Clinical Characteristics of Adult Dermatomyositis with Anti-Transcription Intermediary Factor 1-Gamma Positive: A Systematic Review

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Abstract

Dermatomyositis, an idiopathic inflammatory myopathy, presents with varied clinical manifestations and immune profiles, posing diagnostic and therapeutic challenges. This review describes the clinical features and disease manifestations associated with malignancy in adult dermatomyositis with anti-transcription intermediary factor-1 gamma. PubMed, Scopus, Cochrane Library, and Google Scholar were searched for primary studies that described clinical characteristics of DM with anti-TIF1 gamma positive between January 1, 2013, and December 1, 2023. Twelve studies were included, with a total of 393 patients. Sociodemographic data associated with malignancy and clinical characteristics data were extracted. The descriptions of sociodemographic, malignancy-associated, and clinical characteristics showed predominantly female with a median onset age of 54.2 years; patients were mostly Asian ethnicities. Malignancy was associated with 48.4% of patients, with a median time from DM diagnosis to cancer development of 4.75 months. Common cutaneous manifestations included heliotrope rash 78% and Gottron's sign 58.1%. Musculoskeletal symptoms comprised proximal muscle weakness at 81.6% and myalgia at 36.2%. Pulmonary involvement occurred in 13% of patients. The most frequent malignancies seen in cases of dermatomyositis with anti-TIF1 gamma antibodies include breast 16.2%, ovarian 13.1%, and lung 11% cancers. The mortality rate associated with this condition is noted to be 46.8%. Individuals with this type of dermatomyositis need to undergo regular cancer screening and closely monitor any symptoms or changes in their health. Further research is needed to elucidate underlying pathogenic mechanisms and optimize patient management.

Keywords**:** *adult dermatomyositis, anti-transcription intermediary factor 1 gamma positive, clinical characteristics, cancer-associated dermatomyositis*

1. Introduction

Dermatomyositis was originally identified in 1863 when German pathologist Ernst Leberecht Wagner reported a patient with a peculiar skin rash and muscular weakness. Georges Potain, a French physician, recorded the first instance of dermatomyositis in Europe in 1887. Gustav Stertz, a German dermatologist, was the first to report the link between dermatomyositis and cancer in 1916. (Keitel & Wolff et al., 2016) Anthony Bohan and James B. Peter, two American physicians, categorized dermatomyositis into five categories in 1975, which were used for decades. (Leclair, & Lundberg, 2018) Dermatomyositis is an idiopathic inflammatory myopathy that is clinically diverse and can be challenging to diagnose. Cutaneous signs can vary and may not coincide with myositis and systemic involvement in terms of timing and severity. (DeWane et al., 2020) Multiple myositis-specific autoantibodies (MSAs) were found and reported in the 1990s. These MSAs are used to distinguish dermatomyositis and other idiopathic inflammatory myopathies because they target various cytoplasmic ribonucleoproteins. (Satoh et al., 2017) TIF1- Ab is an autoantibody that directly interacts with TIF1 and is commonly observed in cancer patients, most frequently in adults with dermatomyositis aged 40 to 60. (Qudsiya & Waseem, 2024) It has been shown that cancer is only diagnosed in patients with TIF1- Ab positive 3 years before or 2.5 years after the diagnosis of myositis; early identification of these patients is critical for timely cancer screening and intervention. (McAvera & Crawford, 2020)

Patients with anti-TIF1-gamma antibodies had specific dermatological features such as heliotrope rashes, shawl signs, and Gottron's papules, as well as symptoms like dysphagia and truncal weakness. A total of 96 dermatomyositis patients were studied, and 36 of them tested positive for anti-TIF1-Ab. Heliotrope

rashes, shawl signs, periungual erythema, holster signs, Gottron's papules, dysphagia, and truncal weakness were more common in anti-TIF1-Ab-positive individuals (P<0.05). Interstitial lung disease, polyarthritis, cutaneous ulcers, palmar papules, and mechanic's hands were less common (P<0.05). After 48 months of follow-up, 63.9% of anti-TIF1-Ab-positive patients developed cancer compared to 8.5% of Ab-negative patients (odds ratio 19.1, 95% confidence range 6.1-59.8; P0.001). The most prevalent cancers were nasopharyngeal carcinoma (NPC) and breast cancer, followed by intestinal, lung, and non-Hodgkin lymphoma. The majority of malignancies (78.3%) developed within 13 months after the initiation of dermatomyositis or 4 months following. Anti-TIF1-Ab-positive individuals had a considerably increased death rate. (Chua et al., 2022)

