2024 RDS Annual Meeting Abstract Book

Oral Presentations

Session I:

Lupus Erythematosus

ASSESSING DISEASE SEVERITY IN CUTANEOUS LUPUS PATIENTS USING NATURAL LANGUAGE PROCESSING

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Natural language processing (NLP) in dermatology has great potential to assess disease severity from clinical documentation. The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is primarily used in clinical trial settings but rarely in clinic visits due to time constraints and lack of provider training. Physical examination (PE) descriptions in clinic notes contain necessary information that can estimate CLASI scores. Thus, we performed a pilot study to develop a NLP model that interprets physical examination (PE) documentation in CLE patients and evaluates disease severity. 89 clinical exams of 24 CLE patients were used for a training set, and 35 clinical exams of 26 CLE patients were selected for a test set. The BERT (Bidirectional Encoder Representations from Transformers) model was trained to predict all entities and relationships in the notes and calculate CLASI scores, and applied to the training and test sets. Generated scores were compared to the ground-truth CLASI scores based on human annotation. The model also predicted severity categories (moderate-severe/mild), based on published CLASI score cutoffs, which were compared to ground truths. The model-predicted individual scores had correlations of 0.79 ($p<0.0001$) and 0.82 ($p<0.0001$) with ground truths on CLASI-A and CLASI-D scores, respectively, in the training set, and 0.64 ($p<0.0001$) and 0.88 ($p<0.0001$) in the validation set. For severity category predictions, the model achieved high accuracy of 0.88 (activity) and 0.89 (damage) using the training set and 0.91 (activity) and 0.89 (damage) using the test set. Using PE notes as the input, a BERT-based NLP model can be trained to predict CLASI scores in CLE patients. Limitations include single-center design using documentation from a single clinician. This algorithm can form the foundation of a CLASI calculator that can increase the volume of real-world data with objective disease severity information available for CLE research and clinical decision-making.

Category: Lupus

IMPACT OF AREA DEPRIVATION ON DISEASE SEVERITY IN ADULT PATIENTS WITH DISCOID LUPUS ERYTHEMATOSUS

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Abstract:

The association of area deprivation with outcomes in discoid lupus erythematosus (DLE) remains poorly understood. To determine the association between US Census block measures of deprivation and DLE disease severity, we conducted a cross-sectional analysis of 154 adult DLE patients seen between January 1, 2007, and January 1, 2024, at a single-center referral-based specialty rheumatologic-dermatology clinic in Philadelphia, Pennsylvania. Patients were aged 18-73 years and were enrolled in the University of Pennsylvania's Cutaneous Lupus Erythematosus Database study. Residence in a highly disadvantaged area as geocoded by a state area deprivation index (ADI) was the primary exposure of interest. The main outcome was DLE disease severity as codified by the validated Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) damage and activity scores. A total of 154 patients with DLE (128 women [83%] and 26 men [17%]; mean [SD] age, 43 [13] years; 6 [4%] Asian individuals, 98 [64%] Black individuals, 2 [1%] Hispanic individuals, 46 [30%] White individuals, and 2 individuals [1%] with other race/ethnicity; 78 [51%] with an ADI >5; 43 [28%] current smokers; and 56 [36%] with concurrent systemic lupus erythematosus) were included in the analysis. By multivariable logistic regression, residence within communities with an ADI >5 was associated with nearly 4-fold greater odds of moderate to severe damage (odds ratio [OR], 3.90; 95% CI, 1.27-12.69] and activity (OR, 3.31; 95% CI, 1.27-9.44). Concurrent cigarette smoking was similarly associated with greater odds of moderate to severe damage (OR, 3.15; 95% CI, 1.09-10.29). After controlling for ADI and other confounders, race was not significantly associated with DLE disease severity, suggesting that geospatial disadvantage is associated with disease severity independent of race. This invites a paradigm shift that considers the social context within which racial disparities are observed, highlighting the potential for geographically targeted interventions and policy changes to improve patient outcomes in DLE.

Category: Lupus

Note: This work has recently been published but has not been presented previously. **Faden DF**, Xie L, Stone C, Gomes L, Le T, Ezeh N, Buckingham WR, Kind A, Vleugels RA, Werth VP, Arkin L, Shaw K. Impact of Area Deprivation on Disease Severity in Adult Patients with Discoid Lupus Erythematosus in the Philadelphia Area. *JAMA Dermatology*. July 2024; doi: 10.1001/jamadermatol.2024.2355

HIGH EXPRESSION OF IMMUNE CHECKPOINT VISTA IN CUTANEOUS LUPUS COMPARED TO OTHER INFLAMMATORY SKIN DISEASES

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Immune inhibitory receptor agonists are currently in development for the treatment of autoimmunity. However, little is known about the expression patterns of immune inhibitory receptors, often referred to as immune checkpoints, in inflammatory skin diseases. Identifying potential targets for immune checkpoint agonist therapy will help inform future clinical trials. Programmed death 1 homolog (PD-1H), also commonly called V-domain Ig suppressor of T cell activation (VISTA) is an immune inhibitory receptor of the B7/CD28 gene family that inhibits T cell and myeloid cell functions. Mice that lack PD-1H/VISTA have exacerbated immune pathology in multiple mouse models of autoimmunity, including systemic lupus erythematosus. We previously demonstrated that PD-1H/VISTA knockout mice spontaneously develop cutaneous lupus that resembles human cutaneous lupus erythematosus (CLE). In the MRL/*lpr* lupus model, we found elevated expression of VISTA within CLE-like lesions. Using an agonist anti-VISTA antibody, we showed that VISTA agonist treatment inhibits CLE development and reduces systemic inflammation, including type I interferon production (IFN-α) and autoantibodies. Next, we analyzed 60 skin biopsies from patients with a spectrum of chronic inflammatory conditions, including CLE, lichen planus, psoriasis, acute cutaneous graft-versus-host disease, and dermatomyositis. We found that PD-1H/VISTA is most highly expressed in CLE compared to the other inflammatory skin diseases tested, where 30-80% of cells within skin biopsies of CLE expressed PD-1H/VISTA. As targeting immune inhibitory receptors emerge as a therapeutic option for the treatment of inflammatory skin diseases, our results provide strong rationale for clinical trial development of PD-1H/VISTA agonism for CLE therapy.

Teaching point: VISTA is a highly expressed in CLE and is a potential therapeutic target

Category: Lupus

SPATIAL SINGLE-CELL RNA SEQUENCING OF CUTANEOUS LUPUS REVEALS DISTINCT MOLECULAR, CELLULAR, AND TISSUE LEVEL CHANGES WITH ANIFROLUMAB TREATMENT

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Cutaneous lupus erythematosus (CLE) is a disfiguring autoimmune skin disease with no FDA-approved therapies. Anifrolumab, a monoclonal antibody targeting the type I interferon receptor, has shown promise in treating systemic lupus erythematosus, and emerging data suggest it may be highly effective in CLE. However, the molecular and cellular mechanisms underlying its effects on CLE remain incompletely understood. This study utilizes spatial transcriptomics and single-cell RNA sequencing to explore the impact of anifrolumab on gene expression and cellular composition in CLE-affected skin. Skin biopsies from uninvolved skin (n=3), discoid lupus erythematosus (DLE, n=3), and pre- and post-anifrolumab therapy samples (n=6) were analyzed. Spatial transcriptomics revealed distinct gene expression profiles across different skin compartments, with principal component analysis demonstrating that post-therapy samples shifted towards gene expression profiles characteristic of uninvolved skin. Differential gene expression analysis highlighted compartment-specific changes following anifrolumab treatment, including downregulation of inflammatory keratins (KRT6C, KRT16, KRT17) in the epidermis and upregulation of extracellular matrix genes (COL1A1, COL3A1) in the dermis. Vascular regions showed decreased expression of chemokines CXCL10 and CXCL11. Interferon-stimulated genes were downregulated across all compartments, confirming the on-target effects of anifrolumab. Notably, IFNAR1 expression increased post-treatment, particularly in the epidermis and vasculature, suggesting a potential loss of negative feedback regulation. Integration of single-cell RNA sequencing data revealed a reduction in T and B cell frequencies in lesional skin post-therapy. These findings offer novel insights into the molecular and cellular effects of anifrolumab in CLE, demonstrating its potential to restore skin homeostasis by modulating gene expression and immune cell composition. This study underscores the value of spatial transcriptomics in understanding complex skin diseases and their treatment responses.

Abstract Category: Lupus

DIRECT IMMUNOFLUORESCENCE IgG AUTOANTIBODY SUBCLASS ANALYSIS AS A TOOL TO DIFFERENTIATE BETWEEN BULLOUS SYSTEMIC LUPUS ERYTHEMATOSUS AND EPIDERMOLYSIS BULLOSA ACQUISITA

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Bullous systemic lupus erythematosus (BSLE) and epidermolysis bullosa acquisita (EBA) are autoimmune blistering diseases characterized by the deposition of antibodies against type VII collagen. They have identical histologic presentations of subepidermal blisters with neutrophilic infiltrate in the dermis and direct immunofluorescent staining (DIF) showing linear depositions of IgG and C3 and less commonly IgM and/or IgA along the dermo-epidermal junction (DEJ). Salt-split skin shows dermal deposition of immunoglobulins. Clinically, they both present with erythematous dermal plaques, and tense vesicles and bullae involving the face, trunk, and extensor extremities. Clinico-histopathologic differentiation may be difficult as 30-50% of BSLE may precede SLE, and EBA can present with systemic symptoms of fever, fatigue, non-erosive arthritis and be associated with SLE. Previous studies have performed Western blotting with serum IgG subclasses against recombinant type VII collagen and shown elevated IgG2/IgG3 and IgG1/IgG4 levels in BSLE and EBA, respectively. DIF of IgG subclasses in perilesional skin is a simpler method and may aid in the differentiation between BSLE and EBA. We report 6 patients with clinico-histopathologic differential diagnoses of BSLE (n=2) or EBA (n=4). Frozen tissue slides from perilesional skin were processed for immunofluorescence staining. Primary rabbit anti-human monoclonal antibodies against IgG1, IgG2, IgG3, and IgG4 were added to the tissue and then incubated with goat anti-rabbit antibodies conjugated with Alexa Fluor 488. Images were captured via Olympus microscope and camera at 10x and 20x magnification. Two people blinded to the study evaluated the intensity of the DIF staining. At the DEJ, DIF showed significantly stronger IgG2 and IgG3 staining in BSLE whereas EBA showed significantly stronger IgG1 and IgG4 staining. In cases with features consistent with both BSLE and EBA, tissue DIF IgG subclass staining can be useful to prioritize diagnostic options and to decide therapeutic management.

Category: Lupus

CLINICAL, PATHOLOGICAL AND IMMUNOLOGICAL FEATURES OF TOXIC-EPIDERMAL NECROLYSIS LIKE LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND PROPOSAL FOR DIAGNOSTIC CRITERIA

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Background: Toxic epidermal necrolysis like lupus erythematosus (TEN like LE) is a dermatological emergency associated with significant morbidity and mortality. It requires prompt recognition and differentiation from its mimics.
Methods: We performed a systematic review of studies on toxic epidermal necrolysis like lupus erythematosus published between 1977 and 2024. There were 14 case series and 56 individual case reports/conference papers yielding a total of 112 unique cases of TEN like LE
Results: The mean age was 43.39 years, 86.6% were female. A total of 56/112 (50%) had TEN like LE as presenting manifestation of lupus erythematosus (LE) and 50% had a prior history of LE, (9 Cutaneous LE (CLE), 38 Systemic LE (SLE) and 11 CLE/SLE). Antinuclear antibody (ANA) was reported in 109 patients and was positive in all. The most common identified antibody was SSA/Ro 66(60.55%) followed by dsDNA 56 (50%). Lesions were reported to be photo-distributed in 88 (78.57%) of cases, palmoplantar involvement was seen in 23(20.54%) and mucosal involvement was seen in 63 (56.25%) with 30(26.78%) patients having significant mucosal involvement. Lupus non-specific lesions (chilblains, oral ulcers, facial edema, alopecia, nail-fold capillary changes, urticarial vasculitis) were observed in 28 (25%) patients.
Conclusion: TEN like LE can be the first manifestation of LE in upto half of the cases. Photo distribution, lupus non-specific lesions, ANA positivity or change in ANA type/titre can be important diagnostic clues. Unlike previously believed, mucosal involvement is not uncommon and can be severe. We propose two sets of diagnostic criteria for patients who have either a known diagnosis of LE or no known history of LE. This differentiation is important to differentiate classic TEN from TEN-like lupus in patients who already carry a diagnosis of LE. Further Delphi consensus and prospective comparison with a cohort of drug induced TEN can provide valuable insight.

Keywords:
Systematic review; toxic epidermal necrolysis like lupus erythematosus, anti-nuclear antibody, lupus, photo-distributed

Category: Lupus

CLUES: A Nationwide Siteless Prospective Study to Identify Predictors of SLE Progression in Patients with CLE

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Cutaneous lupus erythematosus (CLE) encompasses a diverse group of autoimmune skin disorders that can cause significant disfigurement and are categorized into distinct subtypes, each with varying risks of progression to systemic lupus erythematosus (SLE). SLE patients face the potential for severe internal organ damage, and despite advancements in treatment, SLE-associated mortality remains concerningly high. Previous population-based studies have identified clinical and serological markers associated with an increased risk of systemic disease progression in CLE, including female sex, acute and subacute CLE subtypes, and positive antinuclear antibodies (ANA). However, there remains a critical gap in molecular signatures that can accurately predict which CLE patients are at the highest risk of SLE conversion on an individual basis. To address this, we have launched a prospective, decentralized study using an innovative approach to longitudinally monitor patients with primary subacute and discoid CLE. Our methodology leverages a smartphone-based digital application, wearable technology, and non-invasive home-based blood and skin sampling techniques, including capillary blood collection, tape stripping, and absorptive microneedles. By employing advanced high-throughput antibody screening and mass spectrometry proteomics, we will perform comprehensive molecular profiling at multiple time points over a five-year period. Our study aims to integrate clinical, genetic, and molecular data to identify a “preclinical signature” that can predict SLE progression in CLE patients. We will employ sophisticated machine learning models, including regularized logistic regression and random forest classifiers, to handle large, multidimensional datasets and build robust predictors of SLE conversion. These models will incorporate variables such as genetic predisposition, antibody and proteomic profiles, stress factors, environmental exposures, and patient behaviors. Using dynamic mathematical modeling, we will iteratively refine our algorithms to determine hazard rates and stable predictors, ultimately aiming to transform risk assessment and clinical management for CLE patients.

ERYTHEMA IN CUTANEOUS LUPUS SIGNIFICANTLY IMPACTS PATIENT QUALITY OF LIFE AND DISEASE COURSE IMPRESSION

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The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is a validated instrument that grades severity of activity (CLASI-A) based on signs including erythema and scale in patients with cutaneous lupus erythematosus (CLE). While erythema is frequently cited in CLE patient quality-of-life interviews, the impact of erythema on CLE patient quality of life and disease course impression is not well characterized. Thus, we performed a prospective longitudinal cohort study to examine how CLASI-A erythema and scale correlate to patient-reported outcome measures (PROM) at baseline and 6 months, respectively. 131 CLE patients were recruited in outpatient dermatology clinics at University of Texas Southwestern Medical Center, Parkland Health, and University of Pennsylvania between July 2018 and November 2023. Demographic and clinical characteristics, CLASI-A scores, and PROMs were collected. Examined PROMs included the CLE Quality of Life Index (CLEQoL), Dermatology Quality of Life Index (DLQI), Patient Impression of Disease Progression (PIDP), and Analogue Pain, Itch, and Fatigue Scales (APIFS). Spearman correlation analyses were performed to examine relationships between CLASI-A erythema or scale and PROMs. At baseline (N = 131), CLASI-A erythema had statistically significant correlation to all PROMs, most notably DLQI (ρ=0.37, $p<0.001$), and mostly stronger correlations compared to the entire CLASI-A scale. Compared to changes in CLASI-A scale, CLASI-A erythema (N=108) at 6 months more often directly correlated to change in PROMs. PIDP had the strongest correlation with changes in CLASI-A erythema, in which patients with larger decreases in CLASI-A erythema scores experienced higher CLE disease improvement (ρ=-0.41, $p<0.001$). These results affirm the substantial impact of erythema in quality of life in CLE patients and demonstrate that improvement in erythema can result in clinically meaningful benefit for CLE patients. They also justify the greater weighting of erythema in CLASI-A scoring, which can be responsive to treatments.

Category: Lupus

Session II:

Sclerosing and Other Connective Tissue Diseases

EOSINOPHILIC FASCIITIS AND MORPHEA SHARE GENE SIGNATURES OF INFLAMMATORY CELL DEATH, SELF-DNA RECOGNITION, AND ENHANCED JAK/STAT SIGNALING

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The pathogenesis of both eosinophilic fasciitis (EF) and morphea is poorly understood. We analyzed skin biopsies from EF and morphea patients compared to adult healthy skin (HS) using gene expression profiling, Ingenuity Pathway Analysis, and immunostaining. EF gene expression changes had many similarities to those observed in morphea. 51/61 differentially expressed genes (DEG), 80/99 canonical pathways, and 40/51 upstream regulators were shared in EF and morphea. Both conditions exhibited robust T cell activation and cytotoxic signatures despite their pauci-inflammatory histological appearance, suggesting small numbers of T cells may drive injury, inflammation, and fibrosis. EF and morphea shared signatures of necroptosis, self-DNA recognition, cGAS/STING activation, induction of types I, II, and III interferon signaling, and fibrosis. 7 JAK/STAT molecules were significantly upregulated in EF, and 9 were upregulated in morphea. Compared to HS, *TYK2* was the most significant JAK molecule upregulated in EF ($p=0.0007$) and morphea ($p=0.0002$). Immunostaining demonstrated activated interferon-related molecules JAK1 and STAT1 in T cells, dendritic cells, and macrophages in both EF and morphea. The numbers of T cells in established fibrotic morphea and EF lesions did not differ from HS, suggesting a potential role for T resident memory cells. Immunostaining revealed increased numbers of T cell associated apoptotic and necroptotic endothelial cells in EF and morphea compared to HS, implicating T cell-driven vascular injury in both conditions. This study provides new insights into the molecular mechanisms of EF and morphea and demonstrates strong pathophysiologic similarities between these two disease states. Our findings indicate that targeted inhibition of JAK/STAT molecules and mediators of necroptosis may be beneficial in treating these fibrotic diseases.

Abstract Category: Sclerotic skin disease

LONGITUDINAL ASSESSMENT OF DISEASE ACTIVITY AND DAMAGE IN ADULT-ONSET MORPHEA

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Morphea, a chronic sclerosing skin disease, exhibits a distinct disease course compared to other conditions, often requiring extended periods to demonstrate significant improvement. However, the precise timeline to disease remission remains undefined. Understanding the short-term disease trajectory is critical for optimizing clinical trial design, determining the time course to remission, and setting realistic patient expectations. In this prospective cohort study, data were collected from the Morphea in Adults and Children (MAC) cohort. Inclusion criteria encompassed adult-onset morphea, a Localized Scleroderma Cutaneous Assessment Tool (LoSCAT) activity score greater than three at one or more visits, and at least one follow-up visit post-flare. Disease activity and damage were evaluated over a two-year period, with all assessments performed by a morphea expert (HTJ), who assigned both activity (LoSAI) and damage (LoSDI) scores. Demographic and treatment data were also gathered. A total of 158 participants met the inclusion criteria, with 82.3% female and 74.1% Caucasian, followed by 13.3% Hispanic/Latino and 5.1% Black, with a mean age of 50 (range 18-88). Generalized morphea was the most common subtype (56.7%), followed by linear morphea (31.8%). The majority (74.1%) of patients were initiated on treatment for their flare, with 36.1% receiving systemic therapy, 8.9% phototherapy, and 29.1% topical treatments. The median LoSAI score decreased from 8.5 at flare onset to 2 at three months, 1 at six months, and 0 at nine months. The median LoSDI score was 14 at flare onset and remained stable at 16 after six months. These findings provide valuable insight into the progression of morphea, establishing essential data for patient counseling and trial design. Future research will extend this work to explore disease activity and damage trajectories in pediatric morphea populations.

Category: Sclerotic skin disease

INTRAVENOUS IMMUNOGLOBULIN FOR THE TREATMENT OF MORPHEA: A RETROSPECTIVE REVIEW OF 2 ACADEMIC MEDICAL CENTERS

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Morphea is a rare, inflammatory disease that manifests with sclerosis and/or atrophy of the skin and subcutaneous tissues. First-line systemic therapies include corticosteroids and traditional steroid-sparing immunosuppressive agents, methotrexate and mycophenolate mofetil. However, some patients may be unable to tolerate, prove refractory, or have contraindications to these standard medications. While intravenous immunoglobulin (IVIg) has demonstrated efficacy in other fibrosing diseases including eosinophilic fasciitis and systemic sclerosis, data supporting its use in morphea is limited. Thus, we conducted a retrospective study of patients with morphea treated with IVIg at Massachusetts General Hospital and Brigham and Women's Hospital from January 2000 to January 2023. Medical records were reviewed to assess demographic data, clinical phenotype, treatment course, and clinical response. Clinical response was defined as complete (resolution of erythema and softening of lesions with no disease progression), partial (incomplete improvement of erythema and/or softening of lesions with no disease progression) or no response (continued disease progression). 13 patients (9 female; mean age 56 [range, 35-76]) met inclusion criteria. Seven patients (53.8%) had complete response, two (15.4%) partial response, and four (30.8%) no response. Of the 10 patients with generalized or pan-sclerotic disease, 70% had complete response, and 20% had no response. By contrast, two of the three linear morphea patients had no response, all of whom had en coup de sabre. Indications for IVIg included failure of or contraindications to standard first- and second-line morphea treatments and pregnancy or breastfeeding concerns. All linear morphea patients started IVIg due to pregnancy, breastfeeding, or plans to become pregnant. Our findings suggest that IVIg can be effective in patients with morphea, particularly generalized or pan-sclerotic subtypes. Response may be subtype-dependent, but IVIg may still be a useful therapeutic option, particularly for women of reproductive age when other medications are contraindicated.

Category: Sclerotic skin disease

INTRAVENOUS EPOPROSTENOL FOR SYSTEMIC SCLEROSIS-ASSOCIATED RAYNAUD'S SYNDROME WITH DIGITAL ULCERATIONS: A RETROSPECTIVE CHART REVIEW

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Epoprostenol is a potent vasodilator and inhibitor of platelet aggregation used to manage severe pulmonary arterial hypertension and other vascular conditions [1]. Epoprostenol has been used for severe Raynaud's, but data for its use has been limited, and more studies have explored the role of iloprost for Raynaud's [2,3,4]. This retrospective chart review describes the clinical outcomes of 12 patients with systemic sclerosis (SSc)-associated Raynaud's syndrome who received intravenous epoprostenol specifically for the treatment of digital ulcers at MassGeneral Brigham. The cohort comprised 4 males and 8 females, with 9 patients having limited SSc, 2 patients having diffuse SSc, and 1 with undifferentiated SSc.

5 patients had undergone surgical debridement or amputation due to ulcer severity at the time of study. Eight patients required prescription pain medication specifically for Raynaud's-related pain prior to IV epoprostenol administration, with seven having used opioids such as dilaudid, oxycodone, or tramadol.

Before initiation of IV epoprostenol, all patients had tried numerous outpatient medications including phosphodiesterase inhibitors (n=9), calcium channel blockers (n=7), nitropaste (n=3), alpha-blockers (n=2), trental (n=1), SSRI (n=1), prostacyclin analogue (n=1), and endothelin receptor antagonist (n=1).The duration of IV epoprostenol administration ranged from 4 to 30 days. Eleven patients received adjunctive botulinum toxin injections, but at least three reported no benefit from this treatment.

Eight patients expressed symptom improvement following IV epoprostenol administration during subsequent encounters. Ulcer healing was documented in three patients: one who received only epoprostenol had complete ulcer resolution in under 187 days, while two who received both epoprostenol and Botox achieved healing in less than 75 and 232 days, respectively.

