915
Race/ethnicity			
White	39/43 (90.7)	43/48 (89.6)	.82
Black	1/43 (2.3)	2/48 (4.2)	
Hispanic	1/43 (2.3)	2/48 (4.2)	
Asian	0/43 (0)	0/48 (0)	
Unreported	2/43 (4.7)	1/48 (2.1)	
Age at primary malignancy, mean (95% CI), y	51.44 (45.90-56.99)	49.39 (45.95-52.83)	.55
APRVP lesion size, median (range), mm	6 (3-50) (n = 17)	5 (1-90) (n = 13)	.736
APRVP primary lesion			
Papule	13/27 (48.1)	10/34 (29.4)	.165
Plaque	4/27 (14.8)	11/34 (32.4)	
Patch	2/27 (7.4)	8/34 (23.5)	
Nodule	5/27 (18.5)	2/34 (5.9)	
Macule	2/27 (7.4)	2/34 (5.9)	
Vesicles	1/27 (3.7)	1/34 (2.9)	
Lesion number			
Single	14/22 (63.6)	24/34 (70.6)	.77
Multiple	8/22 (36.3)	10/34 (29.4)	
Outcomes of lesions (at last date of follow-up)			
Recurrence	10/43 (23.3)	4/48 (8.3)	.141
Stable or better	31/43 (74.4)	43/48 (89.6)	
Angiosarcoma	1/43 (2.3)	1/48 (2.1)	
Recurrence rate/100 person-years (95% CI)‡	6.9 (3.3-12.6)	2.8 (0.8-7.2)	.193
Died	3/43 (7.0)	3/48 (6.3)	>.99

APRVP, Atypical postradiation vascular proliferations; *CI*, confidence interval.
*The Fisher exact test was performed for categorical variables and Wilcoxon rank sum test was performed for continuous variables. Normality assumption was checked for continuous variables, and mean (95% CI) or median (range), depending on the variable distribution, was reported. Categorical data are presented as the number (%).
†Statistically significant ($P < .05$).
‡Includes recurrent APRVP or angiosarcoma.

outcomes may yield additional insights, better informing prognostic recommendations.

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Prevalence of moderate to severe acne in transgender adults: A cross-sectional survey

To the Editor: Moderate to severe acne imposes significant psychosocial and quality-of-life burdens, and may it be triggered by endogenous androgens or exogenous hormone therapy (HT).[1-3] Although moderate to severe acne warranting isotretinoin treatment has been observed in case series,[4] the epidemiology and severity of acne in transgender populations remains to be characterized.

We aimed to determine the prevalence of moderate to severe acne in a cross-sectional survey of transgender adults nested in the multicenter Study of Transition, Outcomes, and Gender (STRONG). The Emory University institutional review board approved this study. STRONG cohort eligibility included enrollment in Kaiser Permanente Northern California, Southern California, or Georgia between January 1, 2006, and December 31, 2014. Participants were adults at least 18 years old with 1 or more transgender-specific International Classification of

Table I. Demographics and prevalence of moderate to severe acne in transgender adults*

Characteristics	All, n (%)	TM, n (%)†	TF, n (%)‡	*P*
Total	696 (100)	346 (49.7)	350 (50.3)	
Age at time of survey, y				<.001
18-29	217 (31.2)	148 (42.8)	69 (19.7)	
30-39	156 (22.4)	104 (30.1)	52 (14.9)	
40-54	168 (24.1)	69 (19.9)	99 (28.3)	
≥55	155 (22.3)	25 (7.2)	130 (37.1)	
Race/ethnicity				.66
Non-Hispanic white	392 (56.3)	191 (55.2)	201 (57.4)	
Non-Hispanic black	20 (2.9)	13 (3.8)	7 (2.0)	
Non-Hispanic Asian/Pacific Islander	48 (6.9)	25 (7.2)	23 (6.6)	
Hispanic	133 (19.1)	68 (19.7)	65 (18.6)	
Other/declined	103 (14.8)	49 (14.2)	54 (15.4)	
History of gender-affirming treatments§				<.001
None	28 (4.0)	11 (3.2)	17 (4.9)	
Hormone therapy only	234 (33.6)	76 (22.0)	158 (45.1)	
Chest surgery without genital surgery	171 (24.6)	142 (41.0)	29 (8.3)	
Genital surgery with or without chest surgery	233 (33.5)	103 (19.8)	130 (37.2)	
Missing information	30 (4.3)	14 (4.1)	16 (4.6)	
Moderate to severe acne diagnosis by a physician‖				<.001
No	449 (64.5)	208 (60.1)	241 (68.9)	
Yes, currently	50 (7.2)	47 (13.6)	3 (0.9)	
Yes, in the past	95 (13.7)	50 (14.5)	45 (12.9)	
Missing information	102 (14.7)	41 (11.9)	61 (17.4)	
Ever diagnosis of moderate or severe acne (current or past)	145 (20.8)	97 (28.0)	48 (13.7)	<.001
Moderate or severe acne linked to hormone therapy				<.001
No	76 (53.9)	33 (34.4)	43 (95.6)	
Yes	65 (46.1)	63 (65.6)	2 (4.4)	
Any visit to a dermatologist	347 (49.9)	154 (44.5)	193 (55.1)	<.001

TF, Transfeminine; *TM*, transmasculine.
*Numbers may not add up to the total number of participants because, unless otherwise specified, we excluded categories with missing data totaling less than 5%.
†TM refers to transgender persons with current gender identity that differs from female natal sex.
‡TF refers to transgender persons with current gender identity that differs from male natal sex.
§Chest surgery referred to any history of mastectomy or breast augmentation, and genital surgery referred to any history of hysterectomy, orchiectomy, vaginectomy, and/or vaginoplasty. The majority (98.3%) of respondents with a history of chest surgery and/or genital surgery had received hormone therapy.
‖We combined the *missing* category with no prior history of moderate to severe acne to produce conservative estimates of current moderate to severe acne prevalence. Acne prevalence may be underestimated in TF persons given higher levels of missing acne data.