Cutaneous features in anti-TIF1-gamma positive patients, including palmar hyperkeratotic papules and psoriasis-like lesions. TIF-1 autoantibodies were found in 55 (41%) of the patients. Patients with anti-TIF-1 antibodies were less likely to experience systemic symptoms such as interstitial lung disease, Raynaud phenomenon, and arthritis/arthralgia. (Fiorentino et al., 2015) Because of the diversity in symptoms, dermatomyositis with anti-TIF1 gamma might be misdiagnosed, resulting in delayed treatment and an increased death rate.

One hundred forty-eight patients were treated with IIM throughout this period, with nine instances being DM with anti-TIF1 gamma positive. There were four and five patients with cancer and without cancer, respectively. Glucocorticoids (GCs) were given to eight TIF1-DM patients, immunosuppressants to four, and intravenous immunoglobulins (IVIG) to seven. All four CA-TIF1-DM patients who were treated had good responses with GC. (Fujikawa et al., 2019) While immunosuppressive therapy remains the mainstay of DM treatment, its role in patients with malignancy-associated DM requires careful consideration, as immunosuppression may influence cancer progression.

Dermatomyositis is known to be related to cancer hence, cancer screening is required for DM patients. Anti-TIF1- antibodies are currently thought to be present in 13-31% of people with DM and 22-29% of children with DM. Lung cancer, breast cancer, and stomach cancer are the most prevalent cancers linked with anti-TIF1-DM. (Ogawa-Momohara et al., 2018) If cancer is discovered, it is critical to treat it as soon as possible since this might lead to an improvement in DM symptoms. (Fiorentino & Casciola-Rosen, 2012; Harada et al., 2022)

Women are more likely than males to have anti-TIF1-DM. (Stuhlmüller et al., 2019) Nevertheless, a recent study indicated that pregnancy might be a potential trigger for the development of anti-TIF1γ antibody-positive dermatomyositis in young adult women (Oya et al., 2020). Nonetheless, numerous cases of dermatomyositis did not show improvement with the treatment of only malignant tumors. This occurrence warrants further investigation, as there may be other underlying mechanisms that need to be clarified. The management of anti-TIF1γ antibody-positive dermatomyositis follows the same approach for other forms of dermatomyositis, including anti-MDA5 and anti-Mi-2 antibody-positive types. The primary treatment consists of prednisolone and immunosuppressants; however, in instances where malignancies are present in patients with anti-TIF1γ antibody-positive dermatomyositis, addressing the malignancies takes precedence. (Lerman, & Richardson, 2019) Additionally, in cases involving dysphagia or resistance to steroids, intravenous immunoglobulin (IVIG) therapy has been noted to be beneficial (Patwardhan, 2020)

2. Objectives

To describe the clinical characteristics and disease manifestations associated with malignancy in adult dermatomyositis with anti-TIF1 gamma positive.

3. Materials and Methods

Figure 1 below shows the flow of the search strategy, which we divided into two parts: identification and screening. For the investigation stage, we first developed keywords in line with the SPIDER mnemonic: dermatomyositis, AND clinical, AND characteristics, AND anti-tif1, AND gamma, AND adult AND cancer-associated dermatomyositis. For each database, we ran an initial basic search and an expanded search using the advanced search function of the databases with the synonyms of the above keywords. We conducted a

series of Boolean search strings of the PubMed, Cochrane, Scopus databases, and Google Scholar (supplementary search) to identify primary studies between the 1st of January 2013 and the 31st of December 2023. The Google Scholar search engine was used to conduct a forward and backward citation on the studies identified at the end of our keyword and database search screening process.

For Google Scholar, we ran a single search using the advanced search function, ensuring systematic reviews were excluded from the search.