Nine received a single course of IV epoprostenol and three underwent multiple courses. This case series suggests that IV epoprostenol may provide symptomatic relief and promote ulcer healing in systemic sclerosis patients with refractory Raynaud's syndrome, though further studies are needed to clarify its role and optimize treatment protocols in this population.

Category: Sclerotic skin disease (e.g. morphea, systemic sclerosis, etc.)

References:

1. Kingma K, Wollersheim H, Thien T. Double-blind, placebo-controlled study of intravenous prostacyclin on hemodynamics in severe Raynaud's phenomenon: the acute vasodilatory effect is not sustained. J Cardiovasc Pharmacol. 1995 Sep;26(3):388-93. doi: 10.1097/00005344-199509000-00007. PMID: 8583779.
2. McHugh NJ, Csuka M, Watson H, Belcher G, Amadi A, Ring EF, Black CM, Maddison PJ. Infusion of iloprost, a prostacyclin analogue, for treatment of Raynaud's phenomenon in systemic sclerosis. Ann Rheum Dis. 1988 Jan;47(1):43-7. doi: 10.1136/ard.47.1.43. PMID: 2449871; PMCID: PMC1003442.
3. Yardumian DA, Isenberg DA, Rustin M, Belcher G, Snaith ML, Dowd PM, Machin SJ. Successful treatment of Raynaud's syndrome with Iloprost, a chemically stable

prostacyclin analogue. Br J Rheumatol. 1988 Jun;27(3):220-6. doi: 10.1093/rheumatology/27.3.220. PMID: 2454140.
4. Rademaker M, Thomas RH, Provost G, Beacham JA, Cooke ED, Kirby JD. Prolonged increase in digital blood flow following iloprost infusion in patients with systemic sclerosis. Postgrad Med J. 1987 Aug;63(742):617-20. doi: 10.1136/pgmj.63.742.617. PMID: 2447572; PMCID: PMC2428395.

INFECTION RISK OF RITUXIMAB MONOTHERAPY VERSUS RITUXIMAB WITH AN ADDITIONAL IMMUNOMODULATOR IN SYSTEMIC SCLEROSIS

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The anti-CD20 monoclonal antibody rituximab (RTX) is a key treatment for systemic sclerosis (SSc), though it carries a risk of infection[1,2]. Often SSc patients are treated with dual immunomodulation by combining RTX with agents like mycophenolate mofetil (MMF) or methotrexate (MTX). However, the impact of combination therapies on infection risk remains unclear. In this retrospective cohort study, we compare infection risks between RTX monotherapy and RTX with either MMF or MTX in patients with SSc.

We reviewed the charts of patients with SSc who were treated with RTX at two large academic medical centers, Brigham and Women's and Massachusetts General Hospitals, from 2014-2024. The RTX active treatment window was defined as 6 months following infusion. The study window was defined as the intersection of the RTX window and any concurrent use of MMF or MTX. Infection risk was assessed by the number of antimicrobial prescriptions during the study window, excluding prophylactic use.

The study included 106 patients (25 male, 82 female) categorized into four groups: RTX monotherapy (n=51), RTX with MMF (n=43), RTX with MTX (n=8), and RTX with both MMF and MTX (n=4). Patients were followed for an average of 23.7 months (range 0.9-115), and 278 antimicrobial prescriptions were recorded (203 bacterial, 27 viral, 48 fungal). The RTX monotherapy group averaged 0.165 antimicrobial prescriptions per month, compared to 0.183 for RTX+MMF (P=0.53, **Figure 1**)**.** Similarly, no significant differences were observed when analyzing bacterial (P=0.58), viral (P=0.52), or fungal (P=0.31) infections separately.

This study provides data to help inform patients and physicians considering combination immunomodulatory therapy. Our findings suggest that adding MMF to RTX therapy in SSc does not meaningfully increase infection risk as assessed by number of antimicrobial therapies. Further studies with larger patient populations are needed to fully characterize this risk for patients on RTX+MTX and triple immunomodulation.

Abstract category: Sclerotic skin disease (e.g. morphea, systemic sclerosis, etc.)

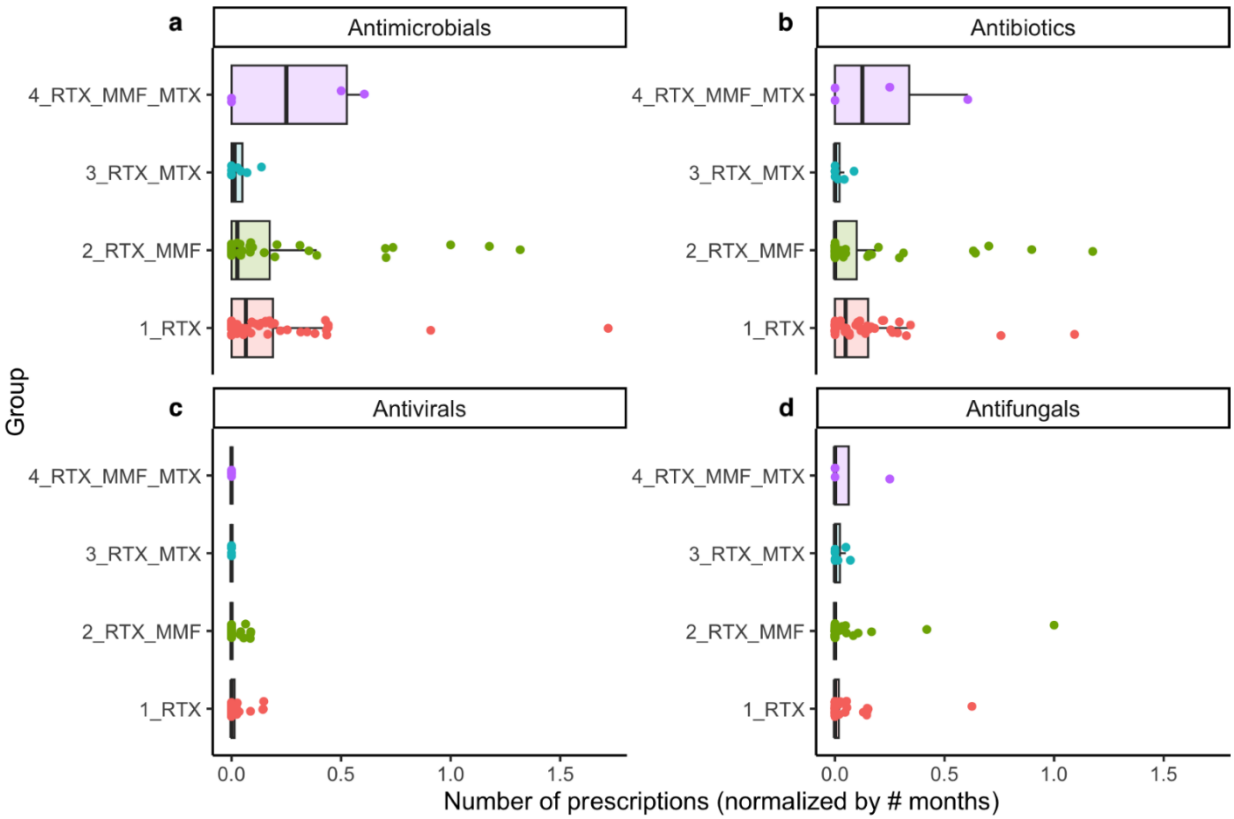

Figure 1. Frequency of antimicrobial prescriptions by immunomodulatory treatment category in systemic sclerosis patients. Boxplots show the number of (**a)** antimicrobial prescriptions, then separated by **(b)** antibiotic, **(c)** antiviral, and (**d**) antifungal prescriptions across patient groups (color). Because the time on immunomodulating treatment differed across patients, the x-axis is normalized by the number of treatment months.

References

1. Ebata, S. et al. Safety and efficacy of rituximab in systemic sclerosis (DESIRES): open-label extension of a double-blind, investigators-initiated, randomised, placebo-controlled trial. *Lancet Rheumatol* **4**, e546–e555 (2022).
2. Varley, C. D. & Winthrop, K. L. Long-Term Safety of Rituximab (Risks of Viral and Opportunistic Infections). *Curr. Rheumatol. Rep.* **23**, 74 (2021).

Session III:
Dermatomyositis

EVALUATION OF THE NEWLY PUBLISHED IMACS GUIDELINES FOR DETECTING MALIGNANCIES IN PARANEOPLASTIC DM PATIENTS

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The International Myositis Assessment and Clinical Studies Group (IMACS) recently published the first consensus-based cancer screening guidelines for patients with idiopathic inflammatory myopathies, including dermatomyositis (DM).[1] Given the known association between IIM and cancer,[2-4] these recommendations aim to provide practical guidance for malignancy screening by stratifying patients as "high," "intermediate," or "low" risk for malignancy based on a constellation of factors including IIM diagnosis, age of disease onset, autoantibody profiles, and clinical features. Recommendations include serologic tests and/or imaging tailored to individual patient risk. We sought to investigate the utility of these guidelines in a prospective cohort of 370 DM patients treated at the University of Pennsylvania Rheumatology-Dermatology specialty clinic from July 2008 to January 2024.[5] Of the 370 DM patients (mean age 48 years, 87% female, 89% non-Hispanic White), 49% had classic DM, 42% amyopathic DM, and 3% hypomyopathic DM. Based on IMACS guidelines, patients were classified as "high" (54%), "intermediate" (37%), and "low" (9%) risk for malignancy. Paraneoplastic DM was identified in 18 patients (4.9%), predominantly in females over 40, classified as "high" or "intermediate" risk. Breast cancer was the most common malignancy, and most cancers were detected either prior to or shortly after DM diagnosis. All malignancies would have been detected using IMACS screening protocols, with five (62.5%) identifiable on "basic" and three (37.5%) on "enhanced" cancer screening. Adverse events included 11 (2.97%) cases of intravenous contrast allergies. This study provides the first external validation of the IMACS cancer screening guidelines. The guidelines demonstrated 100% sensitivity for detecting DM-related malignancies. However, our findings indicate that the IMACS risk-stratification scheme may overestimate the malignancy risk in DM patients, potentially leading to "enhanced" screening protocols where the benefits are uncertain. Specifically, raising the age threshold for "high" risk and considering multiple high-risk factors may improve screening efficiency. Overall, these initial findings highlight the ongoing need to improve risk assessment and cancer screening for DM patients, ensuring a balance between resource use and patient outcomes.

Teaching point: The recently published IMACS guidelines for cancer screening in idiopathic inflammatory myopathies, including dermatomyositis, showed 100% sensitivity for detecting DM-related malignancies but may overestimate malignancy risk, suggesting the need for refined risk stratification to optimize screening efficiency.

Abstract category: Dermatomyositis

References

1. Oldroyd AGS, Callen JP, Chinoy H, et al. International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening: an International Myositis Assessment and Clinical Studies Group (IMACS) initiative. Nat Rev Rheumatol. 2023;19(12):805-17.
2. Moghadam-Kia S, Oddis CV, Ascherman DP, Aggarwal R. Risk Factors and Cancer Screening in Myositis. Rheum Dis Clin North Am. 2020;46(3):565-76.
3. Qiang JK, Kim WB, Baibergenova A, Alhusayen R. Risk of Malignancy in Dermatomyositis and Polymyositis. J Cutan Med Surg. 2017;21(2):131-6.
4. Kang EH, Lee SJ, Ascherman DP, et al. Temporal relationship between cancer and myositis identifies two distinctive subgroups of cancers: impact on cancer risk and survival in patients with myositis. Rheumatology (Oxford). 2016;55(9):1631-41.
5. Stone CJ, Faden DF, Xie L, Lopes Almeida Gomes L, Hejazi EZ, Werth VP, Shaw KS. Application of risk-based cancer screening in patients with dermatomyositis: A retrospective cohort study. *JAMA Dermatol.* Accepted for publication.

Table 1: Risk stratification, demographic data, clinical features, and myositis specific antibody testing profiles of dermatomyositis patient cohort

Non-paraneoplastic DM patients			Paraneoplastic DM patients	
	n=352	95.1%	n=18	4.9%
Risk stratification				
High risk	185	52.6%	15	83.3%
Intermediate risk	135	38.3%	3	16.7%
Low risk	32	9.1%	0	
Sex				
Male[b]	47	13.4%	1	5.6%
Female	305	86.6%	17	94.4%
DM subset				
Amyopathic[b]	149	42.3%	8	44.4%
Classic[a]	174	49.4%	8	44.4%
ASyS[c]	3	0.9%	0	
Hypomyopathic	12	3.4%	0	
Polymyositis[b]	0		0	
IMNM[b]	0		2	11.11%
Juvenile DM	14	4.0%	0	
Myositis panel ordered[e]	244	69.3%	10	55.6%
Anti-TIF1γ+[a]	29	11.9%	2	33.3%
Anti-NXP2 +[a]	6	2.5%	0	
Anti-SAE1 +[b]	8	3.3%	0	
Anti-HMGCR +[b]	1	0.4%	0	
Anti-Mi2 +[b]	18	7.4%	0	
Anti-MDA5 +[b]	14	5.7%	0	
Anti-Jo-1 +[c]	17	7.0%	1	7.7%
Non-Jo-1 Anti-ASSD +[c]	7	2.9%	0	
Other myositis associated antibodies +[d]	64	26.2%	3	21.4%
Avg # high risk factors	1.6534		2.2778	

Avg # intermediate risk factors	0.6705		0.6111	
Avg # low risk factors	1.0454		0.7777	
Clinical features				
Resistant to treatment[a]	15	4.3%	5	27.8%
ILD[c]	73	20.7%	3	16.7%
Inflammatory arthropathy[c]	101	28.7%	3	16.7%
Raynaud's Phenomenon[c]	103	29.3%	4	22.2%
Cutaneous necrosis/ulcer[a]	23	6.5%	1	5.6%
Dysphagia[a]	87	24.7%	7	38.9%

Abbreviations: DM, dermatomyositis; ASyS, anti-synthetase syndrome; IMNM, immune-mediated necrotizing myopathy; ILD, interstitial lung disease; avg #, average number; +, positive; IMACS, International Myositis Assessment and Clinical Studies Group; IIM, idiopathic inflammatory myopathy

[a]'High risk' factors in IMACS guidelines include DM, anti-TIF1g antibody positivity, anti-NXP2 antibody positivity, age>40 years at the time of IIM onset, features of persistent high disease activity despite immunosuppressive therapy (including relapse of previously controlled disease), dysphagia (moderate to severe), and cutaneous necrosis and ulceration

[b]'Intermediate risk' factors in IMACS guidelines include amyopathic DM, polymyositis, anti-SAE1 antibody positivity, anti-HMGCR antibody positivity, anti-Mi2 antibody positivity, anti-MDA5 antibody positivity, and male sex

[c]'Low risk' factors in IMACS guidelines include ASyS, anti-SRP antibody positivity, anti-Jo1 antibody positivity, non-Jo1 ASyS antibody positivity, other myositis-associated antibody positivities (anti-PM-Scl, anti-Ku, anti-RNP, anti-SSA/Ro, anti-SSB/La antibodies), Raynaud phenomenon, inflammatory arthropathy, and interstitial lung disease

Table 2: Summary of cancer diagnoses and diagnostic imaging modalities utilized for cancer detection in paraneoplastic dermatomyositis patients

Type of cancer	n=18	%	Imaging modality used for detection
Breast cancer	9	50.0%	Mammography[a]
Lung cancer	2	11.1%	Chest X-ray[a]
Bladder cancer	1	5.6%	CT-abdomen[b]
Papillary thyroid	1	5.6%	CT-neck[b]
Ovarian cancer	2	11.1%	Abdominal X-ray, CT-abdomen[b]
Renal cell carcinoma	1	5.6%	CT-abdomen/pelvis[b]
Non-Hodgkin lymphoma	1	5.6%	Complete blood count[a]
Adenocarcinoma with unknown primary	1	5.6%	CT-abdomen[b]

[a]Identifiable using basic screening panel as defined by IMACS screening guidelines (this includes age- and sex-appropriate cancer screening; serum ESR; serum CRP; serum protein electrophoresis; urinalysis; and plain chest X-ray radiograph).[1]

[b]Identifiable using enhanced screening panel as defined by IMACS screening guidelines (this includes CT scan of the neck, thorax, abdomen and pelvis; cervical screening; mammography; prostate-specific antigen; CA-125; pelvic or transvaginal ultrasonography for ovarian cancer; fecal occult blood).[1]

EVALUATION OF HEAD AND NECK CANCER IN A U.S.-BASED DERMATOMYOSITIS COHORT

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Dermatomyositis (DM) is an autoimmune cutaneous and myopathic syndrome associated with an increased risk of malignancy. In 2023, the first evidence-based international guidelines for cancer screening in dermatomyositis (DM) were published, recommending CT neck, chest, abdomen, and pelvis for patients with two or more high risk factors for DM-associated malignancy, consideration of upper and lower gastrointestinal endoscopy, and nasoendoscopy in geographic areas with high risk of nasopharyngeal carcinoma (NPC). We present a cohort of 771 adult patients with DM evaluated between 1979 and 2024 at a U.S.-based academic medical center, 128 (17%) of whom had cancer-associated DM defined as malignancy diagnosed within 3 years of DM symptom onset. Of these cases, 7 (5%) had head and neck cancer. All our patients were middle-aged men (mean age 58 at DM symptom onset), and 6 of the 7 were white. Of patients with myositis antibody testing, three were TIF1gamma positive, while two were NXP-2 positive. Clinically, one patient was amyopathic, while all others had myositis, including 4 with severe muscle disease leading to dysphagia. Our patients' cancers were primarily HPV-associated squamous cell carcinoma as opposed to EBV-associated. Four were lifetime nonsmokers**.** Presenting cancer symptoms included "neck lump" in 4 patients, in addition to dysphagia, otalgia, and dysphonia. Malignancy was detected on laryngoscopy in 3 patients, facial MRI in one patient, and CT neck in two patients, while one patient underwent direct excisional biopsy without definitive prior imaging. Amongst this patient cohort, head and neck cancers were not detected on conventional malignancy imaging screens, i.e. CT chest/abdomen/pelvis. Rather, two were ultimately detected on CT neck, which has become a recommendation in the new international guidelines as noted above for patients with two or more high risk features, which all our patients had. We therefore would consider laryngoscopy/nasopharyngoscopy in DM patients even in regions without high risk of NPC. This study seeks to highlight both improvements in screening guidelines and continued challenges in identifying DM-associated head and neck cancer.

Abstract category: Dermatomyositis

SPATIAL TRANSCRIPTOMIC PROFILING OF SKIN IN DERMATOMYOSITIS AND CUTANEOUS LUPUS ERYTHEMATOSUS

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Dermatomyositis (DM) and cutaneous lupus erythematosus (CLE) are distinct autoinflammatory diseases with differing systemic implications. Acute and subacute CLE can manifest similarly to DM with photoexacerbated eruptions of the face, arms, upper chest, and back. Even with routine histology, studies have demonstrated that the two are indistinguishable. Furthermore, amongst DM patients, it is difficult to distinguish between those with cancer-associated DM and those without. Although evaluation of serum autoantibodies has revealed a correlation between transcriptional intermediary factor-γ (TIF1-γ) and nuclear matrix protein-2 (NXP-2) and malignancy, the sensitivity of autoantibody testing is moderate, necessitating a more reliable means of cancer risk detection. This study utilized single-cell and high-resolution spatial data from skin samples derived from patients with cancer-associated DM, non-cancer-associated DM, and CLE patients to identify discriminatory markers.

Punch biopsies of lesional skin from DM and CLE patients were formalin-fixed, paraffin embedded and analyzed using single-cell gene transcriptomics (Single-cell FLEX, 10X Genomics) followed by Xenium In Situ spatial transcriptomics. Evaluation of CLE and DM skin lesions showed upregulation of interferon response and proliferative cell signals at similar levels. Neutrophils were found to predominantly localize to cancer and non-cancer-associated DM samples, but were generally absent from CLE and healthy samples (**Fig 1**). The abundance of Langerhans cells was diminished in lesional CLE samples as compared to overall DM and healthy samples (**Fig 1**). Immune aggregates in non-cancer DM showed a predominance of monocytes, monocyte-derived dendritic cells, and CXCL10+-myeloid cells, while cancer-associated DM immune aggregates consisted of B cells, plasmacytoid dendritic cells, and T cells, which resemble immune aggregates in CLE. Non-cancer DM is associated with IL1B/CXCL10/CXCL11 mediated inflammation and has loss of perivascular antigen-presenting C7+ papillary fibroblasts (**Fig 2**). In summary, our studies identified unique cell states and pathways that can serve as discriminatory markers between DM and CLE skin biopsies as well as between cancer-associated DM and non-cancer associated DM.

Category: Dermatomyositis, Cutaneous Lupus Erythematosus

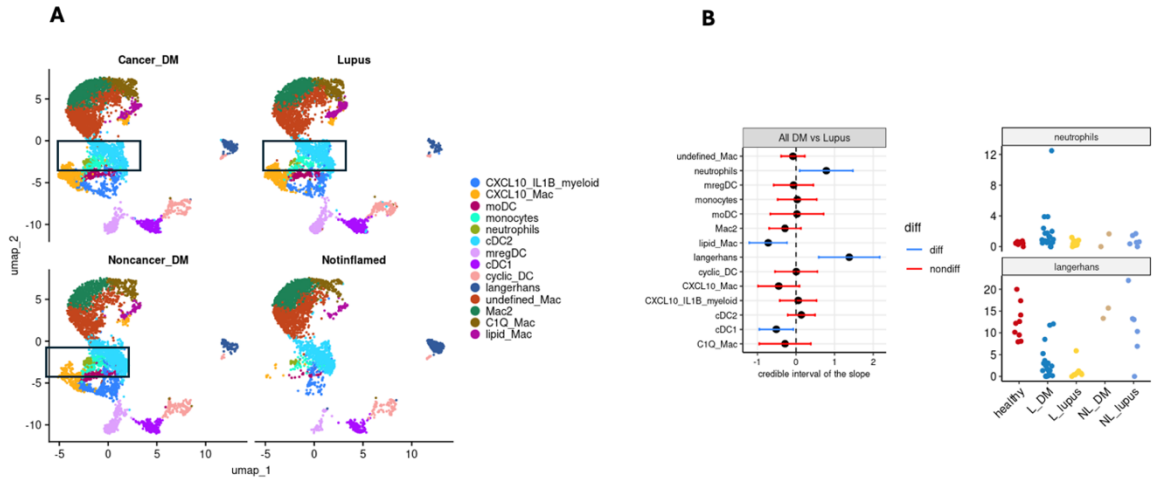

Figure 1. A. UMAP plot of cells in patients with cancer-associated DM, non-cancer associated DM, CLE, and healthy control, demonstrating cluster of 14 major cell types with neutrophils predominantly localizing in cancer and non-cancer DM. **B.** A plot of estimates of differential composition analysis of major cell types for overall DM samples versus CLE samples shows low levels of neutrophils and Langerhans cells in CLE samples as compared to DM. The error bars represent 95% credible intervals.

