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A single-center, retrospective record review of malignancy prevalence in patients with dermatomyositis with anti-transcription intermediary factor 1γ antibodies via line immunoassay versus immunoprecipitation

To the Editor: The association of dermatomyositis (DM) with malignancy has been well established, with a prevalence between 11% and 42%.[1] Patients with DM with transcription intermediary factor 1γ (TIF-1γ) antibodies appear to be at greater risk of malignancy than the broader population of patients with DM, with a malignancy prevalence between 42% and 100%.[2]

The TIF-1 family, consisting of TIF-1α (p140), TIF-1β, and TIF-1γ (p-155), is a subgroup of transcription factors that play crucial propagative and inhibitory roles in carcinogenesis. Cancer-associated myositis is hypothesized to result from the misdirection of an antitumor immune response toward regenerating muscles. It stands to reason that autoantibodies to these proteins may occur as part of an antitumor immune response and lead to the onset of cancer-associated DM.[3]

Previous studies evaluating the prevalence of malignancy in patients with DM positive for TIF-1γ measured TIF-1γ antibodies via immunoprecipitation (IP), but commercially available testing often reports TIF-1γ antibodies via line immunoassay (LIA). The positive percentage agreement between LIA and IP for TIF-1γ antibodies ranges from 50.0% to 73.3%.[4,5] Only 1 small study has evaluated the prevalence of malignancy with TIF-1γ antibodies via LIA testing.[5] Given the reported high prevalence of malignancy in patients with DM with positive TIF-1γ antibodies and the frequent use of LIA testing by commercial laboratories, we aimed to achieve a greater understanding of the clinical utility of commercially available TIF-1γ antibody testing via LIA in predicting cancer.

We performed a retrospective medical record review of patients with DM with positive TIF-1γ antibodies via LIA or IP between January 1, 2014, and September 30, 2019, at the University of Utah. This study was approved by the University of Utah Institutional Review Board. The following information was extracted: age, sex, race, DM diagnosis date, associated malignancies, and date of diagnosis. We excluded those with less than 1 year of follow-up after the DM diagnosis unless malignancy was identified before that time (3 patients). Malignancy screening was not standardized, but generally consisted of age-appropriate cancer screening, computed tomography of the chest, abdomen, and pelvis, and transvaginal ultrasound for women yearly for the first 3 years after diagnosis.

We identified 26 patients using the methods described above (Table I).[6] The average age was 53.3 years, 16 patients were women, and 22 patients were white. All patients were positive for anti—TIF-1γ via IP, and 17 of 21 patients tested were positive for anti—TIF-1γ via LIA. Three patients had a malignancy diagnosis (1 urothelial, 1 gastric, 1 ovarian). The malignancy prevalences among patients positive for TIF-1γ via IP and LIA were 11.5% and 17.6%, respectively. The positive percentage agreement between these 2 methods using paired observation was 81% in the 21 patients in whom both tests were performed.

Our study is one of the largest studies to date evaluating malignancy prevalence in patients with DM who are positive for anti—TIF-1γ and one of the

Table I. Characteristics of dermatomyositis patients with transcription intermediary factor 1γ (*TIF-1γ*) antibodies

Patient	Sex	Age at DM onset, y	Race/ethnicity*	TIF-1γ via LIA[†‡]	TIF-1γ via IP[†§]	Malignancy (primary site)
1	M	77	White	Positive	Weak positive	No
2	M	64	White	Positive	Positive	No
3	F	47	White	Positive	Positive	No
4	F	72	White	Positive	Positive	No
5	F	66	White	N/A	Positive	No
6	M	52	White	N/A	Weak positive	No
7	M	56	White, Hispanic/Latino	Low positive	Positive	No
8	M	48	White	Negative	Positive	No
9	M	65	White	N/A	Positive	No
10	F	71	White	Positive	Positive[‖]	No
11	F	75	White	Positive	Positive[‖]	No
12	M	75	White	Positive	Positive	No
13	F	54	White, Hispanic/Latino	N/A	Positive	No
14	F	69	White	Negative	Positive	No
15	F	22	White	Positive	Positive	No
16	F	18	White	Positive	Positive	No
17	F	29	White	N/A	Positive	No
18	F	58	White	Positive	Positive[‖]	No
19	F	33	White	Negative	Positive	No
20	F	31	White	Positive	Positive	No
21	F	57	Asian	Positive	Positive	Yes (gastric adenocarcinoma)
22	F	54	American Indian/Alaska Native	Positive	Positive	Yes (ovarian serous carcinoma)
23	M	24	White	Negative	Weak positive	No
24	F	65	White	Positive	Positive[‖]	No (benign pancreatic neuroendocrine mucocele—DM resolved with tumor excision)
25	M	49	White	Positive	Positive	No
26	M	75	White	High Positive	Positive	Yes (bladder transitional cell carcinoma)

DM, Dermatomyositis; *F*, female; *IP*, immunoprecipitate; *LIA*, line immunoassay; *M*, male; *N/A*, not available.