Zotero software was used to pool the identified studies from the various database searches and to identify and remove duplicate studies.

For the screening stage, the first step was screening the study titles and abstracts to ensure the relevance to our research question. We had two groups at this stage, depending on the clarity or not of their titles and abstracts. The second step involved an attempt to retrieve the full articles of studies, including sending Emails to study authors requesting the full articles of their studies, and for clarifications on the content retrieved articles, especially those studies for which we were unsure of their relevance to our research question. Each retrieved article was screened for eligibility using our inclusion and exclusion criteria, after which we conducted a checklist review of the study methodology for risk of bias.

We included studies that were in the English language, involving clinical characteristics of adult dermatomyositis with anti-tif1 gamma positive within a time frame of 10 years from January 2013 to December 2023.

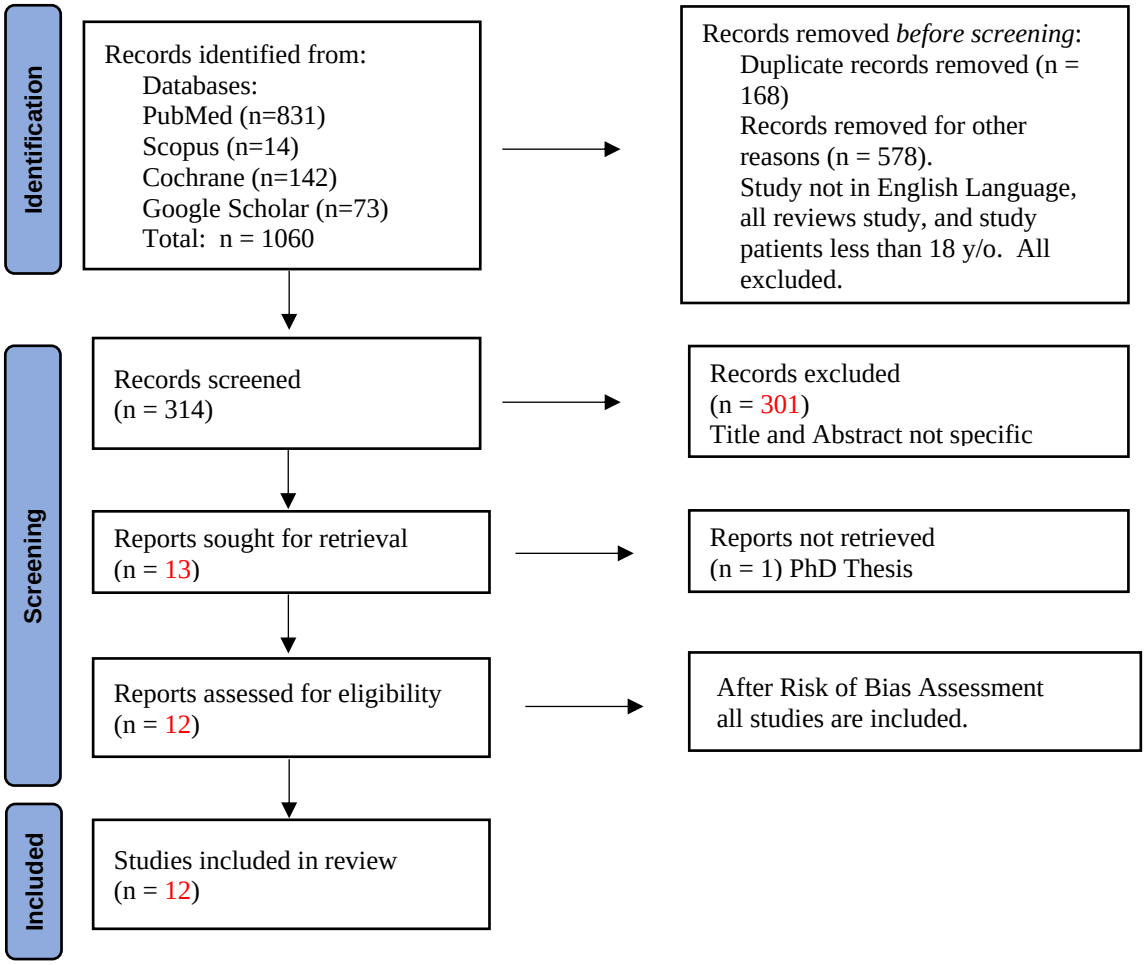

Figure 1 PRISMA flow diagram of search strategy showing the identification and screening phases