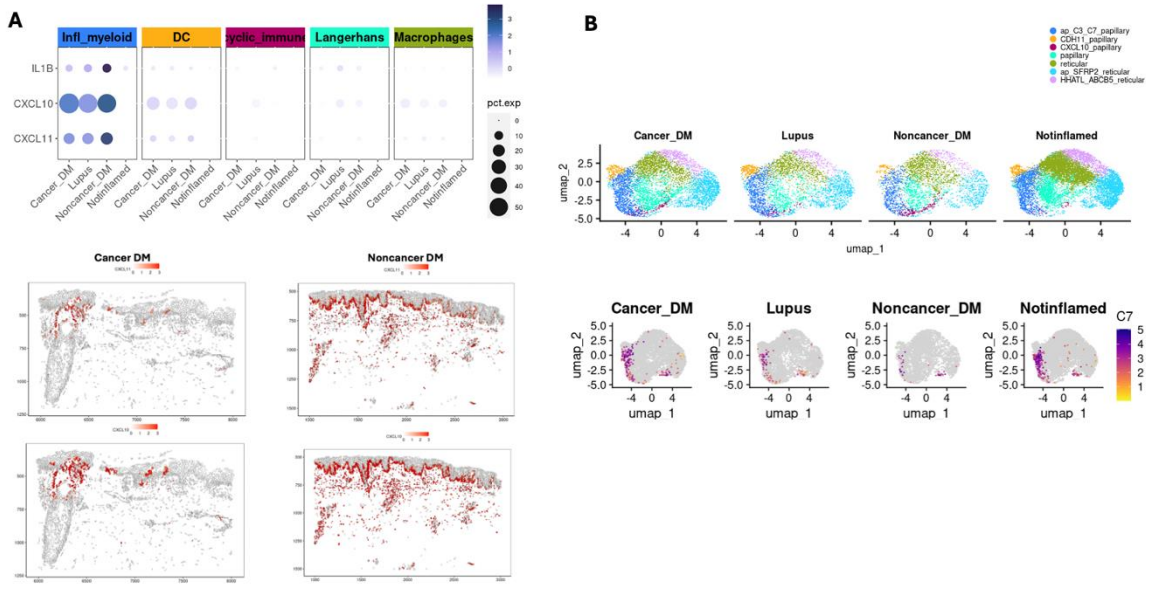

Figure 2. A. Dot plot demonstrating gene expression levels of IL1B, CXCL10 and CXCL11 in different cell types across cancer-associated DM, non-cancer associated DM, CLE and healthy control samples. Inflammatory myeloid cells show elevated gene expression levels amongst non-cancer associated DM samples. Xenium spatial plot further confirms upregulation of CXCL11 and 10 in non-cancer associated DM as compared to cancer-associated DM. **B.** UMAP plot of cells demonstrating loss of C7+ papillary fibroblasts in non-cancer associated DM.

THE DEVELOPMENT OF SUBSEQUENT MACE IN AMYOPATHIC AND MYOPATHIC DERMATOMYOSITIS PATIENTS: A LARGE-SCALE RETROSPECTIVE COHORT STUDY

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Abstract

Dermatomyositis (DM) has been associated with various organ system diseases, including cardiovascular disease (CVD).[1] However, the relationship between DM and the subsequent development of cardiovascular comorbidities remains unclear. Given the established associations between CVD and other rheumatologic conditions such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and rheumatoid arthritis (RA), we aimed to explore the associations between DM and the development of CVD. We conducted propensity matched retrospective cohort analyses using TriNetX, a global electronic medical record database. We compared adult patients with myopathic or amyopathic DM to a control group, excluding individuals with SLE, SSc, and RA. We evaluated the risks of developing major adverse cardiovascular events (MACE), including acute myocardial infarction (MI), cerebral infarction, nontraumatic intracerebral hemorrhage, heart failure, and cardiac arrest, up to 5 years after DM diagnosis. We excluded patients who had experienced MACE prior to their DM diagnosis and patients who developed myocarditis within one year of their DM diagnosis. Both the amyopathic (n= 6,772, RR= 5.33, p< 0.0001) and myopathic (n= 10,362, RR= 7.11, p < 0.0001) DM cohorts demonstrated an increased risk of MACE compared to the control cohort. The amyopathic DM cohort showed an increased association with subsequent acute MI (RR= 4.22, p< 0.0001), cerebral infarction (RR=7.22, p< 0.0001), heart failure (RR= 4.06, p < 0.0001), and cardiac arrest (RR= 3.00, p < 0.0015) compared to the control cohort**.** Similarly, the myopathic DM cohort demonstrated an increased association with subsequent acute MI (RR= 7.49, p < 0.0001), cerebral infarction (RR=6.83, p < 0.0001), heart failure (RR= 7.14, p < 0.0001), and cardiac arrest (RR=4.50, p < 0.0001) compared to the control cohort. Recognizing these associations can direct care guidelines for newly diagnosed DM patients, including regular cardiovascular follow-ups, ensuring comprehensive care for conditions linked to their rheumatologic disease.

References:

1. Shah JT, Shah KT, Mazori DR, Caplan AS, Hejazi E, Garshick MS, Femia AN. Cardiovascular comorbidities are associated with dermatomyositis: A cross-sectional study in the All of Us Research Program. *J Am Acad Dermatol.* 2024;90(5):1013-1016. doi:10.1016/j.jaad.2023.12.037.

Category: Dermatomyositis

THE EFFECTS OF CB2R ACTIVATION ON INFLAMMATORY PATHWAYS IN DERMATOMYOSITIS

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Previous in vitro investigations done by our group into the utility of CB2R activation to treat dermatomyositis (DM) used stimulants that activated pathways not relevant to DM. Here, we tested CB2R activation on amyopathic and classic PBMCs to determine its anti-inflammatory effects on pathways biologically relevant to DM. CB2R positivity data was obtained by analyzing patient PBMCs via flow cytometry. IFNβ was used a marker for inflammation to test CB2R activation and it was stimulated by the following: dsRNA for RIG1, dsDNA for cGAS, LPS for TLR4, and LPS/ATP for NLRP3. The CB2R agonist JWH133 was used to pretreat PBMCs before stimulation. The resulting PBMCs were stained, and flow cytometry data was acquired. CB2R positivity was compared by summing the CB2R FoP for the 10 investigated cell types. Amyopathic DM PBMCS were found to be 101.3% more positive for CB2R compared to classic DM PBMCS ($p=0.0085$). For amyopathic DM PBMCs, the top five cell types accounting for CB2R positivity in decreasing order are the following: pDC, NKT, cDC, NK, M2, and M1. For classic DM PBMCs, the top five cell types accounting for CB2R positivity in decreasing order are the following: NK, NKT, pDC, CD19, and cDC. In amyopathic DM PBMCs stimulated by LPS/ATP to target the NLRP3 inflammasome, CB2R activation resulted in a significant reduction in IFNβ MFI for MoDCs ($p=0.0397$) and Macs ($p=0.0457$) with a similar trend was observed in cDCs relative to classic DM PBMCs. On the other hand, no difference in IFNβ response to CB2R activation was observed across all cell types investigated between classic and amyopathic DM PBMCs stimulated with LPS only to target TLR4. This finding suggests that CB2R activation may be more effective in reducing NLRP3 induced inflammation compared to TLR4 only induced inflammation.

Category: Dermatomyositis

CHECKING OUT IMMUNE CHECKPOINT INHIBITOR USE IN PATIENTS WITH DERMATOMYOSITIS

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Immune checkpoint inhibitors (ICI) are known to induce and aggravate autoimmunity, a complication that can delay or halt treatment. However, little is known about the risk of exacerbating or developing dermatomyositis (DM) during ICI treatment. A meta-analysis was performed in PubMed. Inclusion criteria included any clinical description of DM before, during, and after ICI treatment. Of 518 results, 44 investigations involving 47 patients were utilized. Cases were grouped by etiology determined by the authors of the reviewed manuscript: paraneoplastic DM (PDM) (44.7%), ICI-induced DM (ICI-DM) (46.8%), or uncertain (8.5%). 61.9% of PDM developed DM prior to ICI; 38.1% developed DM during their ICI course. 93.6% utilized systemic corticosteroids (CS) (mean duration 131 days, range 28-690, n=20); 29.8% were treated with CS monotherapy. Intravenous immunoglobulin (IVIg) was the most common CS-sparing therapy (51.1%) (mean duration 6 cycles, range 1-43 cycles, n=13). 95.2% of PDM patients achieved control of DM overall, with 87.5% treated with CS monotherapy versus 100% treated with IVIG achieving control. 86.4% of ICI-DM patients achieved control of DM, with 83.3% treated with CS monotherapy versus 84.6% treated with IVIG achieving control. There was no correlation between DM control and tumor response. In PDM, 14/19 discontinued ICI due to DM and 3/3 tolerated re-challenge. In ICI-DM, 19/20 discontinued ICI and 1/5 tolerated re-challenge. Death from malignancy and autoimmune-related ICI adverse events occurred in 5/11 and 1/11 of PDM and 4/18 and 2/18 of ICI-DM, respectively. All cases without interruption of treatment survived (PDM n= 5; ICI-DM n=1). 78.9% of PDM and 52.4% of ICI-DM tested positive for a DM-associated autoantibody. Four cases were complicated by ILD; all had PDM (p=0.05). Given the high rate of ICI discontinuation amongst patients with DM and potential associated morbidity and mortality, further elucidating the relationship between ICI and DM and establishing a treatment protocol for DM complicating ICI therapy is warranted. This is the first meta-analysis of DM in the ICI setting. Limitations include data heterogeneity, limited details, and publication bias.

Category: Dermatomyositis

STEROID USE AND HAZARD OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE AMONG PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Patients with idiopathic inflammatory myopathies (IIM) experience morbidity from atherosclerotic cardiovascular disease (ASCVD). Steroids, widely used to treat IIM, can increase ASCVD risk through hypertension, hyperglycemia and dyslipidemia. The aim was to assess how steroid use affects the time to ASCVD after International Classification of Disease (ICD) code of DM, PM, dermatopolymyositis (DPM) or juvenile dermatomyositis (JDM). This retrospective analysis used the TriNetX database, a US research network of de-identified data. Patients were identified by two ICD codes separated by at least 6 months, according to their first ICD code (i.e., DM, PM, DPM, or JDM). Patients with an ASCVD code that preceded the ICD code were excluded to capture a new ASCVD event (Figure 1). Steroid exposure was defined by a dispensed (as verified by billed insurance) national drug code. The outcome was time to new ASCVD ICD code (myocardial infarction, ischemic stroke, transient ischemic attack or peripheral arterial disease). Hazard ratios were calculated from first IIM ICD code time to ASCVD event and were adjusted for age at first IIM ICD code, sex, overweight, obesity, hyperlipidemia, hypertension, diabetes, smoking, alcohol, steroid use. In the sample, 16,660 (46.9%) had a NDC code for steroid use. Of these, most, 13642 (38.4%) used steroids on or after the first ICD code for IIM. There was a slightly higher adjusted hazard ratio (aHR) 1.13 (95% CI 1.07, 1.18) for ASCVD for steroid use after IIM ICD code (Table 1). Among patients who were younger at first IIM ICD code, hazards between steroid use and ASCVD was slightly higher (age of 40 at first IIM ICD code had an adjusted hazard ratio of 1.24 compared to age of 70 which had an adjusted hazard ratio of 1.09). Understanding how steroids impact ASCVD risk is critical for future interventions for ASCVD risk reduction.

Category: Dermatomyositis

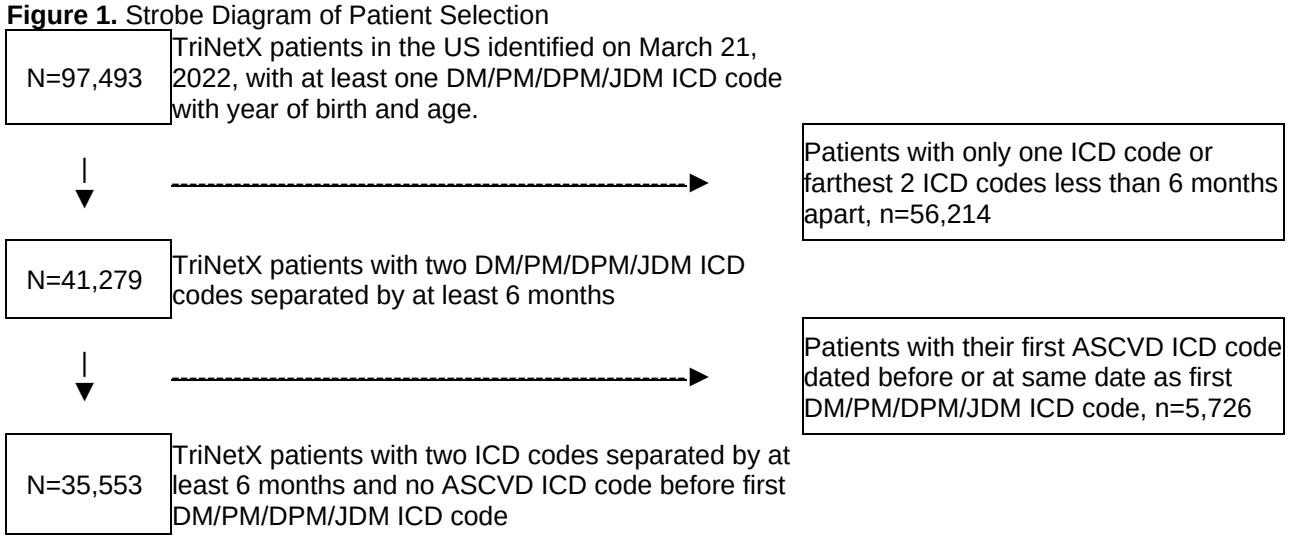
Table 1. Association of steroid use with time to ASCVD, overall (model 1) and by effect modifier using interaction terms (model 2: subtype and model 3: age)

Model	Effects of prednisone use overall or by effect modifier at p<0.05 level	Steroid before first IIM ICD code	Steroid after first IIM ICD code
		aHR (95% CI)	aHR (95% CI)
1	Overall	1.00 (0.94, 1.05)	**1.13 (1.07, 1.18)**
2	PM	**0.92 (0.86, 0.98)**	
	DM	1.07 (0.97, 1.18)	
	DPM	**1.25 (1.09, 1.42)**	
	JDM	ne	
3	Age at first IIM ICD code=40		**1.24 (1.12, 1.36)**
	Age at first IIM ICD code =55		**1.16 (1.10, 1.23)**
	Age at first IIM ICD code =70		**1.09 (1.03, 1.16)**

Abbreviations: aHR: adjusted hazard ratio; CI: confidence interval; ne: not estimable due to small cell counts; IIM: idiopathic inflammatory myopathy; PM: polymyositis; DM: dermatomyositis; DPM: dermatopolymyositis; JDM: juvenile dermatomyositis; ICD: international classification of disease

aHR shown in **BOLD** if statistically significant at alpha=0.05; Adjusted for covariables: age at first IIM ICD code, IIM subtype, sex, history of steroid use and TVCs: overweight, obesity, hyperlipidemia, hypertension, diabetes, smoking, alcohol, steroid use; 5-group generation from year of birth as strata.
Patients were censored at time of last reporting of any ICD code.
Steroid was defined by dispensation by national drug code including: methylprednisolone, prednisone, prednisolone, dexamethasone

Figure 1. Strobe Diagram of Patient Selection



Abbreviations: IIM: idiopathic inflammatory myopathy; PM: polymyositis; DM: dermatomyositis; DPM: dermatopolymyositis; JDM: juvenile dermatomyositis; ICD: international classification of disease; ASCVD: atherosclerotic cardiovascular disease

ANIFROLUMAB IN RECALCITRANT CUTANEOUS DERMATOMYOSITIS

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Dermatomyositis (DM) is an idiopathic, multisystem inflammatory disease characterized by hallmark cutaneous findings and muscular involvement. While muscle symptoms often respond to systemic corticosteroids and traditional immunosuppressants, cutaneous manifestations can persist and significantly reduce patient quality-of-life. With no standardized treatment approach, managing cutaneous DM remains challenging. In case reports, anifrolumab, a type I interferon (IFN) receptor antagonist approved for the treatment of systemic lupus erythematosus, has shown promise in treating recalcitrant cutaneous DM. This multicenter retrospective study aimed to examine the off-label use of anifrolumab in patients with recalcitrant cutaneous DM.

This study included seven DM patients (six female, median age 40) from Boston Children's Hospital, Brigham and Women's Hospital, and NYU Langone Health seen between November 2022 and March 2024 who received □□ 1 dose of anifrolumab. All patients had skin-predominant DM refractory to standard treatments. Three patients with a history of severe muscle disease continued intravenous immunoglobulin (IVIG) alongside anifrolumab, while the remaining four received anifrolumab as monotherapy. The primary outcome was improvement in the Cutaneous Dermatomyositis Area and Severity Index Activity Score (CDASI-A, range, 0-100).

All patients demonstrated substantial improvement in cutaneous disease activity following anifrolumab initiation (**Figure 1)**. The mean decrease [SD] and mean percentage decrease [SD] in CDASI-A scores were 13.0 [6.8] and 49.4 [17.5] after two doses, respectively. Among three patient who received at least 4 doses, further improvement was observed at five months, with mean decrease [SD] and mean percentage decrease [SD] in CDASI-A scores of 19.0 [11.3] and 77.4 [10.1], respectively.

These results highlight anifrolumab's potential as a therapeutic option in recalcitrant cutaneous DM. Limitations of this study include small sample size, lack of control group, and the use of adjunctive IVIG in select patients. Nonetheless, anifrolumab shows promise as a therapeutic option in recalcitrant cutaneous DM and warrants further prospective studies.

Abstract Category: Dermatomyositis

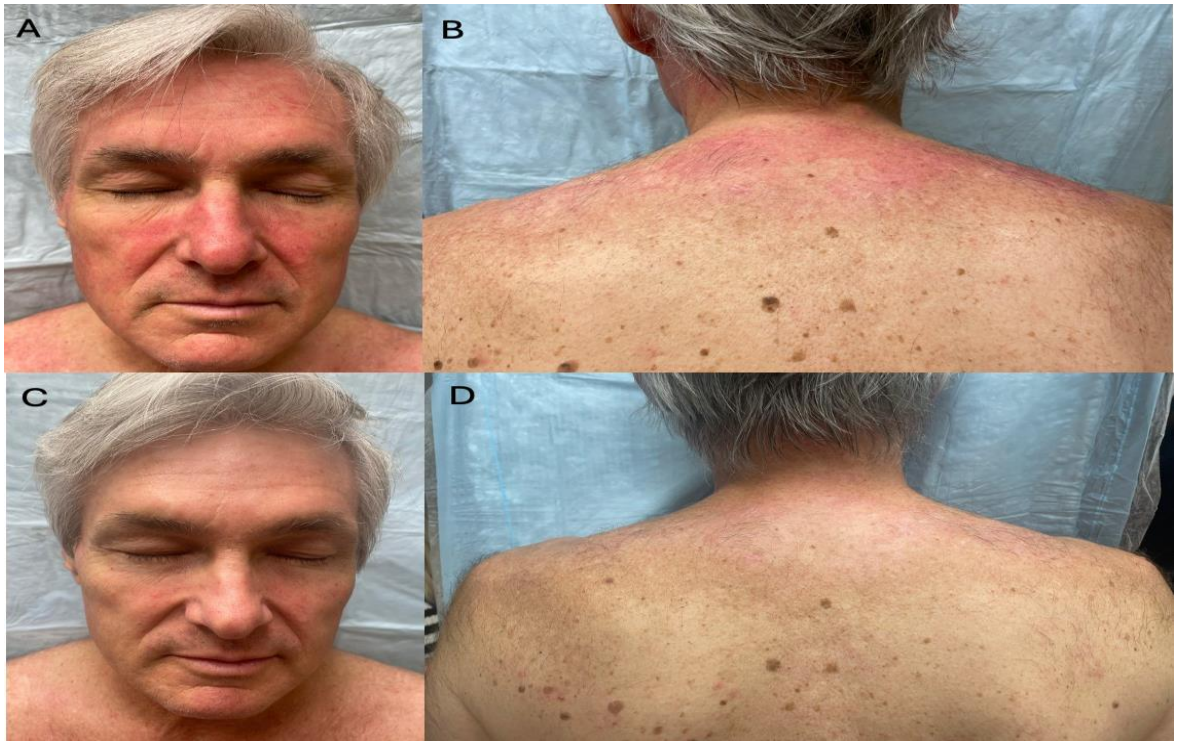

Figure 1: Representative Clinical Images Before and After 2 Months of Treatment with Anifrolumab A man in his 60s with a history of recalcitrant, SAE+ cutaneous DM presented with prominent telangiectatic erythema on his mid-face and forehead (A), chest, and upper back

(B). His cutaneous disease had previously proven refractory to hydroxychloroquine, methotrexate, mycophenolate mofetil, intravenous immunoglobulin, tofacitinib, and upadacitinib. After 2 months of treatment with anifrolumab, the patient experienced improvement in cutaneous DM disease activity as evidenced by marked reduction in erythema and scale (C,D).

SUCCESSFUL TREATMENT OF REFRACTORY CUTANEOUS DERMATOMYOSITIS WITH ANIFROLUMAB

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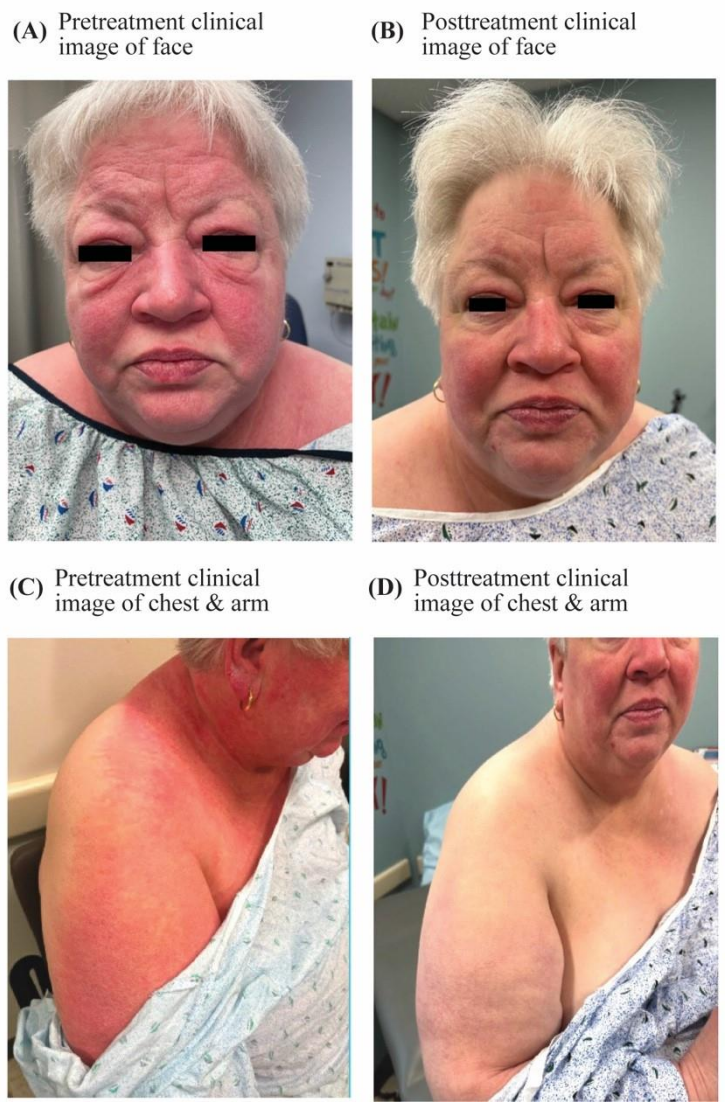
Teaching point: Our findings underscore the critical role of type I interferon signaling in patients with refractory cutaneous TIF-1γ dermatomyositis and highlight anifrolumab as a promising therapeutic option.

Dermatomyositis (DM) is an inflammatory myopathy, characterized by proximal muscle weakness and distinctive cutaneous manifestations, that presents significant therapeutic challenges. Type I interferon (IFN) signaling, elevated in affected skin, muscle, and blood of DM patients, is associated with more active cutaneous disease. Anifrolumab, a monoclonal antibody targeting type I IFN receptor subunit 1, is approved for systemic lupus erythematosus treatment and has shown efficacy in managing cutaneous lupus. We describe a case of refractory cutaneous DM that improved with anifrolumab. A 66-year-old female with a complex medical history, including chronic kidney disease, hypertension, type II diabetes mellitus, deep vein thrombosis, hysterectomy, and salpingo-oophorectomy presented with clinical DM features such as upper eyelid edema, heliotrope rash, and pink scaly patches scattered across her scalp, chest, shoulder, and upper and lower back. The diagnosis was confirmed by the presence of anti-transcriptional intermediary factor-1γ (TIF-1γ) autoantibodies and a skin biopsy revealing interface dermatitis. Despite treatment with intravenous immunoglobulin, methotrexate, mycophenolate mofetil, and steroids, her cutaneous disease persisted. Given her history of blood clots and elevated cancer risk, she was not a good candidate for tofacitinib, a Janus kinase inhibitor. She consented to a trial of anifrolumab, administered intravenously at 300 mg every four weeks. After three infusions, she showed significant improvement in erythema and pruritus, with her Cutaneous Dermatomyositis Disease Area and Severity Index Activity Score (CDASI-A) decreasing from 26 to 11. Her condition has remained well-controlled for over a year without side effects from anifrolumab. Extensive consideration preceded the decision to start anifrolumab, given the risk of IFN blockade in a TIF-1γ DM patient with elevated cancer risk. Recent studies show no increased malignancy risk with anifrolumab compared to placebo. This case underscores the role of type I IFN signaling in refractory cutaneous TIF-1γ DM and supports anifrolumab as a promising treatment.