*Ethnicity is not Hispanic/Latino unless otherwise noted.

[†]TIF-1γ via LIA and IP testing was performed by ARUP Laboratories as part of their Extended Myositis Panel.[6]

[‡]LIA is reported as qualitative values based on the following ranges: "negative" is between 0 and 14 units, "low positive" is between 15 and 35 units, "positive" is between 36 and 70 units, and "high positive" is >70 units.

[§]IP is reported as qualitative values based on the intensity of the band: "negative," "weak positive," or "positive."

[‖]ARUP Laboratories testing for TIF-1γ via IP is reported as negative if antibodies to both p155 (TIF-1γ)[3] and p140 (TIF-1α)[3] are not present. These results were reported as negative for p155/p140 antibodies, but there was a comment that a band corresponding to 155 KDa was observed by IP.

only to evaluate malignancy prevalence in those with LIA. Our study suggests that prevalence of malignancy may be much lower in a United States, primarily white population than reported in the literature. This may be influenced by racial/genetic factors, because most studies thus far have been performed in populations residing outside of North America (primarily Asia).[2]

Our study also suggests that prevalence of malignancy may differ depending on the method of antibody detection. This result is limited in that 5 patients did not undergo LIA because this test was introduced at a later date. If we estimate that 4 of 5 of these patients would have a positive LIA result, given the positive percentage agreement of 81%, then the LIA malignancy rate would be lowered to 14.3%. Much larger studies are needed to ascertain the true risk of malignancy in patients with DM who are TIF-1γ positive and whether LIA testing is a more sensitive predictor of malignancy.

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Smoking and risk of adult-onset atopic dermatitis in US women

To the Editor: Atopic dermatitis (AD) is common in adults, but few studies have examined risk factors for adult-onset AD.[1] Cross-sectional and case-control studies suggest that smoking is associated with AD, but there is insufficient data on the temporality of the association.[2-4] In this study, we examined the association between smoking and risk of incident AD in adult women in the Nurses' Health Study II cohort.

Smoking status and AD were assessed by self-report. In 1989, participants were asked about their lifetime history of 20 or more packs of cigarettes. Smoking status (never, past, or current) was updated biennially. AD was assessed by self-report in 2013. Participants were asked if they ever received a diagnosis of "eczema (atopic dermatitis)" by a clinician and what year this occurred. In 2017, participants who reported a diagnosis of AD were sent a questionnaire to reaffirm their self-report. We excluded prevalent cases of AD at baseline (1995; n = 4575) and participants who had an unknown diagnosis date or reported having AD but did not confirm their report in 2017 (n = 42).[5] We calculated person-years from the return date of the 1995 questionnaire to the first of the AD diagnosis date or the end of follow-up (June 2013).

We used Cox proportional hazards models to calculate age- and multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between smoking and AD. Covariates included age, race (white vs nonwhite), body mass index (kg/m^2), physical activity (metabolic equivalent of task hours/week in quintiles), alcohol intake, asthma, and hay fever. All statistical tests were 2 tailed, and the significance level was set at $P < .05$. We used SAS, version 9.4 (SAS Institute, Inc, Cary, NC).

We included 76,701 women in the analysis. Baseline characteristics of the participants according to smoking status are presented in Table I. Overall, 7,497 (9.8%) participants were current smokers, 17,847 (23.2%) were past smokers, and 51,357 (66.8%) had never smoked. During 1,357,932 person-years of follow-up, we identified 463 incident cases of AD. In our multivariable analysis, neither current (HR, 1.21; 95% CI, 0.86-1.68) nor past smoking (HR, 1.02; 95% CI, 0.82-1.26) were significantly associated with AD compared to never smoking (Table II). Among current smokers, there was no apparent dose-response relationship for the number of cigarettes smoked daily, neither smoking 1 to 14 (HR, 1.25; 95% CI, 0.81-1.94) nor 15 or more (HR, 1.15; 95% CI, 0.72-1.86) cigarettes daily was associated with AD. Among current smokers, risk for AD may have been slightly higher with 25 or more pack-years (HR, 1.25; 95% CI, 0.77-2.01) compared to less than 25 pack-years (HR, 1.18; 95% CI, 0.76-1.82) when both were compared to never