Table 1 Sociodemographic data of adult DM patients with anti-TIF1 γ Positive □

The total number of sample n=393 from 12 studies	**Country***	**Total Number of Adult Patients with DM anti-TIF1γ positive: 393**	**Female 312(79.4%)**	**Median age, years: 54.2(49.5-68.6)**	**Ethnicity: Asian 77.4% Western 33.6% Caucasian 19.2% Latinos 2.3% African-American 0.4% Pacific-Islander 0.8%**	**Smoker 15 from 61 (24.5%)**	**The median time of follow-up duration were 48 months (5-75)**	**The median time diagnosis of DM anti-TIF1 γ until developing cancer is 4.75 months (0-24)**	**median age at Cancer diagnosis 61.75 years (59.5-68.0)**	**Time from diagnosis to death (median) 8.3 months (4.6-12)**
Fiorentino et al. 2015	USA	46	39	49.5	Asian 3 Caucasian 33 Latinos 6 African-American 1 Pacific-Islander 2	0	60.0	0	63.5	0
Chua et al. 2022	Singapore	36	26	61.5	Asian 36	6	2.5	0(-288-22)	0	12
Harada et al. 2022	Japan	14	9	68.6	Asian 14	6	0	18(12-24)	0	0
Zhang et al., 2022	China	80	63	52.0	Asian 80	0	4.5	2.0	60.0	0
Wong et al., 2021	China	28	19	60.8	Asian 28	0	7.5	0	0	0
Didona et al. 2020	German	5	5	45.0	Caucasian 5	0	0	0(-24-24)	60.0	0
Gupta et al. 2021	India	8	8	50.0	Asian 8	0	0	0	59.5	0
Isfort et al. 2021	USA	1	1	45.0	Caucasian 1	0	3.0	0	0	0
Ikeda et al. 2020	Japan	31	21	66.4	Asian 31	0	0	5(0-24)	68.0	0
Shibata et al., 2019	Japan	1	0	71.0	Asian 1	0	0	0	0	4.6
Masiak et al., 2016	Poland	11	8	54.2	Caucasian 11	3	0	7.5(1-18)	0	0
Cordel et al. 2023	Europe	132	112	55.0	Western 132	0	48	12(1-24)	55.0	0

*Countries where the study was conducted.

We proceeded to extract data according to the context of respondents, sociodemographics, clinical characteristics, and the type of malignancy associated.

4. Results and Discussion

4.1 Results

This table summarizes demographic data from 12 studies covering 393 adult patients diagnosed with dermatomyositis with anti-TIF1γ positivity. The majority of patients were female (79.4%), with a median age of 54.2 years (ranging from 49.5 to 68.6 years). Ethnic distribution highlights that most patients were Asian (77.4%), followed by Western (33.6%), Caucasian (19.2%), Latino (2.3%), African-American (0.4%), and Pacific Islander (0.8%). Among patients with available smoking history, 24.5% (15 out of 61) were smokers. The median follow-up duration across studies was 48 months (range: 5-75 months). The median time from DM anti-TIF1γ diagnosis to cancer development was 4.75 months (range: 0-24 months), with a median cancer diagnosis age of 61.75 years. The median time from diagnosis to death was 8.3 months (range: 4.6-12 months), indicating a generally poor prognosis.

Table 2 Provides a comprehensive overview of the cutaneous manifestations observed in a cohort of 393 adult dermatomyositis patients with anti-TIF1 gamma positivity.