Abstract Category: Dermatomyositis

Figure 1. (A-D) Rapid improvement in cutaneous TIF-1γ dermatomyositis with anifrolumab initiation.



RECALCITRANT DERMATOMYOSITIS TREATED WITH ANIFROLUMAB

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Dermatomyositis is an idiopathic inflammatory myopathy characterized by distinctive skin features, muscle weakness, and systemic manifestations. While standard treatments include glucocorticoids and immunosuppressants, some cases remain refractory to these therapies. A 38-year-old male with NXP2-positive dermatomyositis presented with a three-year history of photosensitive rash and proximal muscle weakness. Physical examination (Fig. 1) revealed heliotrope rash, malar rash, Gottron papules, and nailfold capillary changes, with skin biopsy (Fig. 2) confirming vacuolar interface dermatitis. Initial treatment with methotrexate, mycophenolate mofetil, and prednisone led to partial improvement in muscle weakness but did not resolve the cutaneous manifestations. Multiple therapies (Fig. 3) failed to control his cutaneous manifestations including hydroxychloroquine, IVIG, rituximab, azathioprine, baricitinib, and tofacitinib. An extensive malignancy workup was negative. Subsequently, the patient received anifrolumab 300 mg intravenously every four weeks, resulting in significant improvement of skin symptoms within eight weeks and subsequent discontinuation of prednisone without flare. The patient remains stable on a regimen of anifrolumab, mycophenolate, and methotrexate. This case highlights the potential efficacy of anifrolumab, a monoclonal antibody targeting the type 1 interferon (IFN-1) pathway, in treating refractory dermatomyositis. Given the association between IFN-1 dysregulation and dermatomyositis disease activity, anifrolumab offers a promising therapeutic option for patients with difficult-to-treat disease, though further studies are needed to assess its long-term safety and efficacy.

Teaching Point: Anifrolumab may represent an effective therapeutic option for recalcitrant dermatomyositis when traditional therapies fail.

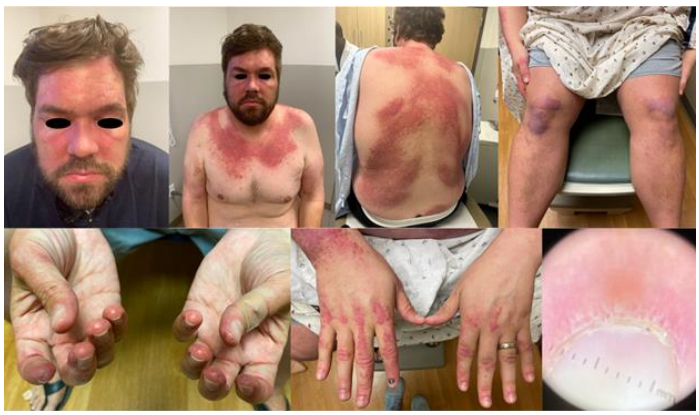

Figure 1. Cutaneous manifestations. Informed consent was obtained from the patient for use of images.

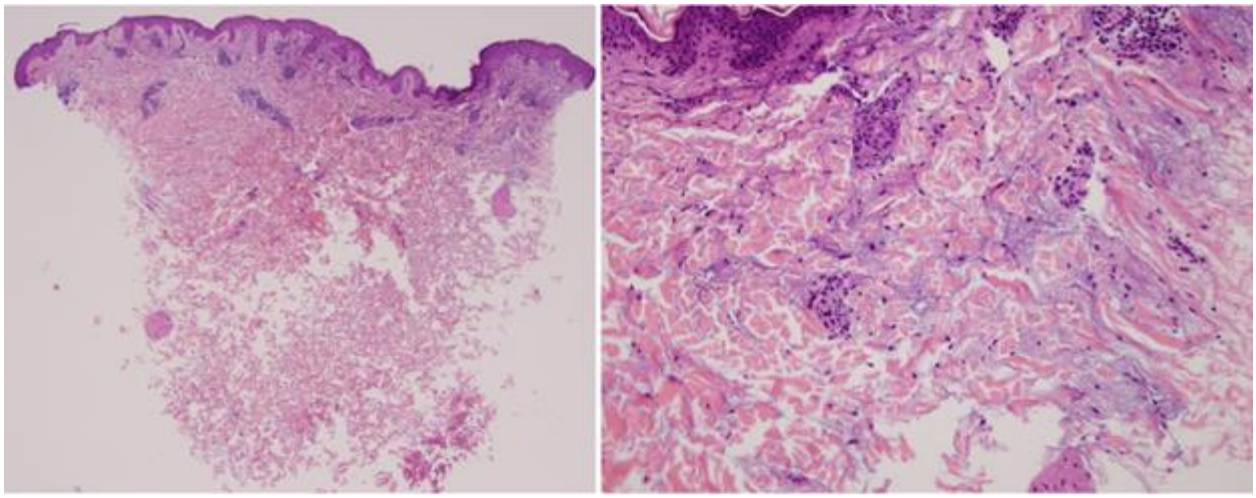

Figure 2. Skin biopsy H&E (a) 2x (b) 40x, Vacuolar interface dermatitis with increased mucin and dermal perivascular lymphoid inflammation.

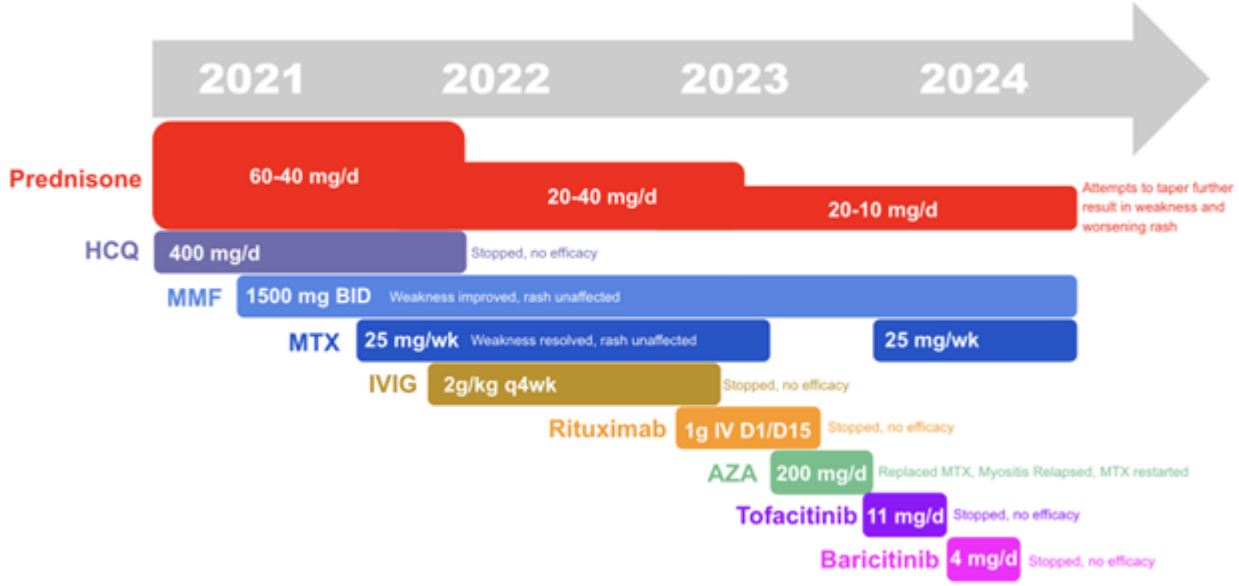

Figure 3. Treatment timeline.

ANCHORING THE CDASI, A CLINICAL OUTCOME ASSESSMENT (COA), TO THE PATIENTS' PERSPECTIVE OF THEIR DISEASE

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Dermatomyositis is an idiopathic acute inflammatory myopathy affecting the skin and muscles, with a prevalence of 1-6 per 100,000 adults in the U.S. The disease is characterized by cutaneous manifestations, assessed using tools such as the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) by physicians and the patient-assessed visual analogue scale (ptVAS). While both measurements exist to generate scores for patients, their relationship has not been evaluated. This retrospective study analyzes data from 216 patients with dermatomyositis to determine the correlation between clinical outcome assessments and patient-reported assessments of disease severity. CDASI and ptVAS scores were extracted from medical records for patients that had at least three visits with complete data for ptVAS score and the associated CDASI. The ptVAS score was utilized to determine the patient's own assessment of their overall global disease, global skin disease, pain, and itch. The visits were paired based on the largest and smallest differences in ptVAS scores between consecutive visits and analyzed using empirical cumulative distribution function (eCDF) curves. The first maximum and minimum difference for each patient in each ptVAS score were determined and separated into five categories, and the corresponding changes in CDASI scores were evaluated. We hypothesized a positive correlation between ptVAS and CDASI score changes, with variations among ptVAS change categories for each of the assessments in ptVAS. eCDF curves for changes in CDASI demonstrated improvement and deterioration that correlated with the changes in ptVAS. There was a statistically significant difference between the maximum changes in CDASI scores between the same two visits for the five different categories for the change in ptVAS scores ($p<1x10^{-7}$ by ANOVA). This study determines that meaningful changes described by the patient correspond with clinician assessment tools in dermatomyositis, providing valuable insights for patient-centered care.

Category: Dermatomyositis

Session IV:
Miscellaneous

CLINICAL CHARACTERISTICS OF POLYARTERITIS NODOSA

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Polyarteritis nodosa (PAN) is a medium-vessel vasculitis occurring in systemic (sPAN) or cutaneous forms (cPAN). Data regarding clinical characteristics and distinguishing features between sPAN and cPAN are limited. This single-center retrospective analysis characterizes clinical presentation, course and treatment amongst 66 PAN patients. cPAN (mean follow-up 6.1 ± 5.3 years) occurred in 33 (50%) and sPAN (8.0 ± 7.1 years) in 24 (36%). Two patients had ocular-limited PAN. Average time from symptom-onset to diagnosis was 172 days; cPAN patients experienced longer delays (287 ± 425 days) than systemic PAN (33 ± 42 days) (p=0.031). Cigarette smoking was over-represented (43.9% vs. 36.0% hospital baseline population) and Asian patients were more likely to be affected (24.2% versus 12.1% hospital baseline population). Asian patients were more likely to test positive for Hepatitis B than other races (p=0.043) and males were more likely to have sPAN (p=0.007). Erythematous nodules and livedo reticularis were the most common presenting features of cPAN (30.3% each); 24.2% experienced ulcerations. 54.2% of sPAN patients had cutaneous involvement although only 38.5% were seen by dermatology; ulcerations occurred in 4.2%. Two sPAN patients presented with skin-only symptoms (mean time to development of systemic symptoms: 3 years). On average 2.95 organ systems were involved in sPAN, most commonly the gastrointestinal tract, neurologic, and urologic/renal systems. Courses were relapsing-remitting (66.7%), chronic (22.2%), or acute (11.1%), without significant differences in course-type between sPAN and cPAN. In relapsing-remitting PAN, mean number of flares was 4.34, or 0.53 flares per year (n=36, mean follow-up 8.2 years). Diagnostic imaging occurred in only 42.4% of cPAN and 83.3% of sPAN patients. 24.1% of tested patients (n=54) had positive ANCA titers, without significant differences between cPAN and sPAN. 79.6% were treated with corticosteroids (average duration: 793 days). 34.9% received steroid-sparing agents (mean time to initiation 1.68 ± 2.47 years, range 0-7 years). 77.8% achieved initial disease control, requiring an average of 1.88 treatments over 1.43 years, but 33.3% of these patients relapsed. Mononeuritis multiplex or peripheral neuropathy occurred in 29.0% and 62.5% of cPAN and sPAN, respectively (p=0.016). This study highlights the long diagnostic delay, high disease burden, prolonged corticosteroid exposure, and high relapse rates in PAN, emphasizing the need for earlier recognition of PAN and optimized treatment strategies.

Category: Vasculitis

CUTANEOUS SMALL-VESSEL VASCULITIS WITH PREDOMINANT IGM OR IGG IMMUNE DEPOSITS ON DIRECT IMMUNOFLUORESCENCE: WHAT DOES IT MEAN IN CLINICAL PRACTICE AND HOW DOES IT FIT WITHIN THE DERMATOLOGIC ADDENDUM TO THE 2012 REVISED INTERNATIONAL CHAPEL HILL CONSENSUS CONFERENCE NOMENCLATURE OF VASCULITIDES? A RETROSPECTIVE REVIEW OF 14 PATIENTS AT MAYO CLINIC.

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In recent years, many clinicians have identified a subset of cutaneous small-vessel vasculitis that clinically appears indistinguishable from IgA vasculitis, however direct immunofluorescence (DIF) reveals IgM and/or IgG dominant or co-dominant perivascular immune deposition without evidence of accompanying IgA deposition. This provisional category of cutaneous vasculitis has since been termed "Cutaneous IgM/IgG immune complex vasculitis" and was not initially included in the 2012 International Chapel Hill Consensus Conference Nomenclature of Vasculitides (CHCC2012). We conducted a retrospective review of our cohort of cutaneous small-vessel vasculitis with IgM and/or IgG dominant or co-dominant deposition on direct immunofluorescence microscopy diagnosed between 2010-2023 at Mayo Clinic. 14 cases were identified and categorized into four subgroups including idiopathic, vasculitis associated with an underlying connective tissue disease, vasculitis associated with a probable etiology, and cryoglobulinemic vasculitis. Of the 14 cases identified, five were idiopathic in nature and ultimately diagnosed as cutaneous IgM/IgG immune complex vasculitis. In all five cases, palpable purpura was present and limited to the lower extremities with accompanying DIF revealing superficial perivascular deposition of IgM, C3, and intermittent fibrinogen. Two cases had associated myalgias and arthralgias, otherwise there was no evidence of systemic involvement in this subgroup. Four (80%) cases were managed with either observation, topical corticosteroids alone, oral corticosteroids alone, or a combination of topical and oral corticosteroids and subsequently experienced complete resolution without recurrence. In conclusion, this study supports the provisional category of cutaneous IgM/IgG immune complex vasculitis as a distinct subtype of vasculitis that is mainly skin-limited and self-resolving or requiring short courses of topical or oral corticosteroids and resulting in complete resolution without recurrence. Further studies evaluating the existence, prevalence, morphology, clinical characteristics, and outcomes are needed to further characterize this provisional subtype of cutaneous small-vessel vasculitis.
Teaching Point: This study supports the provisional category of IgM/IgG immune complex vasculitis as a distinct subtype of cutaneous small-vessel vasculitis that is mainly skin and self-limited.

Category: Vasculitis

IFN-I ENHANCES UVB-INDUCED KERATINOCYTE DAMAGE AND IMMUNE ACTIVATION

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Dermatomyositis (DM) and cutaneous lupus erythematosus (CLE) are autoimmune skin diseases characterized by UVB-induced photosensitivity. Histologically, both DM and CLE present with vacuolar interface dermatitis, associated with the death of basal keratinocytes. Previous studies have identified elevated serum levels of type I interferons (IFN-I) in these diseases, correlating with disease activity. We aimed to investigate how IFN-I promotes UVB-induced skin damage, focusing specifically on keratinocytes (KCs), the first line of defense against UVB radiation. Using single-cell RNA-seq, we found that basal KCs from both lesional and non-lesional skin of DM and CLE exhibit increased interferon-stimulated gene (ISG) expression. Furthermore, monocyte-derived dendritic cells (moDCs) were significantly expanded in the lesional skin of both diseases. In vitro, pre-treatment of cultured human KCs with IFN-β, a key IFN-I family member, significantly increased their susceptibility to UVB-induced pyroptosis, mediated by MAP kinases, caspases, and GSDME. Treating moDCs with supernatant from UVB-irradiated KCs led to their activation; however, inhibiting KC death with MAP kinase inhibitors diminished moDC activation. Interestingly, treating moDCs with an IFN-I receptor-blocking antibody did not reduce their activation, suggesting that IFN-I is not the primary mediator of moDC activation. In vivo, UVB irradiation in healthy volunteers led to an influx of moDCs into the skin. Moreover, UVB irradiation of non-lesional skin in CLE and DM patients increased the concentration of IFN-I-inducible proteins, including Flt3L, in the interstitial skin fluid, which drives the expansion and activation of dendritic cells. Our findings suggest that low but chronic levels of IFN-I in non-lesional skin prime KCs for exaggerated UVB-induced damage, initiating a feed-forward loop involving moDCs that sustains persistent skin inflammation in DM and CLE. These insights highlight a potential therapeutic target for breaking the cycle of photosensitivity in these autoimmune skin diseases.

Category: Miscellaneous rheumatic skin disease

A COMPARATIVE MULTI-OMICS STUDY IN FOUR INFLAMMATORY SKIN DISEASES POINTS TO HETEROGENEITY IN MYELOID CELLS AS A POTENTIAL CAUSE OF PHOTOSENSITIVITY

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Inflammatory skin disorders such as cutaneous lupus erythematosus (CLE) and dermatomyositis (DM) are characterized by heightened photosensitivity, with ultraviolet (UV) exposure acting as a major environmental trigger. UV is known to have immunomodulatory effects and is commonly used as a treatment in psoriasis and vitiligo. It is therefore curious that UV leads to disease exacerbation in CLE and DM. Using single-cell RNA sequencing (scRNA-seq) and high-throughput proteomics of interstitial skin fluid from lesional and non-lesional skin of patients, we identified a robust type-I interferon signature shared between CLE and DM but absent in psoriasis and vitiligo. Further analysis of scRNA-seq data revealed distinct subsets of myeloid cells as the main cellular drivers of each disease. Plasmacytoid dendritic cells (pDCs) were the primary source of IFN-α in CLE, while monocyte-derived dendritic cells (moDCs) produced IFN-β in DM. In contrast, conventional dendritic cells were more abundant in photoresponsive diseases, where cDC1 which mediates antigen cross-presentation was present in vitiligo, and cDC2 which promotes Th17 polarization was expanded in psoriasis. Single-cell spatial transcriptomics confirmed these distinct DC patterns, with pDCs, cDC1, cDC2, and moDCs predominantly localized to the upper dermis. Disease-specific DCs in CLE and DM showed higher colocalization with lymphocytes, suggesting critical immune crosstalk in these diseases. Additionally, a significant spatial relationship was observed between IFN-β-producing moDCs in DM and basal keratinocytes, correlating with elevated interferon-stimulated genes expression in keratinocytes. Using in vitro studies, we explored the interplay between UV exposure, keratinocytes, and moDCs. Interestingly, we discovered that treatment of moDCs with supernatant from UVB-irradiated keratinocytes led to their activation. Moreover, this led to a significant increase in the expression of chemokines known to attract blood-circulating monocytes to the skin. In summary, a disease-specific heterogeneity in skin resident myeloid cells appears to define how distinct inflammatory skin diseases respond to UVB irradiation.

Category: Miscellaneous rheumatic skin disease

ASSOCIATION OF LICHEN SCLEROSUS WITH BREAST CANCER: A CROSS-SECTIONAL STUDY IN THE *ALL OF US* RESEARCH PROGRAM

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Lichen sclerosus (LS) is a chronic inflammatory mucocutaneous condition with a preference for genital areas, but its connection to extragenital malignancies, such as breast cancer (BC), remains unclear. While there is a known risk of vulvar squamous cell carcinoma (SCC) development related to genital LS, studies on an association between LS and BC have shown mixed results. This study evaluates the potential link between BC and LS using data from the NIH-sponsored All of Us Research Program. We conducted a cross-sectional analysis of 144,236 female participants, identifying 667 LS cases and 2,668 matched controls. There were no significant differences between groups in terms of age, race/ethnicity, education, obesity, or other clinical characteristics. LS patients were more likely to report an annual household income over $35,000 and less likely to have smoked. BC prevalence was higher among LS patients (13% vs. 9%), and this association remained significant after adjusting for potential confounders (adjusted OR 1.4, 95% CI 1.1-1.9). In 82% of cases, BC was diagnosed before LS, with a median difference of -3.1 years. This study, utilizing the largest known US-based cohort of LS patients with matched controls, found a 40% increased likelihood of BC among LS patients when adjusting for confounders, consistent with previous research reporting increased co-occurrence and odds of LS in BC patients. The temporal pattern observed may be due to BC treatments, comorbid autoimmunity, or delays in diagnosing LS. Limitations include possible inaccuracies in EHRs and a lack of data on LS severity and subtype. Further research should explore causality and the impact of BC treatment on LS risk.

Category: Miscellaneous rheumatic skin disease

RISK OF DEVELOPING HEMATOLOGIC MALIGNANCY/DYSCRASIAS IN PATIENTS WITH AUTOIMMUNE AND INFLAMMATORY SKIN DISEASES

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Abstract:

Several cutaneous conditions have been linked to hematologic malignancies/dyscrasias, including connective tissue diseases (CTDs) and neutrophilic dermatoses. Autoimmune blistering disorders (AIBDs) may have a weak association, but this is not well-established. Therefore, we assessed cutaneous disorders known or suspected to be associated with hematologic malignancies/dyscrasias to better guide clinical suspicion. We performed a retrospective study utilizing TriNetX calculating the relative risks of developing a hematologic malignancy/dyscrasia over 1-year, 5-year, and 10-year observation periods. We generated cohorts with the cutaneous condition of interest and matched control cohorts. Conditions evaluated included dermatomyositis, discoid lupus erythematosus, eosinophilic fasciitis, erythema elevatum diutinum, leukocytoclastic vasculitis, mixed connective tissue disease, rheumatoid arthritis, Sjogren's syndrome, subacute cutaneous lupus erythematosus, systemic lupus erythematosus, systemic sclerosis, pyoderma gangrenosum, Sweet syndrome, primary amyloidosis, bullous pemphigoid, pemphigus vulgaris, dermatitis herpetiformis, epidermolysis bullosa acquisita, and mucous membrane pemphigoid. All CTDs queried, except dermatomyositis and subacute cutaneous lupus erythematosus, showed significant associations with Non-Hodgkin's lymphoma (NHL) and at least one other hematologic malignancy across all intervals. Strong associations (malignancy: 1-, 5-, 10-year relative risk) included discoid lupus erythematosus (NHL: 4.53, 4.31, 3.81; multiple myeloma: 4.31, 3.00, 3.07), leukocytoclastic vasculitis (NHL: 4.04, 3.96, 2.71), and systemic lupus erythematosus (NHL: 4.33, 3.4, 3.54; Waldenström macroglobulinemia: 3.31, 6.41, 6.65). Among neutrophilic dermatoses, Sweet syndrome was linked to NHL, lymphoid leukemia, and multiple myeloma, with the strongest associations to myeloid leukemia (1-, 5-, 10-year RR: 6.61, 5.26, 6.5) and myelodysplastic syndrome (1-, 5-, 10-year RR: 6.45, 4.99, 4.86). No AIBD demonstrated a significant association. Overall, our findings within 1 year through 5 and 10 years emphasize the importance of longitudinal surveillance in evaluating potential hematologic malignancies/dyscrasias in patients with CTDs and neutrophilic dermatoses. The presence of these associations within 1 year of diagnosis suggests that the development of hematologic malignancies/dyscrasias cannot be solely attributed to long-term immunosuppression.