The total number of sample n=393 from 12 studies	**Heliotrope sign 78%**	**Gottron sign 58.1%**	**Gottron's papules 43.1%**	**V sign 43.1%**	**Shawl sign 40%**	**Periungual erythema 36.5%**	**Facial edema & erythema 31.5%**	**Holster sign 24.6%**	**Scalp rash 16.2%**	**Pruritus 15.4%**
Fiorentino et al. 2015	78.2%	78%	67%	98%	0%	91%	96%	71%	87%	87%
Chua et al., 2022	72.2%	0%	72%	0%	50%	69.4%	0%	22.2%	0%	0%
Harada et al. 2022	64%	43%	0%	0%	57%	0%	0%	0%	0%	0%
Zhang et al., 2022	91.3%	70%	0%	80%	60%	0%	0%	0%	0%	0%
Wong et al., 2021	96.4%	96.4%	96.4%	0%	96.4%	0%	0%	96.4%	0%	0%
Didona et al. 2020	100%	0%	60%	0%	40%	0%	0%	0%	20%	20%
Gupta et al. 2021	100%	0%	0%	0%	0%	0%	100%	0%	0%	0%
Isfort et al. 2021	100%	100%	0%	0%	0%	100%	0%	0%	0%	0%
Ikeda et al. 2020	48.4%	80.6%	77.4%	0%	0%	83.9%	90.3%	0%	0%	0%
Shibata et al., 2019	0%	0%	100%	0%	100%	0%	0%	0%	0%	0%
Masiak et al., 2016	27.2%	9%	0%	36.3%	0%	9%	27.2%	0%	0%	0%
Cordel et al. 2023	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%

Table 3 provides a comprehensive overview of the musculoskeletal involvement and pulmonary complications associated with malignancy and mortality observed in a cohort of 393 adult dermatomyositis patients with anti-TIF1 gamma positivity.

The total number of sample n=393 from 12 studies	**Proximal muscle weakness 31 from 38 (81.6%)**	**Amyopathy 20.4% (53)**	**Myalgia 36.2% (94)**	**Muscle weakness 35% (91)**	**Arthritis / Arthralgia 9.6% (25)**	**Dysphagia 42.8% (162)**	**ILD[1] 13.0% (46)**	**Highest Creatinine Kinase, median (U/L): 498 (342-17698.5)**	**Associated with malignancy 48.6% (191)**	**Mortality 46.8% (29)**
Fiorentino et al. 2015 n=46	0%	26%	0%	0%	36%	37%	5%	342	22%	0%
Chua et al., 2022 n=36	80.6%	19.4%	0%	0%	0%	41.7%	5.6%	473	63.9%	36.1%
Harada et al. 2022 n=14	0%	7.1%	21%	64%	0%	71%	0%	-	86%	86%
Zhang et al., 2022 n=80	21.3%	68.8%	68.8%	0%	46.3%	25%	0%	-	37.5%	0%
Wong et al., 2021 n=28	0%	35.7%	0%	0%	10.7%	32.1%	21.4%	496	53.6%	0%
Didona et al. 2020 n= 5	0%	0%	0%	0%	0%	0%	0%	-	40%	0%
Gupta et al. 2021 n=8	0%	0%	0%	0%	0%	0%	0%	-	50%	0%
Isfort et al. 2021 n=1	100%	0%	100%	100%	100%	0%	0%	-	0%	0%
Ikeda et al. 2020 n=31	0%	19.4%	80.6%	80.6%	9.7%	61.3%	12.5%	987.8	51.6%	0%
Shibata et al., 2019 n=1	100%	0%	100%	100%	0%	100%	0%	500	100%	100%
Masiak et al., 2016 n=11	0%	0%	81.8%	0%	27.2%	36.3%	0%	17698.5	36.3%	27.2%
Cordel et al. 2023	0%	0%	0%	0%	0%	43.4%	11.0%	0%	54.5%	0%

[1]Interstitial lung disease.

Table 4 Provides a detailed breakdown of the organ locations of cancers observed in a cohort of 191 adult dermatomyositis patients with anti-TIF1 gamma positivity, categorized by gender and presented as both raw numbers and percentages.

Total number of samples n=191 from 12 studies	**NPC[1]**	**LC[2]**	**BC[3]**	**OC[4]**	**CC[5]**	**GC[6]**	**NHL[7]**	**BLC[8]**	**UC[9]**	**TC[10]**	**CVC[11]**	**FTC[12]**	**KC[13]**	**Unknown**
Fiorentino et al. 2015 n=10	-	-	-	-	-	-	-	-	-	-	-	-	-	M≠F[14]: 10
Chua et al., 2022 n=23	M[15]:3 F[16]:3	M:1 F:1	F:6	-	M:1 F:2	-	M:1 F:1	-	-	F:1	F:1	F:1	F:1	-
Harada et al. 2022 n=14	-	M:1 F:2	F:2	F:1	M:1 F:1	M:1	M:1	-	F:2	-	-	-	-	M:1 F:1
Zhang et al., 2022 n=30	-	-	-	-	-	-	-	-	-	-	-	-	-	M≠F: 30
Wong et al., 2021 n=15	M≠F:7	M≠F:4	-	F4	-	-	-	-	-	-	-	-	-	-
Didona et al. 2020 n=2	-	F2	-	-	-	-	-	-	-	-	-	-	-	-
Gupta et al., 2021 n=4	-	-	-	-	-	-	-	-	-	-	-	-	-	M≠F: 4
Isfort et al. 2021 n=0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ikeda et al. 2020 n=16	M:1	M:1	F:4	F:4	M:1 F:1	M:2	-	M:2	-	-	-	-	-	-
Shibata et al., 2019 n=1	-	-	-	-	-	M:1	-	-	-	-	-	-	-	-
Masiak et al., 2016 n=4	-	F:1	-	F:1	F:1	M:1	-	-	-	-	-	-	-	-
Cordel et al., 2023	M≠F:5	M≠F:8	F:19	F:15	M≠F:3	-	M≠F:4	M≠F:1	M≠F:1	-	M≠F:2	-	M≠F:1	-
Total n, % patients with Cancer based on sex	M:4 F:3 M≠F:12 10%	M:3 F:6 M≠F:12 11.%	F:31 16.2%	F:25 13.1%	M:3 F:5 M≠F:3 5.8%	M:5 4.2%	M:2 F:1 M≠F:4 3.7%	M:2 M≠F:1 1.6%	F:2 M≠F:1 1.6%	F:1 0.8%	F:1 M≠F:2 1.6%	F:1 0.8%	F:1 M≠F:1 1.1%	M:1 F:1 M≠F: 44 38.7%

[1] Nasopharyngeal cancer, [2]Lung cancer, [3]Breast cancer, [4]Ovarium cancer, [5]Colon cancer, [6]Gastric cancer, [7]Non Hodgkin's Lymphoma, [8]Bladder cancer, [9]Uterus cancer, [10]Thyroid cancer, [11]Cervix cancer, [12]Falopian tube cancer, [13]kidney cancer, [14]Unknown sex, [15]Male, [16]Female.

4.2 Discussion

4.2.1 Sociodemographic of adult DM patients with anti-TIF1 gamma-positive

This systematic review from the 12 analyzed cohort studies for a total of 393 dermatomyositis adult patients with anti-TIF1 gamma positive. Found that 7 studies were from Asian countries with a predominant

Asian Ethnicity of 202 (77.4%). (Chua et al., 2022; Gupta et al., 2021; Harada et al., 2022; Ikeda et al., 2020; Shibata et al., 2019; Wong et al., 2021; Zhang et al., 2022). Two studies were from the USA (Fiorentino et al., 2015; Isfort et al., 2021), and 3 others were from Europe (Cordel et al., 2023; Didona et al., 2020; Masiak et al., 2016). These 4 studies were predominantly Caucasian ethnicity 50(19.2%). This study confirmed that the female sex predominant in 312 (79.4%). (Chua et al., 2022; Cordel et al., 2023; Fiorentino et al., 2015; Harada et al., 2022; Ikeda et al., 2020; Masiak et al., 2016; Wong et al., 2021; Zhang et al., 2022). Smoking prevalence (24.5%) in 15 out of 61 patients from 3 cohort studies (Chua et al., 2022; Fiorentino et al., 2015; Masiak et al., 2016). Suggests that a notable proportion of these patients may be at an even higher risk for developing lung cancer due to the combined effects of smoking and their underlying condition. The median duration of follow-up was 48 months, indicating that patients were longitudinally monitored for an extended period. The median time from diagnosis of dermatomyositis with anti-TIF1 gamma positivity to the development of cancer was 4.75 months, with a median age at cancer diagnosis of 61.75 years. A substantial proportion of adult DM patients with anti-TIF1 gamma positivity were found to be associated with malignancy (191) 48.6%. This result is similar to 3 previous meta-analyses showing, respectively, an OR for CAD of 27.26 (95% CL 6.59- 118.82) and RR for CAD of 5.57 (95% CL 2.91-10.65) (Best et al., 2019; Lu et al., 2014; Trallero-Araguás et al., 2012) suggesting that anti-TIF1 gamma autoantibody should be considered a valuable tool for predicting cancer associated with dermatomyositis (CAD) in adult patients.