Category: Miscellaneous rheumatic skin disease

PYODERMA GANGRENOSUM ASSOCIATED WITH IGA MONOCLONAL GAMMOPATHY DEMONSTRATE IGA AND C5A EXPRESSION

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Pyoderma gangrenosum (PG) is a neutrophilic dermatosis characterized by the rapid development of painful sterile ulcers and is often associated with an underlying systemic disease. Approximately 20% of PG patients have an underlying monoclonal gammopathy (MG), of which IgA gammopathy is the most common subtype. Patients with PG and associated IgA MG may develop recurrent and recalcitrant disease suggesting an involvement of IgA in the pathogenesis of PG. IgA and IgA immunocomplexes have been shown to induce neutrophil extracellular traps (NETs). Furthermore, IgA and NETosis can activate the complement system resulting in further neutrophil infiltration. Hence, our aim is to investigate the expression of IgA and C5a in the skin lesions of PG patients with and without IgA MG. Frozen tissue slides from lesional skin were processed for immunofluorescence staining from PG patients with (n=3) and without (n=5) associated IgA MG. A biopsy specimen of IgA vasculitis and a healthy skin tissue were used as a positive and negative control, respectively. Rabbit anti-human monoclonal antibodies against IgA, IgM, IgG and C5a were used as primary antibodies. Tissue sections were then incubated with secondary goat anti-rabbit antibodies conjugated with Alexa Fluor 488. Images were captured via Olympus microscope and camera at 10x and 20x magnification. Two people blinded to the study evaluated the intensity of the immunofluorescence staining. All 3 patients with PG and IgA MG showed strong perivascular IgA and overlapping C5a staining, whereas all 5 PG patients without IgA MG showed non-specific or no staining. None of the specimens showed staining for IgM or IgG. Our results show a possible pathogenic role of IgA and C5a in the recurrent and recalcitrant nature of PG patients with IgA MG. Use of C5a inhibitors or treatment of underlying MG may have therapeutic benefit in these patients.

Category: Miscellaneous rheumatic skin disease

PROCOAGULANT EXTRACELLULAR VESICLES IN PATIENTS WITH LIVEDO RETICULARIS

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Procoagulant activity is an important property of EVs (extracellular vesicles). This study investigates the role of EVs in livedo reticularis (LR). We isolated EVs from plasma of 12 patients and 7 healthy controls (HC), measured tissue factor (TF) procoagulant activity and analyzed their content and cellular origin. TF procoagulant activity was increased in the plasma of LR patients. We detected increased TF activity in small but not in large EVs. The concentration of vesicles in plasma was not increased, implying the procoagulant properties of EVs may not be explained by a higher abundance, but possibly by their cargo. Hence, we sought to analyze their protein content. A total of 304 differentially expressed proteins (DEP) were identified. Five were upregulated and 269 downregulated. LR patients revealed a distinct expression pattern. A subset with profound vasculopathy showed a different pattern and for patients in remission the pattern was similar to HCs. Overrepresentation analysis revealed enrichment of proteins associated with homeostasis, coagulation, and vascular endothelial growth factor signaling pathways. Amongst the DEPs, Krueppel-Like Factor 8 (KLF8) exhibited the most prominent difference with a decrease by a fold change of 4.6 ($p<0.001$). KLF8 is expressed in vascular endothelium and regulates angiogenesis and vessel contractility. With regard to cellular origin, LR patients exhibited an increase in leukocyte-derived EVs and a decrease in platelet-derived EVs. No significant changes were observed in the fraction of EVs that originated from endothelial cells. This may be indicative of a shift from baseline homeostasis in health to an inflammatory EV profile in LR. In conclusion, EVs exert a procoagulant effect in LR. Increased TF activity and a shift in EV release from primarily platelet-driven to leukocytes are possible mechanisms underlying this effect. Our findings suggest that a reduction in KLF8 within EVs may be a key regulatory factor in LR.

Category: Miscellaneous rheumatic skin disease.

Clinical Cases of the Year

SURGICAL EXCISION OF CALCINOSIS CUTIS AMONG DERMATOMYOSITIS PATIENTS

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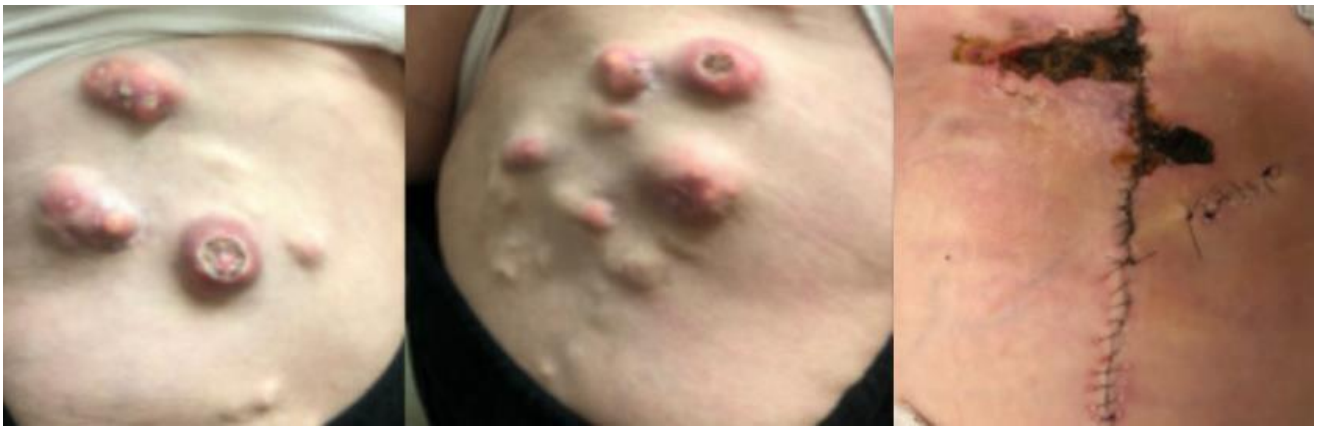
Among juvenile and adult dermatomyositis (DM) patients, calcinosis cutis is primarily associated with NXP2 and MDA-5 autoantibodies. Given limited treatment success with calcinosis specific interventions, the mainstay treatment of calcinosis has primarily focused on controlling the underlying disease activity. However, anecdotally, we have noticed that calcinosis may occur among patients even while other aspects of their disease activity has remained well-controlled. Previously, surgical resection of calcinosis was thought to be contraindicated due to the risk of recurrence. The purpose of this study is to evaluate the short-term and long-term outcomes of surgical resection of calcinosis among DM patients. Surgical excision was indicated due to a history of soft tissue infection, functional impairment, or pain for the patient. In a retrospective case series, eight patients were identified who had severe enough calcinosis to warrant surgical excision. Baseline demographics and clinical characteristics, including phenotypic features of DM, autoantibody, site of calcinosis, medications at the time of surgery, and surgical indication were recorded. In addition, the short-term and long-term outcomes were reported. Overall, there were limited reports of recurrence. Once lesions were excised, patients reported an improved quality of life with reduced pain and burden of disease. Surgical resection in tandem with physical therapy resulted in an improved range of motion and gait. Many patients were able to ambulate without the use of assistive devices. The most frequent perioperative complication was infection. However, most patients who reported infection had been using corticosteroids prior to surgery. While some patients continued to report pain after surgery, the pain was associated with any residual areas of calcinosis. After consistent physical therapy, patients experienced a reduction in any calcinosis-related pain.

Teaching Point: Surgical resection of calcinosis results in an overall improved functionality and pain for the patient with limited reports of recurrence.

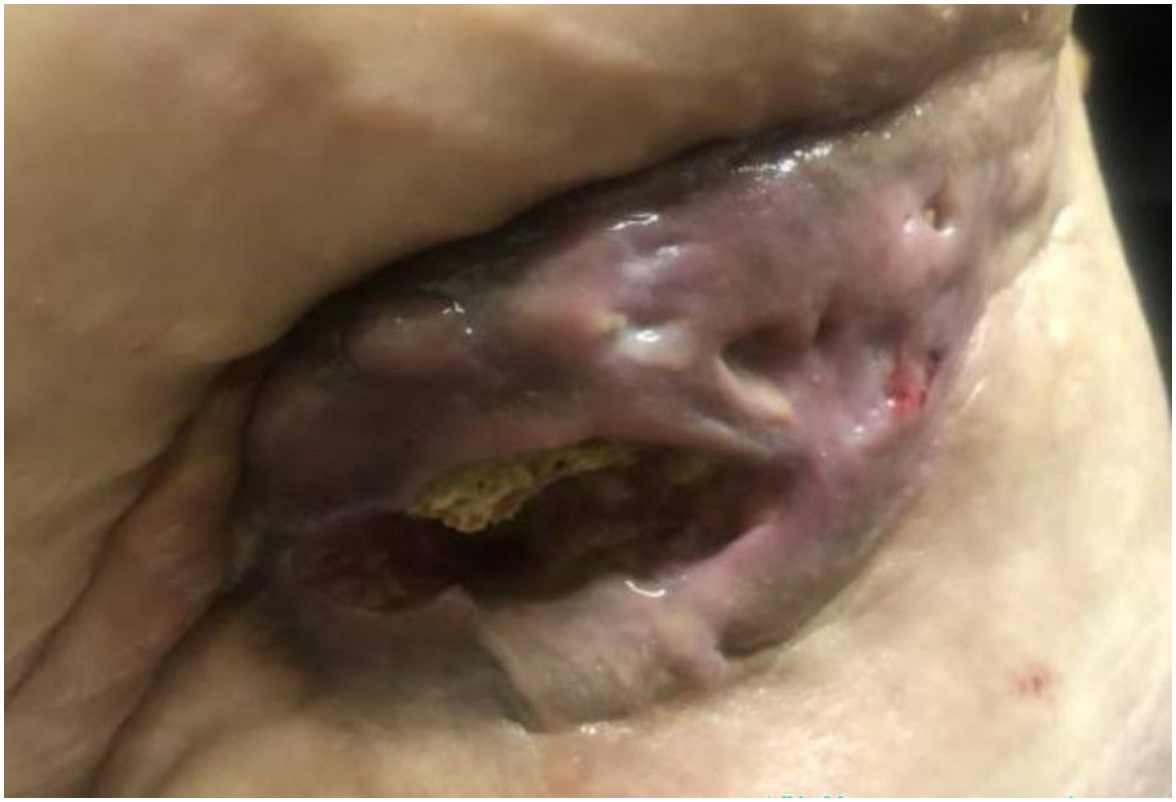
Category: Dermatomyositis

Figure 1



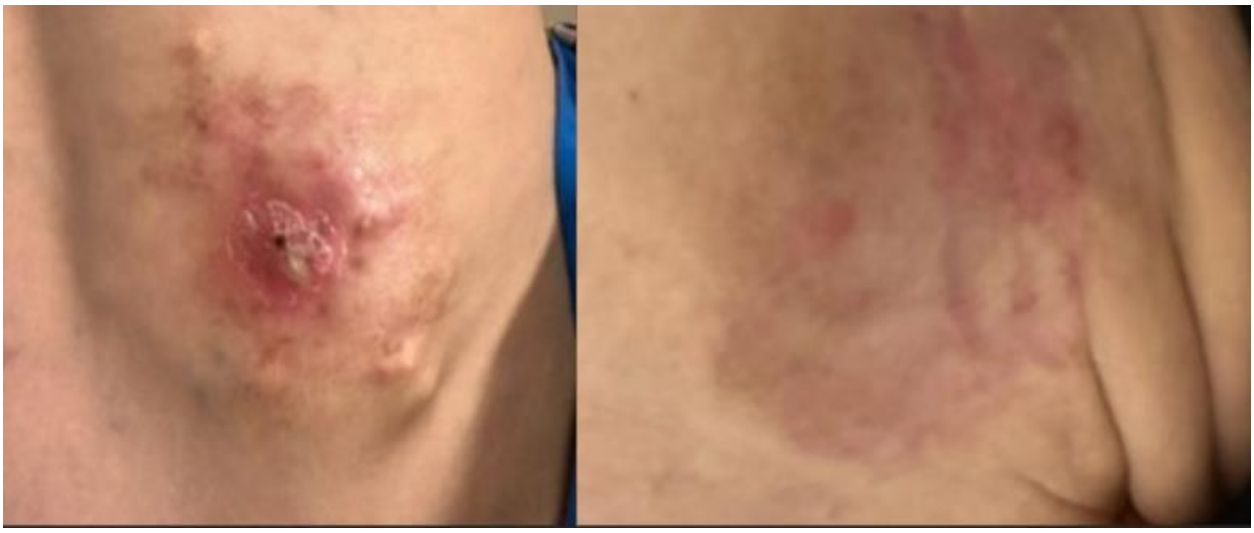
A. R Hip *B. L Hip* *C. Post-Op of L Hip*

Figure 2



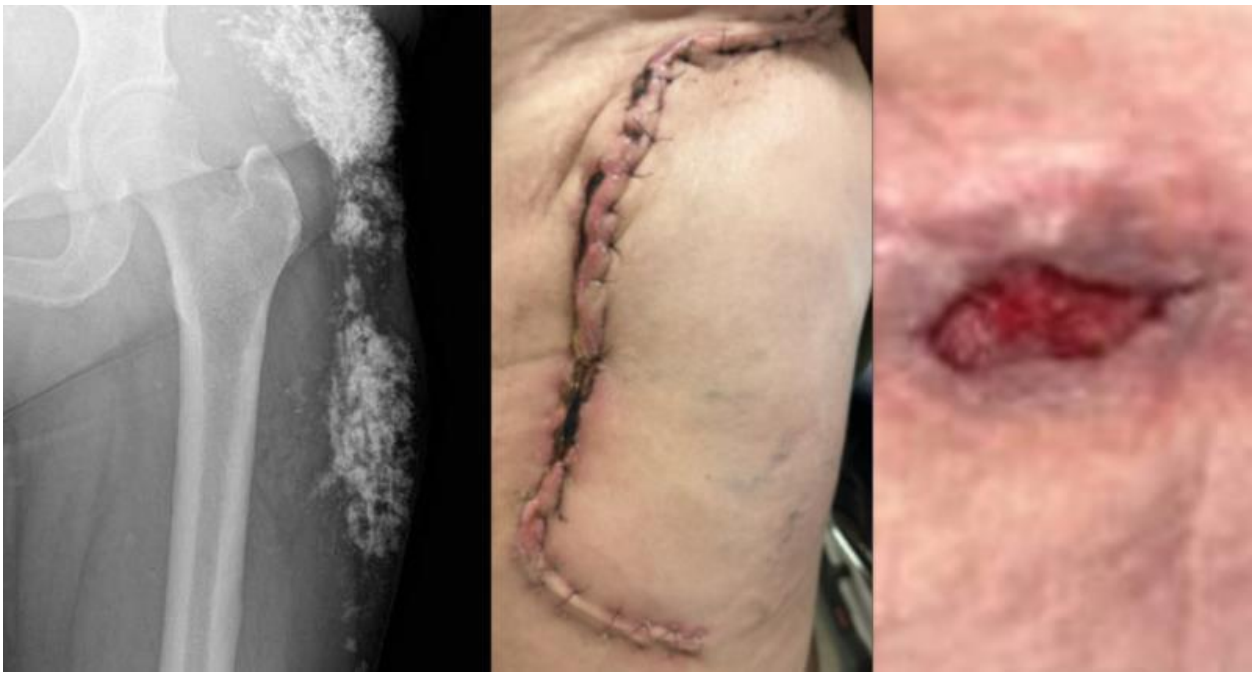
L Hip

Figure 3.1



A. L Proximal Thigh *B. L Hip*

Figure 3.2



A. Pre-Op XR of L Hip *B. S/p excision, L Hip* *C. Three months s/p post op*

EN COUP D'UNE VEINE: ANATOMY OF A NOVEL MORPHEA MIMICKER

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Linear morphea, particularly the *en coup de sabre* variant, is a rare and potentially disfiguring condition that primarily affects the forehead and scalp. This form of morphea is characterized by indurated linear plaques that can extend deeply into the skin, sometimes involving underlying structures such as bone and meninges, leading to severe complications. Early identification and treatment are crucial to prevent progression. However, the diagnosis can be challenging, as other conditions can mimic its presentation. We describe three cases from our combined Rheumatology-Dermatology clinic referred for suspected morphea *en coup de sabre*. Each patient exhibited subtle, 1-2mm linear indentations on the paramedian forehead without any associated sclerosis or changes to the epidermis. Two patients had faint bluish hyperpigmentation of the affected skin. One patient experienced localized paresthesia and tested positive for anti-SCL70, while the other two had unremarkable serological findings. None of the individuals reported a history of connective tissue disease. Imaging, including brain MRI and bedside ultrasound, showed no signs of fibrosis or soft tissue anomalies. Color doppler revealed a compressible vessel aligned with the supratrochlear vein within the indentation. We hypothesize that these depressions represent prominent supratrochlear veins, made visible by age-related skin thinning and sun damage, rather than early morphea. Such cases underline the importance of thorough clinical and imaging evaluation to avoid misdiagnosis. This benign anatomic variant mimics the appearance of morphea *en coup de sabre* and has not been previously reported in the connective tissue disease literature. Recognizing this phenomenon is vital to avoid unnecessary diagnostic tests, prevent inappropriate and potentially harmful interventions, and alleviate patient anxiety.

Teaching Point: Identifying benign anatomical variations, such as prominent supratrochlear veins, can prevent misdiagnosis and unnecessary treatment for morphea *en coup de sabre*.

Category: Sclerotic skin disease (e.g., morphea, systemic sclerosis, etc.)

References

1. Ferrell C, Gasparini G, Parodi A, Cozzani E, Rongioletti F, Atzori L. Cutaneous Manifestations of Scleroderma and Scleroderma-Like Disorders: a Comprehensive Review. *Clin Rev Allergy Immunol.* 2017;53(3):306-336.

2. Peterson LS, Nelson AM, Su WP, Mason T, O'Fallon WM, Gabriel SE. The epidemiology of morphea (localized scleroderma) in Olmsted County 1960-1993. *J Rheumatol*. 1997;24(1):73-80.
3. Fett N, Werth V (2011) Update on morphea: part I. epidemiology, clinical presentation, and pathogenesis. J Am Acad Dermatol 64(2):217–228

USE OF EXTRACORPOREAL PHOTOPHORESIS IN MORPHEA: A CASE SERIES

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Extracorporeal photopheresis (ECP) is an immunomodulatory therapy involving photosensitization of peripheral blood mononuclear cells with 8-methoxypsoralen followed by exposure to ultraviolet light which is used for treatment of cell-mediated autoimmune conditions. Prior studies have investigated ECP in treatment of systemic sclerosis but reports in morphea (localized scleroderma) are limited[1-3]. This study aims to assess the efficacy of ECP in morphea. We identified patients who underwent ECP between 2012 and 2024 at our institution. Retrospective chart review was conducted to characterize demographics, treatment details, and clinical outcomes (table 1). Five patients were included in our analysis. Median age was 52 (26-64). Patients were predominantly female (n=3) and White (n=4) with recalcitrant disease (n=3). Morphea subtypes included generalized plaque morphea (patients 1, 3, and 5), pansclerotic morphea (patient 4) and mixed connective tissue disease with features of deep morphea and lupus panniculitis (patient 2). In four patients, systemic treatments were administered concurrently with ECP including methotrexate (n=1), corticosteroids (n=3), JAK inhibitors (n=2), and hydroxychloroquine (n=1). ECP was administered every two (n=4) or four (n=1) weeks. Median treatment duration was 12 months. Patient outcomes were assessed by physical exam of affected body surface area. Patients 1 and 2 experienced initial improvement but discontinued ECP after 6 and 11 months due to lack of sustained improvement or disease progression. Patient 3 experienced sustained increase in mobility and skin softening. In patient 4, disease progression was halted. Patient 5 achieved remission which was sustained for several years following discontinuation of ECP. Our limited analysis represents the first case series of ECP in morphea. In our cohort, ECP demonstrates variable efficacy, with patients achieving no effect, temporary or sustained improvement, or complete remission. ECP may be considered for severe or recalcitrant disease, although implementation may be limited by lack of insurance coverage and patient adherence.

Category: Sclerotic skin disease

References:

1. Cribier B, Faradji T, Le Coz C, Oberling F, Grosshans E. Extracorporeal photochemotherapy in systemic sclerosis and severe morphea. *Dermatology*. 1995;191(1):25-31. doi:10.1159/000246481
2. Neustadter JH, Samarin F, Carlson KR, Girardi M. Extracorporeal photochemotherapy for generalized deep morphea. *Arch Dermatol*. Feb 2009;145(2):127-30. doi:10.1001/archdermatol.2008.547
3. Pileri A, Raone B, Raboni R, Giudice V, Patrizi A. Generalized morphea successfully treated with extracorporeal photochemotherapy (ECP). *Dermatol Online J*. Jan 15 2014;20(1):21258.

Table 1. Characteristics and treatment regimens of five patients with morphea treated with ECP. MCTD – mixed connective tissue disease with features of morphea profunda and lupus panniculitis; MTX – Methotrexate; HCQ – hydroxychloroquine; MMF – mycophenolate mofetil.

Patient	Gender	Diagnosis	Prior therapies	Concurrent therapies	ECP regimen	ECP duration	Adverse events	Response
1	F	Generalized morphea	HCQ	Clobetasol ointment 2%	q4 weeks	6 months	Dorsal pedal erythema during treatments;	Generalized skin softening after 1 treatment, sustained at 2- and 3-month

							increasing fatigue	follow-ups. Treatment discontinued due to lack of sustained improvement
2	F	MCTD	prednisone, cyclophos-phamide, Azathioprine Belimumab	MTX, HCQ, MMF, prednisone, cyclophos-phamide, pregabalin, colchicine	q2 weeks	11 months	–	Improvement in pain and appearance of lesions at 2 months; treatment discontinued due to development of new lesions
3	F	Generalized morphea	•	tofacitinib, prednisone	q2 weeks	12 months	–	Increased mobility at 2 months, increased skin suppleness at 6 months; evidence of reversal of fibrosis at 9 months
4	M	Pansclerotic morphea	Prednisone, cyclosporine, cyclophos-phamide, thalidomide	topical triamcinolone	q2 weeks	4 years	–	Stable disease
5	M	Generalized morphea	Prednisone, PUVA	clobetasol 0.05% ointment, tofacitinib, prednisone, baricitinib	q2 weeks	20 months	–	Improvement in lesion appearance noted at 10 months, remission later achieved and sustained at least 2 years after discontinuing ECP

REMISSION OF REFRACTORY PEMPHIGUS VULGARIS WITH EFGARTIGIMOD

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Pemphigus Vulgaris (PV) is an autoimmune disorder characterized by IgG autoantibodies to desmoglein 1 and/or desmoglein 3, essential components of the desmosomes which bind keratinocytes. We report a case of refractory PV in which treatment with efgartigimod (an anti-neonatal Rc receptor blocker) resulted in sustained remission. A 38-year-old woman presented with PV impacting approximately 60% body surface area (BSA). She had high antibody levels to both desmoglein 1 and desmoglein 3. The patient had been refractory to many therapies, including cyclophosphamide, steroid tapers, mycophenolate mofetil, azathioprine, methotrexate, IVIG, and dapsone. She experienced anaphylaxis (including a desensitization protocol) to rituximab three times. On physical examination, widespread erosions were noted around the eyes, mouth, armpits, buttocks, lower legs, and in the intertriginous areas, in addition to severe stomatitis. Malignancy screening two years prior was unremarkable. The presenting flare was preceded by missed doses of cyclophosphamide. During an ICU admission, the patient responded well to five rounds of plasmapheresis. Ocrelizumab (anti-CD20 antibody approved for multiple sclerosis) was discussed as an option, but was denied by insurance. The decision was made to integrate efgartigimod into the patient's treatment regimen. She received efgartigimod (10 mg/kg) infusions weekly for 4 weeks, followed by a single dose every 4 weeks. The following medications were continued: prednisone 20 mg daily, CellCept 1.5 g daily for oral solution and IVIG every four weeks. This treatment regimen was well tolerated and resulted in tremendous and rapid improvement. Our patient also developed cutaneous ulceration on bilateral calves while on this medication which was not consistent with pemphigus and could be attributable to efgartigimod. There is a need for medications that allow PV patients to attain lasting remission while minimizing dependence on corticosteroids. This case contributes to the growing body of evidence demonstrating the value of efgartigimod in the treatment of PV.

Teaching Point: Efgartigimod may be an effective therapeutic option for pemphigus vulgaris, particularly that which has been refractory to standard therapy.