4.2.2 Clinical characteristics identified in adult dermatomyositis with anti-TIF1 gamma positive

The majority of patients exhibited characteristics of cutaneous manifestations, with the heliotrope rash being the most prevalent 78.0%, followed by Gottron's sign 58.1 %, Gottron's papules 43.1%, and V sign 43.1 %. Similar to Fiorentino et al. (2015) a single cohort of 46 adult dermatomyositis patients with anti-TIF1 gamma positive in which all of these cutaneous manifestations were presented with a high percentage in adult dermatomyositis patients with anti-TIF1 gamma positive. Musculoskeletal manifestations were common among the patients with myalgia at 36.2%, muscle weakness at 35% being predominant, and proximal muscle weakness was observed in the largest subset of patients 81.6% (31 out of 38 patients) (Chua et al., 2022; Isfort et al., 2021; Shibata et al., 2019). Highlight the potential impact on functional status and quality of life. Interstitial lung disease (ILD) was documented in a notable proportion of patients 13% (46 out of 353 patients) (Chua et al., 2022; Cordel et al., 2023; Fiorentino et al., 2015; Ikeda et al., 2020; Wong et al., 2021; Zhang et al., 2022). The research by Fiorentino et al. (2015), Cordel et al. (2023), Chua et al. (2022), and Wong et al., 2020. Collectively suggest that pulmonary complications were less common among individuals in the anti-TIF1 gamma-positive group.

4.2.3 Type of malignancy based on sex and organ location affected

Breast cancer was the most common malignancy observed, accounting for 16.2% of a total of 191, followed by Ovarian cancer, which was the next most frequent, each comprising 13.1% of cancer cases with higher prevalence in females. Lung and Nasopharyngeal cancer were the next most frequent, each comprising 11% and 10% of total cancer cases, respectively. Notably, breast and ovarian cancer was exclusively observed in female patients, this study is aligned with a previous meta-analysis study done in Asians in which Nasopharyngeal, Lung, Breast, Gastric, Colon, and Ovarian cancer were the most predominant in their research. (Ungprasert et al., 2013) Other less common cancer types included bowel, gastric, non-Hodgking lymphoma, bladder, uterine, kidney, B-cell chronic lymphocytic leukemia (B-CLL), gallbladder, thyroid, fallopian tube, pancreatic, and esophageal cancers, each representing a smaller proportion of total cancer cases. This study is aligned with previous Systematic and Meta-analyses, which confirmed a higher prevalence of solid cancers than hematological malignancies in adult DM with anti-TIF1 gamma (Hill et al., 2001; Best et al., 2019).

There were notable gender differences in the distribution of certain cancer types. For instance, nasopharyngeal cancer was more prevalent in males, while lung, breast, and ovarian cancers were observed in females. This gender disparity may reflect underlying biological differences or environmental exposures. A significant proportion of 38.7% of cancer cases were categorized as "unknown" in terms of organ location

and sex. This highlights a limitation in the data collection or reporting process, as the specific anatomical site and sex of these patients were not documented. (Cordel et al., 2023; Fiorentino et al., 2015; Gupta et al., 2021; Wong et al., 2021; Zhang et al., 2022) The findings provide valuable insights into the spectrum of malignancies associated with anti-TIF1 gamma-positive dermatomyositis and underscore the importance of comprehensive cancer screening and surveillance in affected individuals. The observation of a diverse range of cancer types affecting various organ systems highlights the multisystem nature of the disease and emphasizes the need for a multidisciplinary approach to patient management. The gender differences in cancer distribution suggest potential underlying biological and hormonal factors influencing cancer susceptibility in anti-TIF1 gamma-positive dermatomyositis. A significant percentage of mortality was found in this study, 46.8% (29) of 62 patients, most of them were clinically presented with advanced malignancy at older ages. (Chua et al., 2022; Harada et al., 2022; Masiak et al., 2016; Shibata et al., 2019).