Category: Clinical Case

Figure 1: Pemphigus vulgaris initial presentation before treatment

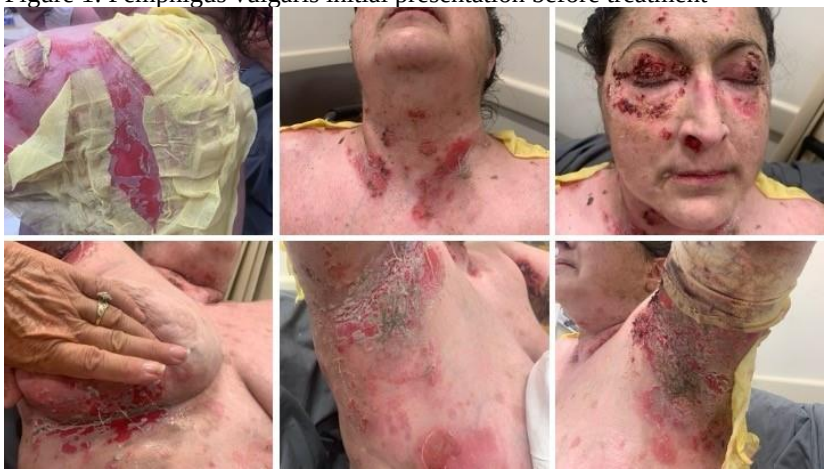
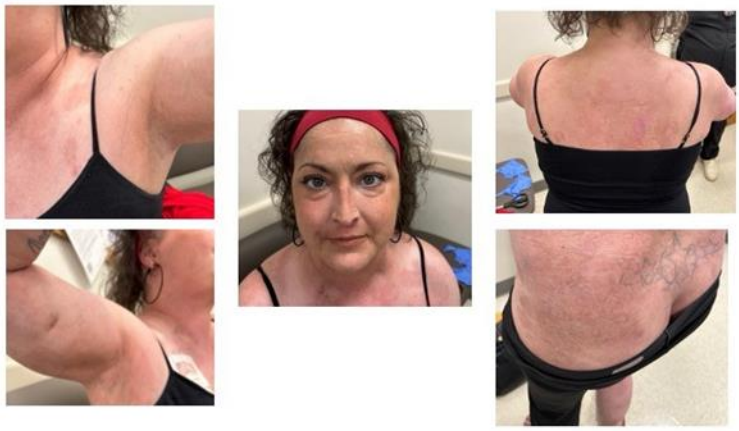


Figure 2: Pemphigus vulgaris post-plasmapheresis

Figure 3: Pemphigus vulgaris eight weeks after treatment with efgartigimod



TRAUMA-INDUCED UNILATERAL PROGRESSION OF SCLEROSIS IN A PATIENT WITH LIMITED CUTANEOUS SYSTEMIC SCLEROSIS

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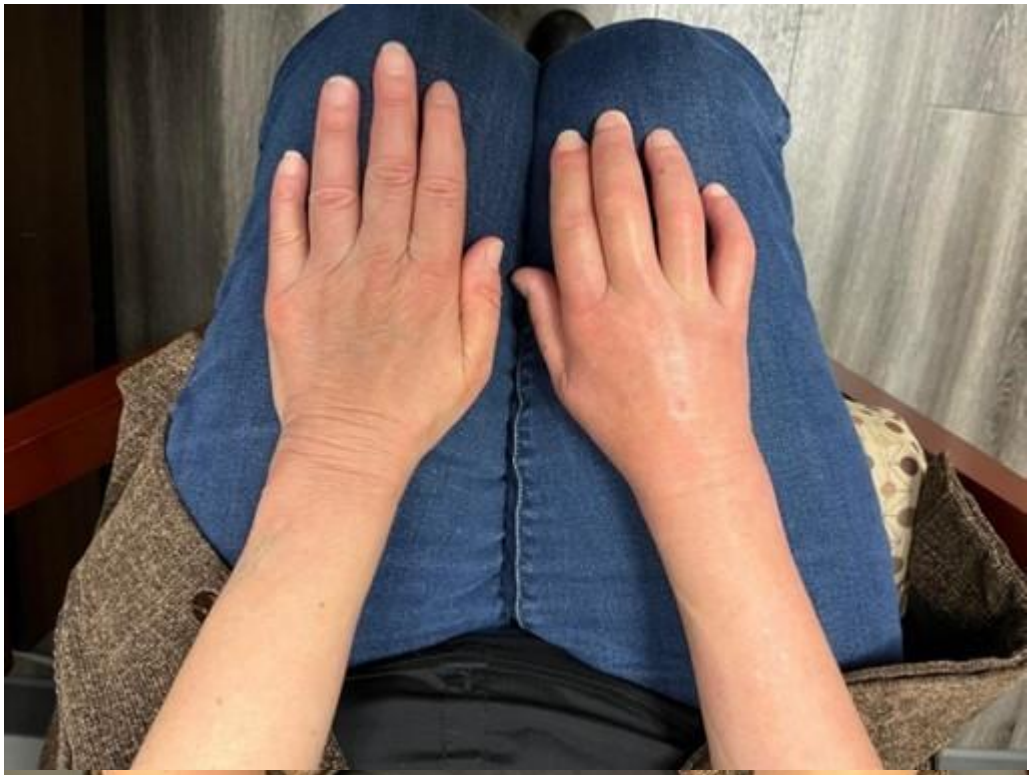
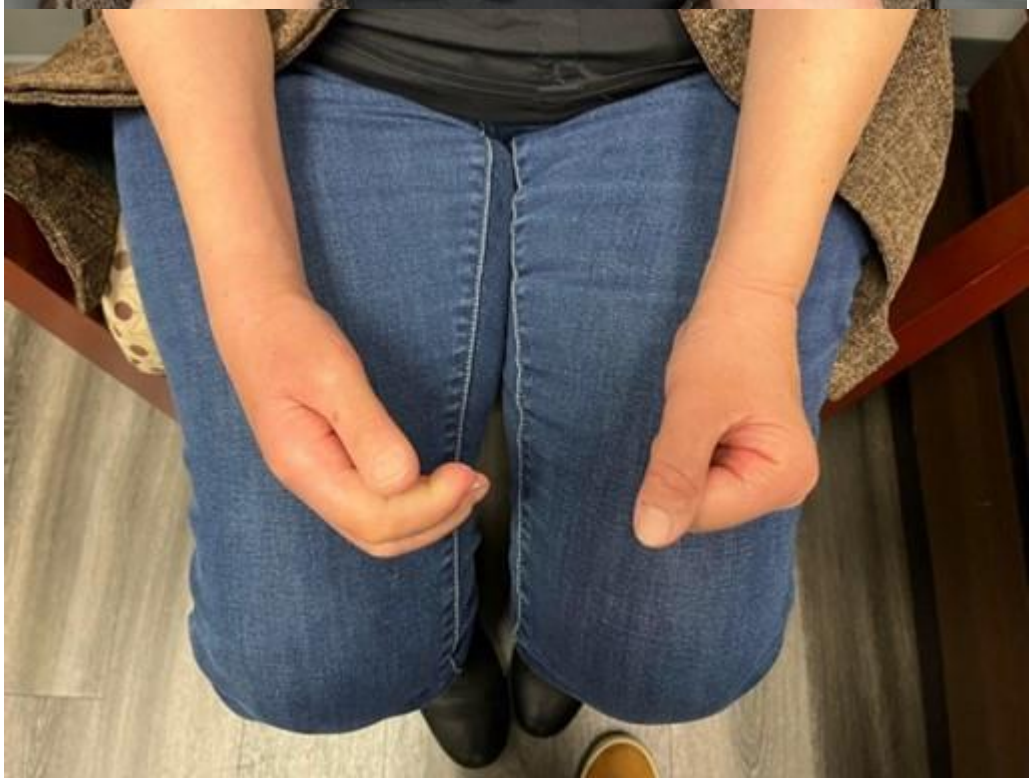
Systemic sclerosis (SScl) is a rare autoimmune disease that typically presents with bilateral cutaneous symptoms. Unilateral presentation or progression of SScl is an extremely rare phenomenon with few cases in existing literature all of which were associated with various external insults. Further investigation into this unique presentation may advance our understanding of the pathogenesis and potential inducing etiologies of SScl. We report a case of rapidly progressive unilateral hand sclerosis in a 63-year-old female following injury and immobilization. The patient had a history of limited-cutaneous SScl with bilateral Raynaud's phenomenon and mild sclerodactyly of her digits that remained stable for 11 years. However, six months following a right radial fracture that required casting, she presented with advanced biopsy-proven sclerosis and decreased mobility involving her entire right hand that extended towards her distal forearm. Interestingly, her left hand remained unchanged. Physical trauma is a known precipitating factor in morphea, which may present with similar unilateral skin changes, however the presence of stark sclerodactyly eliminates morphea as a diagnosis in this case. There have only been 2 reports of trauma-induced SScl and in both cases the patients suffered diffuse bilateral skin changes, which highlights the rarity of unilateral SScl progression seen in our case. Although the pathogenesis for SScl is incompletely understood, it is postulated that vascular injury, which may be induced by physical trauma, disrupts local microcirculation and activates a wound healing cascade resulting in excessive collagen deposition in genetically predisposed individuals. This may explain the unique unilateral progression seen in our case and highlight the potential role of external physical injury in the pathogenesis of SScl. Currently, there exists no definitive treatments for SScl and further investigation into potential inducing etiologies may advance our understanding and management of the disease.
Teaching Point: Physical trauma may play an integral role in precipitating systemic sclerosis and lead to atypical presentations of the condition.

Category: Clinical Case





A VASCULITIS MIMICKER: NICOLAU SYNDROME AFTER INADVERTANT HYALURONIC ACID INJECTION INTO THE INFERIOR LATERAL GENICULAR ARTERY

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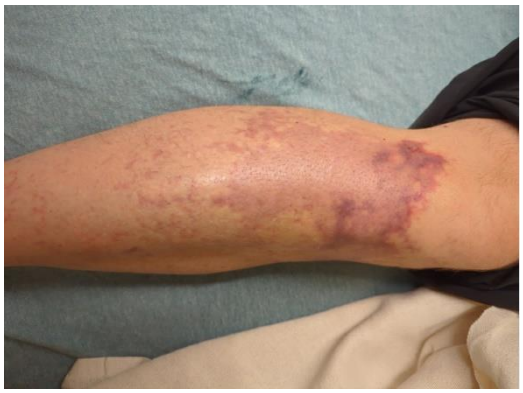
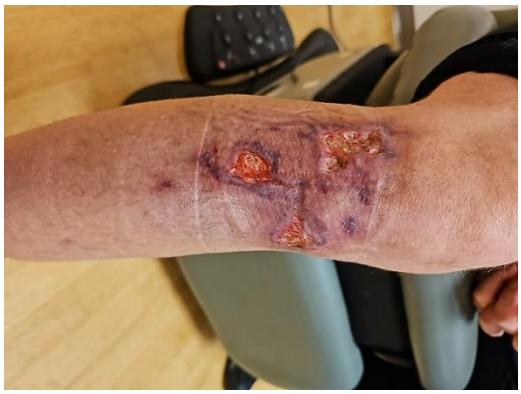
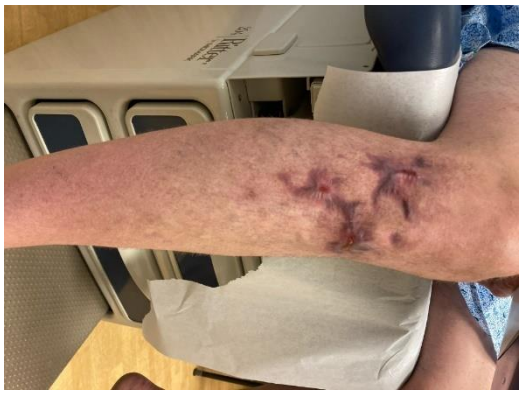
We present the case of a 57-year old male with Nicolau syndrome following sodium hyaluronate injection for treatment of knee arthritis. This case represents a rare, iatrogenic complication of viscosupplementation that is underrecognized as only seven cases have been reported in the literature. Our patient experienced pain immediately following injection to his right knee and later developed an ecchymosis-like rash and limb swelling. He was initially evaluated by orthopedics where point of care doppler demonstrated patent genicular arteries and laboratory work up was negative for infection. At day nine post-injection, he was referred to dermatology for work up of vasculitis. He presented with dusky livedoid and stellate purpura of the right knee suggestive of medium vessel disease. Nicolau syndrome secondary to inadvertent arterial injection of sodium hyaluronate was suspected. His symptoms initially improved with intralesional injection of hyaluronidase (450 units), which was repeated twice. However, this injection was performed too late in the natural history of his disease as he developed ulceration. Viscosupplementation by hyaluronic acid intra-articular injection is a common and generally well-tolerated intervention for knee osteoarthritis. Nicolau syndrome is a severe, iatrogenic complication following intramuscular, subcuticular, intraarticular or subacromial injection of medications and is thought to represent inadvertent intraarterial injection, embolus, or vessel compression from drug deposit. In the case of sodium hyaluronate, prompt recognition of this unintended consequence and immediate treatment with hyaluronidase can improve disease course. In the seven published cases, amorphous blue-grey material can be found intravascularly on biopsy, consistent with embolization of hyaluronic acid. Consistent with the etiology, laboratory work-up is unremarkable for acute phase reactants suggestive of vasculitis. In similar cases with earlier intervention with hyaluronidase injection, the clinical course is milder, thus prompt recognition of this vasculitis mimicker is required for timely intervention.

Teaching point: Distinguishing vasculitis from an iatrogenic complication from viscosupplementation is important for early intervention in Nicolau syndrome secondary to hyaluronic acid injection.

Category: Clinical case







DRUG INDUCED LUPUS ERYTHEMATOSUS IN A PHASE II TRIAL OF ANTI-C1Q MAB ANX005 STUDY PARTICIPANT

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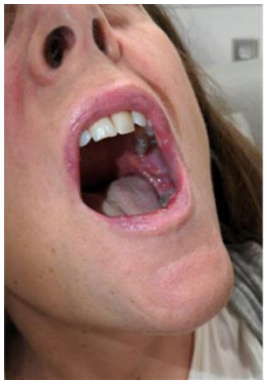
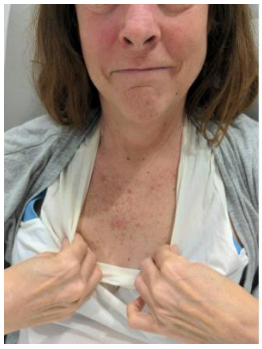
Huntington's Disease (HD) is a rapidly progressive and fatal movement disorder. In HD, complement C1q inappropriately activates and amplifies the classical complement pathway, leading to neural inflammation and synapse loss. ANX005 is a novel monoclonal antibody (mAb) that targets and blocks C1q. We present the case of 52-year-old female with HD participating in a Phase II Trial of ANX005 who dropped out of the study due to development of drug-induced lupus erythematosus (DIL). The patient was on week 20 of biweekly infusions of ANX005 when she developed oral ulcerations and an eruption on the face and chest. She had accompanying fatigue, malaise, lightheadedness, photosensitivity, and alopecia. She was initially treated by her primary care physician with a 7-day course of daily valacyclovir 1000mg and one 40mg intramuscular injection of triamcinolone for suspected herpes simplex infection. Her cutaneous symptoms worsened, and she subsequently developed nausea and vomiting that led to a hospital admission for electrolyte derangements. Dermatology service was consulted, and examination revealed skin findings consistent with acute and subacute cutaneous lupus erythematosus including mucosal ulcerations and erosions, malar rash, and papulosquamous lesions on the chest/neck. Laboratory evaluation was significant for lymphopenia, positive RNP antibody, positive Sm antibody, negative anti-histone antibody, ANA 1:320 speckled, and low levels of C3 and C4, 68 and 15, respectively. Biopsy of the chest revealed findings consistent with acute to subacute lupus, which led to a diagnosis of DIL. The patient was treated with daily prednisone 15mg and hydroxychloroquine 300mg which led to resolution of her cutaneous symptoms. It is well known that deficiency of complement C1q is associated with the development of systemic lupus erythematosus (SLE). Although ANX005 has shown promise for slowing of disease progression in HD, development of DIL is an important adverse effect that warrants change in management. Teaching Point: ANX005 is a novel anti-C1q mAb developed for the treatment of Huntington's Disease that can cause drug-induced lupus erythematosus.

Category: Clinical Case

7/29/2021 Clinical images:





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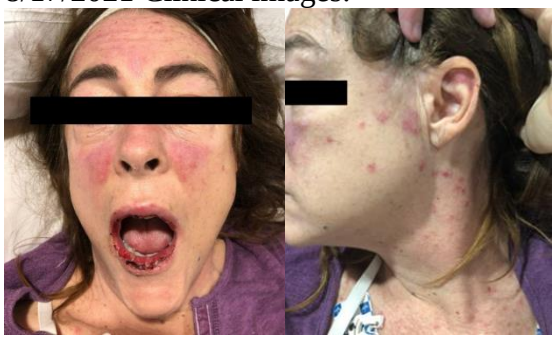

Poster Presentations

CASE SERIES AND RETROSPECTIVE COHORT STUDY OF CONCURRENT PSORIASIS AND DERMATOMYOSITIS

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Psoriasis and dermatomyositis (DM) are autoimmune-mediated, inflammatory conditions that rarely occur in the same patient. Herein, we describe patients with both diseases. Searching medical records at the University of California Irvine for ICD-10 codes for "psoriasis" and "dermatomyositis" yielded 16 patients: 12 were likely DM with psoriasis originally misdiagnosed. Four had true concomitant disease. A 42-year-old woman with 25-year-history of DM developed psoriasis on scalp, trunk, and thighs; she improved with topical steroids. Second, a 35-year-old man with juvenile DM presented 11 years later with psoriasis on elbows and knees and psoriatic arthritis, for which he failed apremilast, etanercept, tofacitinib, and ustekinumab; deucravacitinib was effective. Third, a 56-year-old woman with DM developed psoriasis on scalp and elbows 8 years later which improved on risankizumab. Lastly, a 76-year-old woman had limited psoriasis on methotrexate; 10 years later, she developed DM with facial involvement, Gottron's papules and V-neck sign, improving with prednisone, methotrexate, and azathioprine. A literature search identified 20 additional cases of concomitant psoriasis and DM (total 24). The average age was 43 (range 4-76 years) with 2:1 female-to-male-ratio. Of patients with documentation, 75% (3/4) had relatives with autoimmune conditions, and 42% (5/12) had other autoimmune conditions. Most (13/24, 54%) were diagnosed with DM before psoriasis, an average 7.2 years between diagnoses. A significant portion had juvenile DM (33%, 8/24). Only two patients developed malignancies. DM most commonly presented with Gottron's papules, Gottron's sign, and heliotrope rash. Psoriasis most affected scalp, elbows, and knees/legs. Overall, distinguishing between concurrent psoriasis and DM versus psoriasiform rashes in DM may be challenging. Concurrent disease should be suspected in those with other autoimmune diseases and when rashes of differing morphology appear years apart. Careful consideration is required when selecting therapy, as treatment of one condition could flare the other, and some therapies treat both conditions.

300 words maximum, single spaced, single paragraph, Times New Roman font, 12 pts size.

Category: Dermatomyositis or Clinical Case

SERONEGATIVE CUTANEOUS RHEUMATOID NODULES WITH POSITIVE RESPONSE TO TOFACITINIB

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Treatment guidelines for rheumatoid arthritis (RA) include non-steroidal anti-inflammatory drugs, glucocorticoids, disease-modifying anti-rheumatic drugs and biologics. Tofacitinib, a Janus kinase (JAK) inhibitor, was approved for RA in 2012 by the Food and Drug Administration and has been relatively well tolerated.[1] Tofacitinib has been used in granulomatous diseases with success.[2] There are cases of lung rheumatoid nodules successfully treated with tofacitinib.[3,4] Here we describe a case of seronegative cutaneous rheumatoid nodules with positive response to tofacitinib. A 29-year-old female with history of seronegative RA presented with severe pain and stiffness of the wrists and ankles. Medication trials included intralesional steroid injections, methotrexate, anakinra, infliximab, sulfasalazine, rituximab, abatacept, systemic corticosteroids and hydroxychloroquine with some relief. Examination showed chronic nodules of the arms and legs and ulcerated nodules and plaques over the metacarpophalangeal joints and cheeks (Fig 1). Severe synovitis was noted in the wrists and ankles. Biopsy showed fibrinoid necrobiotic granulomata with plasma cells, consistent with rheumatoid nodules (Fig 2). Due to severity of pain and resistance to treatments, she was started on tofacitinib 5 mg twice daily. Chronic rheumatoid nodules improved, and there was reduction in flares and ulcers. Exam showed scarred and atrophic plaques and nodules over the cheeks, arms, elbows, and hands with emphasis at extensor joints, knees, ankles, and shins (Fig 3). Ability to ambulate and perform activities of daily living also improved. Cytokines involved in the pathogenesis of RA, such as interleukin-6, interferons, granulocyte-macrophage colony-stimulating factor and common gamma chain cytokine family, act through JAK-signal transducer and activator of transcription pathway.[5] Tofacitinib inhibits JAK1, JAK3, and mildly JAK2 and may reduce inflammatory pathways that lead to rheumatoid nodule formation. Our patient case demonstrates cutaneous rheumatoid nodules with positive response to tofacitinib. Tofacitinib should be further studied as a potential therapy for patients with cutaneous rheumatoid nodules.

Teaching Point: Patients with cutaneous rheumatoid nodules may show positive response to tofacitinib as several cytokines involved in the pathogenesis of rheumatoid arthritis act through the JAK-STAT pathway.
Abstract Category: Clinical Case

Figures:

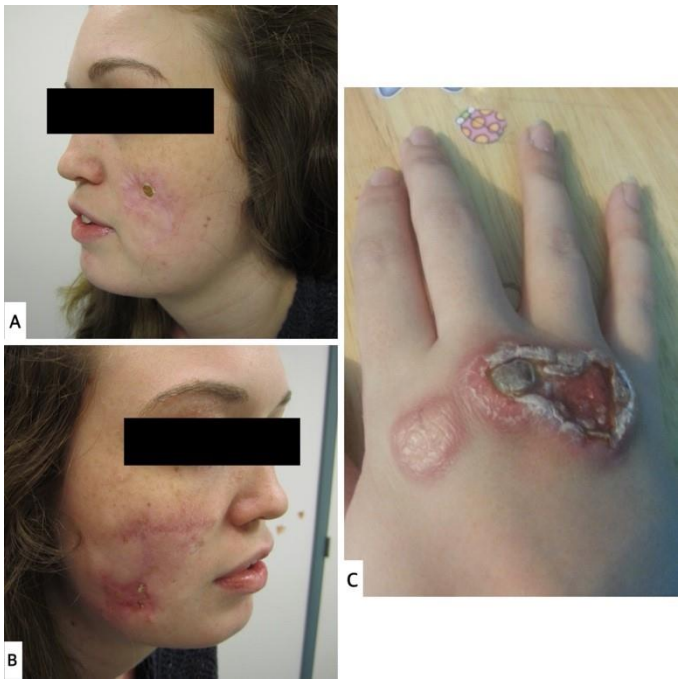

Fig 1. Open nodules of the left cheek (A), right cheek (B), and over the metacarpophalangeal joints of the right hand (C) before treatment with tofacitinib.

Fig 2. (A) 2x: Palisading granulomas with central area showing fibrinoid necrosis. (B) 4x: Palisading granulomas surrounding fibrin, with necrobiosis. (C) 20x: Granulomatous inflammation surrounding fibrin admixed with plasma cells.

Fig 3. Scarred and atrophic plaques and nodules of the face (A), bilateral elbows (B,C), and metacarpophalangeal joints (D) after treatment with tofacitinib.