Additionally, the high proportion of cancers categorized as "unknown" underscores the importance of standardized reporting practices and thorough documentation of clinical data to facilitate more accurate epidemiological studies and improve our understanding of the relationship between dermatomyositis and malignancy. Addressing these limitations will be critical for optimizing patient care and informing clinical decision-making in this complex disease setting. We had limitations while analyzing data from the 12 cohort studies; it became evident that some studies lacked complete information regarding treatments administered and specific types of malignancies observed. This limitation hindered the comprehensiveness of the analysis, as the absence of such crucial data restricted our ability to fully explore the associations between treatments, malignancy types, and clinical outcomes among adult dermatomyositis patients with anti-TIF1 gamma positivity. As a result, the incomplete dataset may influence the interpretation of findings, and further research with more comprehensive data collection is warranted to address this limitation and enhance the understanding of this patient population.

5. Conclusion

In this study analyzing 393 adult dermatomyositis (DM) patients with anti-TIF1 γ, we observed a predominance of females 79.4% with a median age of symptom onset at 54.2 years. The majority of patients were of Asian ethnicity, 77.4%, followed by Western ethnicity, 33.6%, with a smaller representation of Caucasian, Latino, Pacific Islander, and African American individuals. Notably, 24.5% of patients were smokers. The median follow-up duration was 48 months, and the median time from DM diagnosis to cancer development was 4.75 months. The median age at cancer diagnosis was 61.75 years, with a median time from diagnosis to death of 8.3 months. A significant association between anti-TIF1 γ-positive DM and malignancy was observed, with 191 patients, 48.6% developing cancer, and a significant number of Mortality, 46.8%.

Cutaneous manifestations were frequent, with heliotrope rash at 78.0%, Gottron's sign at 58.1%, and Gottron's papules at 43.1% being the most common. Musculoskeletal manifestations included proximal muscle weakness 81.6%, amyopathy 20.4%, myalgia 36.2%, and muscle weakness 35.0%. Dysphagia was reported in 42.8% of patients. Interstitial lung disease was present in 13.0% of cases.

The most common malignancies encountered were breast cancer 16.2%, ovarian cancer 13.1%, followed by lung cancer 11% and nasopharyngeal cancer 10%. Other notable malignancies included bowel, kidney, uterus, bladder and gastric cancers. A considerable proportion of malignancies were categorized as "unknown" in terms of sex and organ location 38.7%

Across the studies reviewed, it is evident that adult DM patients with anti-TIF1 gamma positivity exhibit a distinct clinical profile compared to DM patients without this antibody. These individuals often present with specific cutaneous features such as the classic heliotrope rash, Gottron’s papules, and a higher prevalence of malignancy-associated dermatomyositis. Furthermore, they tend to have a higher risk of internal organ involvement and malignancies and a low risk of interstitial lung disease, arthritis, and arthralgia. The association between anti-TIF1 gamma positivity and cancer risk highlights the importance of diligent cancer screening and surveillance in these patients.

Additionally, the prognosis of anti-TIF1 gamma-positive DM patients appears to be less favorable compared to other DM subsets, with higher rates of disease relapse, treatment resistance, and overall

mortality. This underscores the need for personalized treatment approaches tailored to the specific needs of these patients, including aggressive immunosuppressive therapy and close monitoring for disease progression and complications.

Overall, the findings from the reviewed cohort studies provide valuable insights into the clinical characteristics and outcomes of adult DM patients with anti-TIF1 gamma antibody positivity. However, further research is warranted to elucidate the underlying mechanisms driving the distinct phenotype observed in these patients and to develop targeted therapeutic strategies to improve their long-term outcomes.

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