References:

1. Álvaro-Gracia, J. M., García-Llorente, J. F., Valderrama, M., Gomez, S., & Montoro, M. (2021). Update on the Safety Profile of Tofacitinib in Rheumatoid Arthritis from Clinical Trials to Real-World Studies: A Narrative Review. *Rheumatology and therapy*, *8*(1), 17–40. https://doi.org/10.1007/s40744-020-00258-9

2. Rosenbach M. (2020). Janus kinase inhibitors offer promise for a new era of targeted treatment for granulomatous disorders. *Journal of the American Academy of Dermatology*, *82*(3), e91–e92. https://doi.org/10.1016/j.jaad.2019.06.1297

3. Her, M., Park, J., & Lee, S. G. (2024). A large pulmonary nodule in a rheumatoid arthritis patient treated with tofacitinib. *International journal of rheumatic diseases*, *27*(1), e15013. https://doi.org/10.1111/1756-185X.15013

4. Kondo, M., Murakawa, Y., Honda, M., Yanagawa, T., Nagasaki, M., Moriyama, M., Watanabe, Y., & Kakimaru, H. (2021). A case of rheumatoid arthritis with multiple lung rheumatoid nodules successfully treated with tofacitinib. *Modern rheumatology case reports*, *5*(1), 1–5. https://doi.org/10.1080/24725625.2020.1777677

5. Palmroth, M., Kuuliala, K., Peltomaa, R., Virtanen, A., Kuuliala, A., Kurttila, A., Kinnunen, A., Leirisalo-Repo, M., Silvennoinen, O., & Isomäki, P. (2021). Tofacitinib Suppresses Several JAK-STAT Pathways in Rheumatoid Arthritis *In Vivo* and Baseline Signaling Profile Associates With Treatment Response. *Frontiers in immunology*, *12*, 738481. https://doi.org/10.3389/fimmu.2021.738481

SYNDROME OF REMITTING SERONEGATIVE SYMMETRICAL SYNOVITIS WITH PITTING EDEMA WITH COMORBID EARLY LIMITED SYSTEMIC SCLEROSIS

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A 78-year-old female was referred to rheumatology with sudden onset swelling of the hands and feet and joint pain for 3 months. The symptoms quickly resolved with oral steroids and recurred upon discontinuation. Review of systems revealed longstanding history of Raynaud's and chronic cough, but no acid reflux, chronic joint pain, or perception of skin tightening. Exam showed pitting edema of the dorsal hands and feet, synovitis of metacarpophalangeal and proximal interphalangeal hand joints, and nailfold capillary abnormalities. Labs were notable for positive ANA (>1:1280) and anti-centromere antibody (>1:1280), negative RF, anti-CCP, remaining scleroderma and lupus panels and normal chemistry and blood counts. Hands and feet x-rays showed soft tissue swelling, degenerative changes, but no erosions. The patient was diagnosed with syndrome of remitting seronegative symmetrical synovitis with pitting edema (RS3PE) and re-started on low dose prednisone. Subsequently, dermatologic exam identified telangiectasias on palms and dorsal hands and skin tightening involving dorsal hands and fingers. Biopsy showed sclerosing dermatitis, therefore a concomitant diagnosis of early limited systemic sclerosis (SS) was made. CT imaging demonstrated no interstitial lung disease or underlying malignancy. RS3PE is characterized by seronegative symmetric polysynovitis and arthritis of the distal limbs with acute onset pitting edema on the dorsal hands and feet in patients above the age of 50, rapidly responsive to steroids[1]. It can be associated with underlying infections, medications, autoimmune diseases and malignancy, in which case may not respond to steroids[2]. Early SS presenting with edematous hand changes without sclerosis has been misdiagnosed as RS3PE and treated with high dose steroids which presumably contributed to subsequent renal criris[3]. Importantly edematous (usually non-pitting, rarely pitting) hand changes[4] of early SS are not expected to develop suddenly, are more common on distal fingers rather than dorsal hands and should not resolve rapidly with steroids like in RS3PE.

Teaching Point: RS3PE may present in association with limited systemic sclerosis, and is characterized by sudden onset and pitting edema, that is steroid responsive.

Abstract Category: Clinical Case

References
[1]McCarty DJ, O'Duffy JD, Pearson L, Hunter JB. Remitting seronegative symmetrical synovitis with pitting edema. RS3PE syndrome. JAMA. 1985 Nov 15;254(19):2763-7.
[2]Lakhmalla M, Dahiya DS, Kichloo A, Fatima T, Edigin E, Wani F. Remitting seronegative symmetrical synovitis with pitting edema: a review. J Investig Med. 2021 Jan;69(1):86-90.
[3]Gambichler T, Susok L, Doerler M, Westhoff TH, Seibert FS. Very Early Systemic Sclerosis Mimicking Remitting Seronegative Symmetrical Synovitis With Pitting Edema. J Clin Rheumatol. 2021 Jan 1;27(1):e13-e14.
[4]Englert H, Low S. Pitting oedema in early diffuse systemic scleroderma. Ann Rheum Dis. 2001 Nov;60(11):1079-80.

RAPID IMPROVEMENT OF SUSPECTED RUBELLA VIRUS-ASSOCIATED GRANULOMATOUS DERMATITIS WITH ADALIMUMAB TREATMENT

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Rubella virus (RuV) associated granulomatous dermatitis has an unclear pathogenesis in which either vaccine-derived or wild-type virus is identified in cutaneous or visceral biopsy specimens. Treatments with antimicrobials and immunomodulatory therapy have shown varying degrees of success, complicating patient management. In this report, we present the case of a 57-year-old white female with a 4-year history of recalcitrant maculopapular, pigmented and itchy rash with patchy ulcerations extending from left knee to the ankle. Interestingly, within a year after onset of skin lesions, she was diagnosed with stage 4 diffuse large B-cell lymphoma and successfully treated with R-CHOP chemotherapy. Her skin disease went into remission during chemotherapy but then relapsed involving the entire left lower extremity (Figure 1a). Moderate to higher doses of corticosteroids initially worked well, but lower doses led to persistent disease activity (Figure 1b). She was then treated with hydroxychloroquine and methotrexate due to concern for sarcoidal versus paraneoplastic dermatitis, but with disappointing results (Figure 1c). Infectious testing and rheumatologic serology for HIV, Hepatitis B/C, fungal infections, Anti-nuclear antibody, rheumatoid factor and anti-neutrophilic cytoplasmic antibodies were negative. Multiple skin biopsies were taken, and pathology depicted necrotizing and non-necrotizing granulomatous processes with mixed features of sarcoidosis, fibrosing granuloma annular and necrobiosis lipoidica. This indicated an extreme granulomatous dermatitis from B-cell lymphoma (Figure 2). Microbial stains and cultures remained negative. Tissue was sent to Centers for Disease Control for further histologic and immunohistochemical staining and resulted positive for RuV, indicating potential diagnosis of RuV associated granulomatous dermatitis. Due to the patient's severe, debilitating presentation and lack of response to other treatments, interdisciplinary collaboration between Rheumatology, Oncology, and Dermatology agreed on starting adalimumab 40mg injections every 2 weeks. On follow-up 3 months later, physical exam showed notable improvement with granulation tissue and no active ulcerations (Figure 1d).

Teaching point: The case encourages clinicians to consider RuV-associated granulomatous dermatitis in patients with atypical, recalcitrant cutaneous granulomatous lesions. To our knowledge, this would be the first case of successful treatment of RuV-associated granulomatous dermatitis with an anti-TNF monoclonal antibody and emphasizes adalimumab as a viable treatment option for patients non-responsive to other corticosteroid sparing therapies.

Abstract Category: Clinical Case

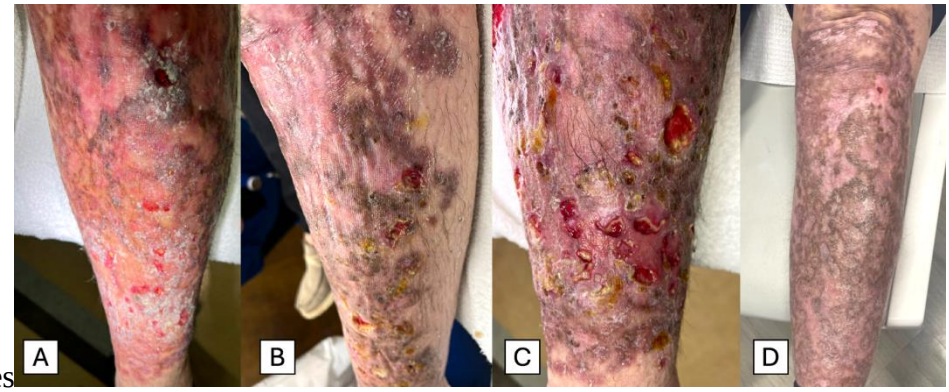

Figure 1. Clinical Images

A. Initial presentation of erythematous papules and nodules with few ulcerations after 1 year of remission

B. Improvement with moderate to high dose oral corticosteroids

C. Worsening of lesions with increased ulceration after hydroxychloroquine and methotrexate combination treatment

D. Substantial improvement in granulomatous ulceration seen after 14 weeks of treatment with adalimumab

References:

1. Zhang D, Wanat KA, Perelygina L, et al. Cutaneous granulomas associated with rubella virus: A clinical review. *J Am Acad Dermatol*. 2024;90(1):111-121. doi:10.1016/j.jaad.2023.05.058

2. Perelygina L, Chen MH, Suppiah S, et al. Infectious vaccine-derived rubella viruses emerge, persist, and evolve in cutaneous granulomas of children with primary immunodeficiencies. *PLoS Pathog*. 2019;15(10):e1008080. Published 2019 Oct 28. doi:10.1371/journal.ppat.1008080

3. Tl VL, Am CV, I GJ, et al. Rubella virus-associated cutaneous granulomatous disease in an immunocompetent woman. *Eur J Clin Microbiol Infect Dis*. Published online April 22, 2024. doi:10.1007/s10096-024-04828-5

4. Shields BE, Perelygina L, Samimi S, et al. Granulomatous Dermatitis Associated With Rubella Virus Infection in an Adult With Immunodeficiency. *JAMA Dermatol*. 2021;157(7):842-847. doi:10.1001/jamadermatol.2021.1577

5. Dhossche J, Johnson L, White K, et al. Cutaneous Granulomatous Disease With Presence of Rubella Virus in Lesions. *JAMA Dermatol*. 2019;155(7):859-861. doi:10.1001/jamadermatol.2019.0814

6. Wanat KA, Perelygina L, Chen MH, et al. Association of Persistent Rubella Virus With Idiopathic Skin Granulomas in Clinically Immunocompetent Adults. *JAMA Dermatol*. 2022;158(6):626-633. doi:10.1001/jamadermatol.2022.0828

CHARACTERIZATION OF SEX-BASED DISPARITIES IN DERMATOMYOSITIS PATIENTS ADMITTED TO JOHNS HOPKINS HOSPITAL: A RETROSPECTIVE COHORT STUDY

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This retrospective cohort study investigated sex-based differences in a cohort of 40 male and 108 female dermatomyositis (DM) patients who were admitted to Johns Hopkins Hospital between October 2013 and February 2024. Patients admitted to Johns Hopkins with a diagnosis of DM were 2.7 times more likely to be female than male. Male and female DM patients did not differ significantly by race, age at diagnosis and admission, duration of DM, insurance status, and smoking status. Male patients experienced more complications than female patients, with longer hospital stays (16.8 days vs. 8.6 days, p=.024) and greater susceptibility to infections during their admission (42.5% vs. 17.6%, p=.003). Moreover, DM in men was associated with a higher incidence of lung involvement (65% vs. 40.7%, p=.015) and a history of skin cancer (20% vs. 1.9%, p<.001; adjusted odds ratio (AOR) 8.50 (95% confidence interval (CI): 2.39, 30.21)). Compared to female sex, male sex was significantly associated with previous melanoma diagnosis (10.0% vs. 0.0%, p = 0.006) and squamous cell carcinoma (SCC) diagnosis (12.5% vs. 0.93%, p = 0.007). A possible hypothesis for the higher risk of melanoma and SCC history in males with DM includes increased UV exposure, which may also predispose males to DM, as UV exposure can trigger or exacerbate autoimmune diseases.[1] DM antibodies also varied by sex: females exhibited a significantly higher likelihood of being anti-TIF-1γ positive compared to males (14.8% vs. 2.5%, p=.042), while anti-NXP2 prevalence was higher in males (15% vs. 4.6%, p=.070). This study highlights the longer hospital stays, higher infection rates, and greater prevalence of skin cancer among male DM patients, underscoring the importance of considering sex-specific factors when managing DM inpatient. Further research is warranted to elucidate the underlying mechanisms driving these disparities and to optimize care for DM patients.

Category: Dermatomyositis

References

1. Bernard JJ, Gallo RL, Krutmann J. Photoimmunology: How ultraviolet radiation affects the immune system. *Nature Reviews Immunology*. 2019;19(11):688–701. https://doi.org/10.1038/s41577-019-0185-9. doi: 10.1038/s41577-019-0185-9.

CLASSIFICATION CRITERIA FOR CUTANEOUS FEATURES IN DERMATOMYOSITIS: A PROSPECTIVE VALIDATION STUDY

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Dermatomyositis (DM) is an heterogenous autoimmune disease that may be challenging to classify, especially in skin-predominant patients. The current international effort, comprised of rheumatologic dermatology experts, aims to develop more inclusive classification criteria for cutaneous DM. A Delphi iterative process retained 23/54 clinical and laboratory candidate items generated from literature review and expert discussions. They were further validated in a prospective case-control study across 14 sites in North America, Europe, and Asia. A total of 270 subjects

including 161 cases and 109 comparable controls were enrolled. Among the cases, 97 were classic, 57 clinically amyopathic and 7 juvenile DM. Univariable associations with DM were assessed using Chi-square or Wilcoxon tests for demographic variables, and all candidate items. Elastic net logistic regression analysis was performed to identify significant predictors and to develop a scoring system based on regression coefficients. The dataset was split into 70:30 for training and testing sets to reduce overfitting. Receiver Operating Characteristic curve and Area Under the Curve were computed on the testing set. Twenty items (all except scalp pruritus, erythematous/violaceous erythema and scalp/palmar/lateral thigh involvement) were associated with DM. The final model included papules/erythema over joints, periorbital/eyelid erythema +/- oedema, nasolabial folds, nailfold capillaries/erythema, cuticular dystrophy, poikiloderma, V sign, Shawl sign, elbow/knee, lateral digit involvement, interface dermatitis and increased dermal mucin. Several points-based scoring systems and models combining clinical variables with/without skin histology were created to refine the sensitivity and specificity while optimizing practicability. This dataset-derived preliminary weighting will undergo forward validation and adjustment, such as with expert-based method, to conjunctly reflect clinical decision making. The final model may be used as a standalone for skin-predominant DM or be integrated within the current larger effort in improving myositis classification criteria.

Category: Dermatomyositis

RISK OF INTERSTITIAL LUNG DISEASE IN ADULT DERMATOMYOSITIS PATIENTS TAKING METHOTREXATE

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Abstract:

Interstitial lung disease (ILD) constitutes a potentially severe extra-muscular manifestation of dermatomyositis (DM)[1]. Methotrexate (MTX) is considered a first-line treatment for DM, but its association with pulmonary toxicity in rheumatoid arthritis patients has raised concerns about its potential to increase ILD risk in DM patients[2]. While a recent study using the *All of Us* Research Program found no association between MTX use and ILD development in DM patients, the interpretability of the authors' findings are limited by small sample size, reliance on electronic health records, lack of subtype data, and challenges establishing temporality between DM and ILD diagnosis in this database[3]. Thus, we sought to utilize a large, longitudinal, and prospective DM database to explore any potential association between MTX use and ILD risk across DM subtypes. In this cohort study, we analyzed 558 DM patients at the University of Pennsylvania Rheumatology-Dermatology clinic from January 2007 to May 2024. Patients with ILD at first visit and follow-up of less than one year were excluded. Inclusion criteria were DM diagnosis and initiation of immunomodulating treatment (IMT). We stratified MTX use with demographics, DM subtype, and other IMTs including mycophenolate mofetil (MMF), which is often used to stabilize lung function in DM due to its anti-fibrotic properties[1]. 236 patients met the inclusion criteria, of which 39.41% were started on MTX, 38.56% on MMF, and 22.03% on other IMTs (Table 1). After excluding patients who were on MTX or MMF for less than 75% of their total follow-up time, there were no significant differences in ILD development: 9 (12.16%) patients on MTX and 10 (14.09%) patients on MMF developed ILD (Table 2). Reflecting standard-of-care practice, myopathic and amyopathic patients were equally likely to be started on MTX or MMF. We found no differences in ILD rates across DM subtype. Taken together, our study provides strong evidence that there is minimal risk of pulmonary toxicity with MTX use in DM patients.

Category: Dermatomyositis

References

1. Cobos, G.A., A. Femia, and R.A. Vleugels, *Dermatomyositis: An Update on Diagnosis and Treatment.* American Journal of Clinical Dermatology, 2020. **21**(3): p. 339-353.
2. Fragoulis, G.E., et al., *Methotrexate-Associated Pneumonitis and Rheumatoid Arthritis-Interstitial Lung Disease: Current Concepts for the Diagnosis and Treatment.* Frontiers in Medicine, 2019. **6**.
3. Shah, J.T., et al., *Methotrexate Use and Risk of Interstitial Lung Disease in Dermatomyositis.* JAMA Dermatol, 2024. **160**(6): p. 676-678.
4. Pandya, R., et al., *Clinical characteristics and symptom progression of dermatomyositis subtypes: A retrospective analysis of a prospective database.* Journal of the American Academy of Dermatology, 2024. **91**(1): p. 31-36.
5. Hu, Q., et al., *Characteristics and risk of interstitial lung disease in dermatomyositis and polymyositis: a retrospective cohort study in Japan.* Scientific Reports, 2023. **13**(1): p. 17172.

Table 1: Demographic, clinical, and treatment characteristics of adult DM patients stratified by IMT use

	On MTX N=93	**On MMF** N=91	**Other IMT[3]** N=52	**P-Value**
Age, median (IQR)	53.24 (44-63.75)	51.95 (44-64)	58.16 (49.5-65.25)	p = 0.86
Sex[1]:				
Female	81 (90.00%)	79 (86.82%)	51 (98.08%)	p = 0.70
Male	9 (10.00%)	12 (13.19%)	1 (1.92%	
Race[1]:				
Black	0 (0.0%)	0 (0.00%)	4 (7.69%)	**P = 0.001**
White	88 (94.62%)	85 (93.40%)	47 (90.38%)	
Asian	5 (5.38%)	6 (6.60%)	0 (0.0%)	
Ever smoker	32 (34.41%)	21 (23.08%)	20 (38.46%)	P = 0.28
DM Subtypes[1]				
Classic/Myopathic	44 (47.32%)	44 (48.35%)	17 (32.69%)	p = 0.36
Amyopathic	44 (47.32%)	43 (47.25%)	33 (63.46%)	
Other[2]	5 (3.57%)	4 (4.40%)	2 (3.85%)	
Other Medications				
Hydroxychloroquine	67 (72.04%)	65 (71.43%)	45 (86.54%)	p = 0.09
Chloroquine	11 (11.83%)	11 (12.08%)	4 (7.69%)	p = 0.69
Quinacrine	29 (31.18%)	30 (32.91%)	25 (48.98%)	p = 0.10
Azathioprine	19 (20.43%)	8 (8.79%)	6 (11.54%)	p = 0.06
IVIg	15 (16.13%)	25 (27.47%)	4 (7.69%)	**p = 0.01**
Dapsone	1 (1.08%)	2 (2.20%)	2 (3.85%)	p = 0.54
Cyclosporine	1 (1.08%)	3 (3.30%)	0 (0.00%)	p = 0.29
Rituximab	3 (3.22%)	3 (3.30%)	3 (5.77%)	p = 0.71
MTX	93 (100%)	19 (20.88)	0 (0.00%)	
MMF	19 (20.43%)	91 (100%)	0 (0.00%)	

Abbreviations: DM, dermatomyositis; IVIg, intravenous immunoglobulin; MTX, methotrexate; MMF, mycophenolate mofetil; IMT, immunomodulating treatment

[1] Missing data for 2 or fewer patients

[2] Other includes hypomyopathic or unknown subtypes

[3] Other IMT includes hydroxychloroquine, chloroquine, quinacrine, azathioprine, IVIg, dapsone, cyclosporin, rituximab

Table 2: ILD development in adult DM patients stratified by IMT use

	On MTX n=74	**On MMF** N=71	**Other IMT** N=52	**P-Value**
Overall ILD Development*	9 (12.16%)	10 (14.09%)	6 (11.54%)	p = 0.77
Months after DM diagnosis to ILD diagnosis, median (IQR)	37.8 (14-57.56)	29.04 (11.25-37.0)	24 (15.5-32)	
Myopathic ILD Development	4 (9.09%)	6 (13.64%)	3 (17.64%)	p = 0.63
Months after DM diagnosis to ILD diagnosis, median (IQR)	63.75 (15.25-110.25)	43.63 (13.5 – 57)	22.33 (17.5-28.5)	
Amyopathic ILD Development	5 (11.36%)	4 (9.30%)	3 (9.09%)	p = 0.93
Months after DM diagnosis to ILD diagnosis, median (IQR)	34.33 (14.5-53.75)	49.20 (12-78)	25.25 (17-34.75)	

Abbreviations: DM, dermatomyositis; IVIg, intravenous immunoglobulin; MTX, methotrexate; MMF, mycophenolate mofetil; IMT, immunomodulating treatments; PFT, pulmonary function test

*excluded patients who were diagnosed with ILD at first visit

ERYTHEMA VARIATION IN DERMATOMYOSITIS ACROSS SUBTYPES AND RACIAL GROUPS: IMPORTANCE OF OUTCOME MEASURE FOR DERMATOMYOSITIS CLINICAL TRIALS

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Abstract:

Dermatomyositis (DM) is a chronic autoimmune disease that presents with characteristic skin manifestations and skeletal muscle weakness, with some patients only exhibiting cutaneous findings. Currently, most clinical trials focus on improving muscle symptoms while excluding skin involvement. Two measurement tools are used to assess DM skin disease activity: Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) and the Cutaneous Dermatomyositis Investigator Global Assessment (CDM-IGA)[1]. As DM studies become more inclusive of cutaneous disease, it is important to utilize a scoring tool that accurately captures changes in skin activity. We aim to assess variability in erythema presentation across DM subtypes and among racial groups to help describe an outcome measure that reflects improvement in DM skin disease. Our cross-sectional study included 464 DM patients enrolled in the Penn Dermatomyositis Database from January 2007 to May 2024. 84.5% of our cohort was female. 89% were White, 6.3% were Black and 3.2% were Asian. Classic (49.1%) and amyopathic (48.3%) subtypes were the most prevalent subtypes. The primary outcome of mean erythema was calculated using the CDASI-A total erythema score divided by areas affected during patients' first visit. The result was categorized as "pink" (1.00-1.49) or "red" (≥1.50) as surrogate estimates of the CDM-IGA score. White (1.29±0.02), Black (1.11±0.05), and Asian (1.14±0.11) patients were all considered "pink", but White patients had significantly increased average erythema compared to Black patients. CDASI severity differed across race: Whites [n=419: 50.4% mild], Blacks [n=29: 72.4% mild], and Asians [n=15: 33.3% mild] (p=0.026). However, this difference would not be observed using average erythema scores, as scored by the CDM-IGA, suggesting this measurement tool would not accurately record skin disease activity. With the need to standardize DM trial outcome measures for cutaneous disease, our findings support the use of the CDASI as the primary scoring tool in cutaneous trial outcomes.

Category: Dermatomyositis

References

1. Pandya, R., et al., *Validation of Cutaneous Dermatomyositis Disease Area and Severity Index Activity Score and Other Efficacy Outcomes as Measures of Skin Disease in Dermatomyositis in the Lenabasum Phase 3 Trial.* Journal of Investigative Dermatology, 2023. **143**(12): p. 2378-2385.e7.

DISPARITIES IN DERMATOMYOSITIS HEALTHCARE UTILIZATION BASED ON PUBLIC VERSUS PRIVATE INSURANCE PLANS: A RETROSPECTIVE COHORT STUDY

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Socioeconomic status (SES) is increasingly studied as a predictor of healthcare utilization and disease outcomes. Patients with connective tissue diseases such as dermatomyositis are often challenged by SES-related disparities in insurance benefits and limited FDA-approved therapies. To explore the relationship between insurance coverage, healthcare utilization, and therapeutic management in dermatomyositis, we conducted a retrospective review of patients seen at University of California Irvine Medical Center between January 2016 and June 2024. Patients diagnosed with adult-onset dermatomyositis per ACR/EULAR criteria were stratified by insurance type. Public insurance included government-based plans like Medicare and Medicaid. Private insurance included private-company health insurance plans. Of the included 118 patients, 58.4% (69/118) held public insurance. These individuals were more likely to be Hispanic (odds ratio [OR] 2.8, p=0.02). Public insurance holders received intravenous immunoglobulin (IVIg) therapy sooner after diagnosis (<3 months since diagnosis) compared to those with private insurance (OR 3.6, p=0.02). Similarly, rituximab (RTX) initiation was sooner (<4 months since diagnosis) (OR 5.3, p=0.04). Those with public insurance had significantly more emergency department visits and/or hospitalizations (OR 3.6, p=0.02). Longer diagnostic delays and prolonged high-dose corticosteroid use were also observed amongst public insurance holders, however these differences were not statistically significant. Overall, these findings suggest that public insurance holders experience difficulties in receiving timely care, which might result in more severe disease presentation and thus longer time on corticosteroids and sooner initiation of aggressive therapies. Such trends align with broader patterns observed in dermatology, in which patients with public insurance consult less outpatient care, present with more severe disease, and experience increased mortality rates. This study demonstrates that dermatomyositis patients with public health insurance experience less favorable management and outcome patterns compared to patients with private insurance, highlighting the need for continued reform to achieve equitable, accessible care for patients with complex dermatologic diseases.

Teaching Point: Differences in health insurance benefits may impact healthcare utilization and therapeutic management of patients with dermatomyositis.

Category: Dermatomyositis

DEMOGRAPHICS AND COMORBIDITIES OF CLINICAL INTEREST AMONG PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS IN A LARGE US ELECTRONIC HEALTH RECORD DATABASE STUDY

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Few population-based observational studies have examined demographic and clinical characteristics of cutaneous lupus erythematosus (CLE) patients since four new CLE codes were introduced in the International Classification of Disease-10, Clinical Modification (ICD-10 CM) system in 2015. Utilizing algorithms informed by Guo et al.[1] to identify CLE patients, this cross-sectional study describes demographics and comorbidities of a large CLE patient cohort in the US, using the Optum® de-identified Electronic Health Record data set (N=~113 million) between 2016 and 2022. Among 10,025 CLE patients, 84% were female; 62% were Caucasian, 25% African American (AA), and 3% Asian (**Figure 1**). The mean (standard deviation) age at diagnosis was 51 (±16) years. CLE subtypes overall presented as 64.3% discoid lupus erythematosus (DLE), 13.7% other local lupus erythematosus (LE), 9.5% subacute CLE (SCLE), 8.2% both DLE and SCLE, and 4.4% undetermined; among AA these percentages were 82.9%, 7.2%, 2.2%, 5.3%, and 2.5%, respectively. Coexisting systemic lupus erythematosus (SLE)[2] was observed in 47% (n=4,718) of CLE patients. The proportion of AAs was ~10% higher among CLE patients with SLE (29.5%) versus CLE-only patients (20%). Comorbidities of clinical interest included SLE-related conditions such as renal involvement (glomerular disease [7.5%], tubulo-interstitial disease [0.8%]), lung involvement (2.1%), pericarditis (1.8%), nonspecific organ involvement (14.6%); mental health disorders such as anxiety disorder (30.1%), depression (25.6%); and cardiovascular risk factors such as essential hypertension (45%), disorders of lipids (36%), obesity (27.9%), and type 2 diabetes (13.9%). This large EHR-based study provides valuable insights into the demographics of CLE patients in the US, overall, by subtype, and by coexisting SLE status. The comorbidities that were identified, highlight areas for future research in a landscape where no CLE-specific therapies exist and emerging treatments are being developed.

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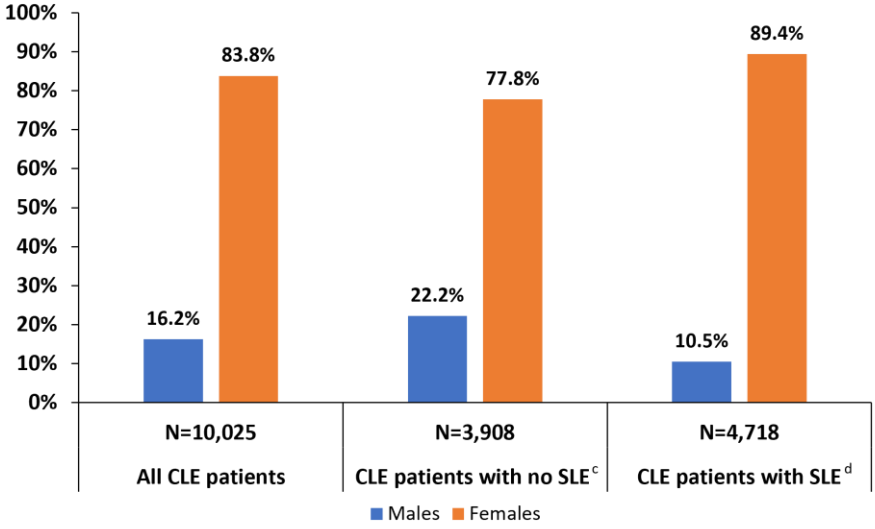
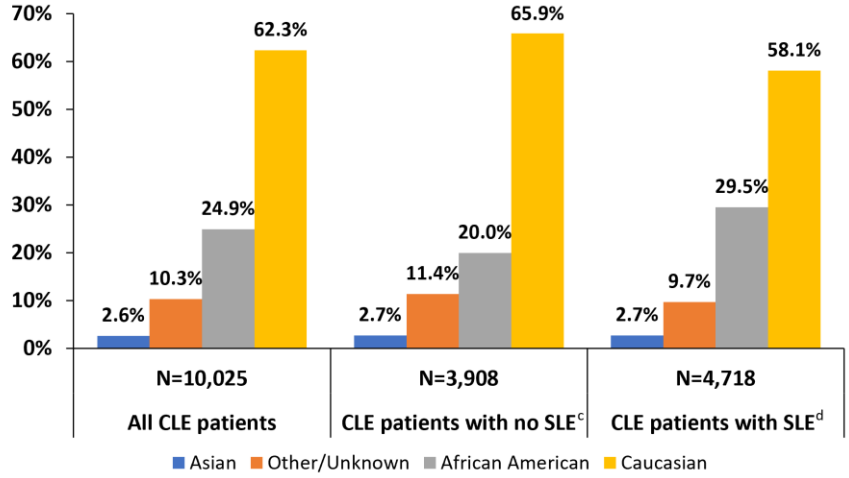
Abstract Category: Lupus

Figure 1 Demographic characteristics of CLE patients in the Optum® de-identified Electronic Health Record data set (Optum® EHR) 2016–2022, overall and by coexisting SLE status[a,b]

1a. Sex distribution among CLE patients in the Optum® EHR 2016–2022, overall and by coexisting SLE status



1b. Race distribution among CLE patients in the Optum® EHR 2016–2022, overall and by coexisting SLE status



[a]Overall CLE was defined by ≥2 CLE ICD-10 CM codes, with ≥1 ICD-10 CM code from a dermatologist OR a rheumatologist between 2016–2022.

[b]SLE was defined by ≥3 ICD-9/10 CM codes for SLE (ICD-9 CM: 710; ICD-10 CM: M32)[2] between 2007–2022. The numbers of CLE patients with and without SLE do not add up to the total number of all CLE patients because individuals with <3 SLE codes are not counted as having coexisting SLE.

[c]CLE without coexisting SLE was defined by overall CLE with no ICD-9/10 CM codes for SLE[2] ever

[d]CLE with coexisting SLE was defined by overall CLE with ≥3 ICD-9/10 CM codes for SLE[2]

Abbreviations: CLE: Cutaneous Lupus Erythematosus; EHR: Electronic Health Record; ICD-9/10 CM, International Classification of Disease-9/10 Clinical Modification, SLE: Systemic Lupus Erythematosus.

References:

[1]Guo L, et al. Arthritis Rheumatol 2022;74(Suppl. 9) (Abstract 0318)
[2]Barnado A, et al. Arthritis Care Res (Hoboken) 2017;69:687–693

LASER THERAPY IN THE TREATMENT OF POST-INFLAMMATORY HYPERPIGMENTATION AND ATROPHY SECONDARY TO DISCOID LUPUS ERYTHEMATOUS LUPUS IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Discoid lupus erythematosus (DLE) is a chronic scarring form of cutaneous lupus, commonly resulting in dyspigmentation and atrophy. We present the case of a 46-year-old Hispanic female with systemic lupus erythematosus (SLE) and clinically quiescent DLE with prominent post-inflammatory hyperpigmentation (PIH) and atrophy. Her initial SLE diagnosis was established 20 years ago, and her course was complicated by severe cutaneous manifestations, grade IV lupus nephritis, and severe Raynaud's phenomenon with ulcerations. In recent years, both her systemic and cutaneous disease have remained largely quiescent on methylprednisolone 4mg daily and mycophenolate mofetil 1000mg twice daily. Despite adequate control of her lupus, the patient experienced significant distress and impaired quality of life due to PIH and atrophy involving the bilateral eyelids, nasal bridge, and medial cheeks. Initial management of PIH with topical hydroquinone (HQ) was unsuccessful. Subsequently, the patient was treated with a compounded cream containing kojic acid, niacinamide, and azelaic acid, with strict sun protection. Due to the persistence of PIH and atrophic scars, the patient consented to non-ablative fractional skin resurfacing (Fraxel) treatment. Areas were pre-treated and post-treated with HQ to reduce risk for worsening PIH in Fitzpatrick Skin Type V, and strict sun protection was emphasized. After one treatment with Fraxel, the patient had improvement in both atrophy and PIH. No adverse effects were observed, and the patient plans to have additional Fraxel treatments. This case highlights the potential for using Fraxel to treat PIH and atrophy in patients with well-controlled DLE, including in the setting of SLE. Given the limited literature on laser and energy-based therapy in patients with DLE and/or SLE due to concerns for re-activation of disease, our case provides valuable insight into the safe utilization of this treatment modality.

Teaching point: In treating discoid lupus erythematosus (DLE), it is pivotal to treat both the inflammation and the sequela of disease—i.e. post-inflammatory hyperpigmentation and atrophy—to optimize patient quality of life. Laser and energy-based devices can be safely and effectively used in patients with both skin of color and well-controlled DLE and/or SLE to manage these symptoms without triggering a lupus flare and resulting in worsening PIH.

Category: Lupus

DYSCHROMIA IN DISCOID LUPUS ERYTHEMATOSUS: UNLOCKING BIOLOGIC MECHANISMS TOWARDS ADVANCING TREATMENT AND PREVENTION IN MINORITY HEALTH POPULATIONS

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Discoid Lupus Erythematosus (DLE) usually presents as a well circumscribed, indurated, hypopigmented plaque, and a hyperpigmented rim[1]. The mechanism of dyspigmentation is unclear but hypothesized to be secondary to basement membrane inflammation where majority of melanocytes reside. Even when the disease process is well controlled, the outcome is a healed scar that can present as vitiligo-like depigmentation or hyper-pigmentation, and ultimately leads to permanent disfigurement[2]. Available treatments targets inflammation to heal the lesions but do not address the resultant dyspigmentation[3]. This research aims to identify dyschromic DLE histomorphometric traits for potential therapeutic targets. Six DLE patients with dyschromia were enrolled. Punch biopsies of hyper-, hypo-, and normally pigmented skin (NS) were analyzed. Melanin index (MI) was measured non-invasively for each pigment phenotype. Demographic and dermatology life quality index (DLQI) data were collected. Statistical analyses were performed in Graphpad prism. The patient population was predominantly female (66.67%), black (83.33%), Fitzpatrick skin type V or VI, and reported an average DLQI of 6.17 ± 7.40. Hyper- regions had higher MI compared to hypo- and NS (877.86 $\pm$ 19.54 vs. 702.27 $\pm$ 44.78, 826.67 $\pm$ 40.1) however these differences were not significant. The rete ridge ratio (RRR) of normally pigmented skin was above 1 (1.39 $\pm$ 0.08) and higher compared to the hypo- or hyper-phenotype, 1.16 $\pm$ 0.14 ($p>0.05$), 1.10 $\pm$ 0.10 ($p<0.001$), respectively. Hyper- and hypo- sites lacked dermal appendages and had increased epidermal and dermal thickness vs. NS. Both dermal and epidermal pigment granules were observed in hyper- sites. DLE dyschromia in our population predominantly affects black females. Histologically, DLE dyspigmented skin showed fewer rete ridges which may explain a decreased epidermal barrier function. Treating DLE dyschromia is challenging, but identifying distinct dyschromic histomorphometric characteristics could reveal potential therapeutic targets. Future efforts may focus on molecular targets and prevention.

Abstract Category: Lupus Erythematosus

References:

1. Farley-Loftus R, Mahlberg M, Merola JF, et al. Generalized discoid lupus erythematosus. Dermatol Online J. 2009;15(8):18.

2. Panjwani S. Early diagnosis and treatment of discoid lupus erythematosus. J Am Board Fam Med. 2009;22(2):206-213.

3. Garza-Mayers AC, McClurkin M, Smith GP. Review of treatment for discoid lupus erythematosus. Dermatol Ther. 2016;29(4):274-283.

CHANGES IN ERYTHEMA AND SCALE TREND SIMILARLY OVER SIX MONTHS IN PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS

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Erythema comprises most of the Cutaneous Lupus Erythematosus Disease Area and Severity Index activity (CLASI-A) scoring, followed by scale. Comparing how CLASI-A erythema and scale scores change over time in relation to total CLASI-A scores in patients with cutaneous lupus erythematosus (CLE) would determine whether or not one component fluctuates more. Thus, we conducted a six-month prospective study of 115 CLE patients on standard-of-care therapies with regular two-month follow-up intervals to elucidate trends in erythema and scale. Patients were recruited from outpatient dermatology clinics at the University of Texas Southwestern Medical Center, Parkland Health, and the University of Pennsylvania from July 2018 to May 2023. The primary and secondary outcomes were mean change and mean percent change (MPC) of total CLASI-A, CLASI-A erythema, and CLASI-A scale between baseline and each follow-up visit. Predictor variables associated with disease activity trends were analyzed with linear mixed-effects modeling adjusted for baseline CLASI, time, and within-subject correlation. Mean and mean percent changes in CLASI-A over six months were -4.3±8.6 and -19.8%±72.0% for total CLASI-A, -2.7±5.9 and -20.4%±63.9% for CLASI-A erythema, and -1.1±2.9 and -16.4%±71.0% for CLASI-A scale, respectively. No significant differences existed between the MPC of CLASI-A erythema and scale at visit 4 (p=0.65). Mean changes of CLASI-A erythema and scale at visit 4 were -3.1±5.6 and -1.2±3.1 for White Non-Hispanic patients (n=39), -2.9±6.0 (p=0.21) and -1.3±3.0 (p=0.07) for Black patients (n=68), -1.5±3.0 and -0.4±1.1 for localized discoid lupus erythematosus (DLE) (n=34), -2.2±6.9 (p=0.14) and -1.2±3.6 (p=0.23) for generalized DLE (n=56), and -5.4±6.1 (p=0.60) and -2.2±2.9 (p=0.69) for subacute CLE (n=31), respectively. CLASI-A erythema and scale have similar 6-month trends in patients with CLE, even when divided by race/ethnicity or CLE subtype. Our results highlight that changes in erythema do not predominantly drive changes in total CLASI-A, despite erythema carrying more weight than scale.

Category: Lupus

TRUNCAL INVOLVEMENT IN LUPUS ERYTHEMATOSUS PANNICULITIS PATIENTS ARE LINKED WITH CALCINOSIS CUTIS

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Lupus erythematosus panniculitis (LEP) is a rare variant of chronic cutaneous lupus that typically presents as indurated nodules or plaques. Calcinosis cutis (CC) is a potential complication of this disease with limited treatment modalities and significant quality of life issues. The prevalence and risk factors of CC in LEP are not well understood. Thus, we conducted a retrospective cohort study on patients with LEP to quantify the rate of those with CC and to identify risk factors associated with presence of CC. This study analyzed data from 26 LEP patients recruited in outpatient dermatology clinics at University of Texas Southwestern Medical Center and Parkland Health from April 2009 to August 2024. Primary outcome measure was presence of CC based on clinical diagnosis from a dermatologist, biopsy, and/or radiographic imaging. Data collected included demographics, smoking history, disease duration, treatments, lesion location, pathology, and autoantibodies. Predictor variables associated with CC were analyzed either by Mann-Whitney U or Fisher's exact tests. 11/26 (42.6%) LEP patients had CC during the evaluation period. LEP patients with truncal lesions had calcinosis cutis at a higher rate (9/11, 81.8%) compared to those without (5/15, 33.3%) ($p=0.02$). Other predictor variables including autoantibodies, smoking history, demographics, or medications were not significantly associated with CC. This study was limited by its single-center design, retrospective nature, and small sample size. Nonetheless, with a larger group of LEP patients than previously investigated, we reported almost half of LEP patients developed CC and identified truncal LEP lesions being associated with CC. CC is a common complication of LEP that requires close monitoring by clinicians. Larger longitudinal studies are needed to confirm these findings and better understand temporal development of CC in LEP patients.

Category: Lupus

GEOGRAPHIC DISTRIBUTION AND ENVIRONMENTAL TRIGGERS OF CUTANEOUS LUPUS ERYTHEMATOSUS IN MASSACHUSETTS FROM 2018-2023

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Cutaneous Lupus Erythematosus (CLE) is a form of lupus erythematosus that primarily affects the skin, representing a localized dermatologic manifestation without systemic involvement. The exact causes of CLE are not known, and little research has been done studying patients who have CLE and their exposures to environmental toxins from superfund sites and toxic release inventory sites. Superfund sites and toxic release inventory sites are EPA recorded contaminated sites that contain hazardous materials. This study aimed to determine whether CLE cases aggregate near superfund and toxic release inventory sites by investigating the geographic distribution of CLE in Massachusetts. Data from Massachesetts from 2018-2023 was obtained from TriNetX. TriNetX is a global health analytics platform that provides de-identified clinical data from healthcare institutions. There were 1,444 with a diagnosis of CLE who were included in the study, and 116 different zip codes. Data on superfund sites and toxic release inventory sites were found via the United States Environmental Protection Agency database. ArcGIS, a geographic information system (GIS) mapping software, was used to analyze geographic distribution of CLE in Massachusetts and to determine distances and zip codes of superfund and toxic release inventory sites. There was a presence of clustering of CLE cases in Massachusetts, especially in the zip codes of 01005 (33 cases in a population of 4,837), 01009 (24 cases in a population of 699), 01068 (16 cases in a population of 1585) and 01083 (11 cases in a population of 2539). In addition, a Pearson correlation was conducted and was -0.67, which found a strong association between CLE and short distance (less than 85 kilometers) from a superfund and toxic release inventory sites. This study provides closer insight into the correlation between CLE and exposure to environmental toxins.

Category: Lupus

SYSTEMIC LUPUS ERYTHEMATOSUS IS A RISK FACTOR FOR HAVING MULTIPLE SUBTYPES OF CUTANEOUS LUPUS ERYTHEMATOSUS

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Cutaneous lupus erythematosus (CLE) is an autoimmune skin disease that can be classified into acute, subacute, or chronic subtypes. The frequency and associated risk factors of having multiple CLE subtypes have not been well characterized. We performed a cross-sectional study of 319 CLE patients recruited in outpatient dermatology clinics at University of Texas Southwestern Medical Center and Parkland Health between January 1, 2009 and December 31, 2021. Patients below 18 years of age or with unknown CLE subtype information were excluded. Univariate and multivariable analyses were performed to identify significant risk factors associated with having multiple CLE subtypes. 59 patients (18.5%) were diagnosed with two or more CLE subtypes. Univariate analyses identified SLE diagnosis [86.4% (≥1 CLE subtype) vs. 45% (1 CLE subtype), $p<0.001$]; history of positive anti-nuclear antibody (89.8% vs. 68.8%, $p<0.001$); arthritis (50.8% vs. 25%, $p<0.001$); renal disorder (33.9% vs. 13.5%, $p<0.001$); and serositis (7.31% vs. 18.6%, $p=0.01$) as risk factors associated with multiple CLE subtypes. In the multivariable analysis, only SLE diagnosis was statistically significant (odds ratio: 5.09, 95% CI: 1.89-13.68, $p<0.01$). Thus, our study showed that almost one out of five CLE patients have multiple CLE subtypes, with SLE diagnosis being a significant risk factor. Clinicians can monitor CLE patients for developing multiple subtypes and account for systemic manifestations and laboratory abnormalities associated with SLE diagnosis. Limitations include the single-center cross-sectional nature and small sample size. Future directions include prospective studies that examine the temporal progression of developing multiple CLE and its associated risk factors. We also plan to examine whether having multiple CLE subtypes affects patient outcomes, such as treatment response and quality of life.

Category: Lupus

INTER-RATER AND INTRA-RATER RELIABILITY OF THE CUTANEOUS LUPUS ACTIVITY-INVESTIGATOR GLOBAL ASSESSMENT-REVISED (CLA-IGA-R) INSTRUMENT

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Background: Valid and clinically meaningful outcome measures to assess the efficacy of emerging therapies for Cutaneous Lupus Erythematosus (CLE) remains an unmet need. There has been a regulatory call for an Investigator's Global Assessment (IGA)-based instrument to complement current instruments. IGA-based instruments also offer a feasible tool for use in clinical practice and represent an easily interpreted outcome for both patients and providers across specialties (i.e., clear/almost clear). The Cutaneous Lupus Activity-Investigator Global Assessment-Revised (CLA-IGA-R) was developed by our group and it is currently in use for multiple phase 2/3 clinical trials. The CLA-IGA-R is a 5-point scale (*0=clear, 1=almost clear; 2=mild; 3=moderate; 4=severe*) that evaluates the severity/activity of CLE in three subscales: (a) erythema, (b) other morphologic characteristics (OMC) (i.e., scale, infiltration, erosion) and (c) hair follicle involvement via follicular plugging (an exploratory subscale).

Objective: To assess the inter- and intra- rater reliability of the erythema and OMC subscales of the CLA-IGA-R.

Methods: A hardcopy booklet with 222 high-resolution photographs of CLE lesions was provided to six dermatology experts. Four dermatologists and two dermatologist-rheumatologists completed a standardized investigator training module and were then asked to score the severity of lesions using the CLA-IGA-R. Inter-rater reliability was assessed using intraclass correlation (ICC). Inter-rater reliability results for erythema were stratified by Fitzpatrick skin types: 1-2, 3-4, and 5-6. Intra-rater reliability was evaluated using a linear mixed-effects model.

Results: Overall, the inter-rater ICC for erythema and OMC were 0.901 and 0.902, respectively. In subgroup analysis, the inter-rater ICC for erythema was 0.888 Fitzpatrick skin types 1-2, 0.837 for Fitzpatrick skin types 3-4, and 0.859 for Fitzpatrick skin types 5-6. Intra-rater ICC was 0.774 for erythema and 0.700 for OMC.

Conclusion: The erythema and OMC domains of the CLA-IGA-R demonstrated high inter-rater and intra-rater reliability. Evaluation of the responsiveness of CLA-IGA-R is underway.

Abstract Category: Lupus

ADVERSE EVENTS ASSOCIATED WITH ANIFROLUMAB

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Anifrolumab, a monoclonal antibody against the type I interferon receptor, was FDA-approved in 2021 for the treatment of moderate-to-severe systemic lupus erythematosus (SLE). Since that time, it has shown promise particularly for cutaneous and musculoskeletal manifestations in lupus.[1] Studies on the safety profile for anifrolumab have overall been favorable, but the medication is not without side effects. A meta-analysis of the MUSE, TULIP-1, and TULIP-2 trials demonstrated that 86.9% of patients receiving anifrolumab experienced at least one adverse event (AE).[2] However, AEs led to discontinuation in only 4.1% of patients receiving anifrolumab.[2] Herein, we present a case series of 16 patients treated with anifrolumab at Boston Medical Center, the largest safety-net hospital in New England. All patients had a diagnosis of SLE and received monthly infusions of anifrolumab 300mg. The mean and median number of total infusions administered was 10 and 8, respectively. Within our cohort, 8 patients (50%) experienced AEs related to anifrolumab. Four patients experienced serious AEs – 2 with pneumonia, 1 with headaches, and 1 with serum sickness-like reaction – while four experienced milder AEs – 2 with upper respiratory infections, 1 with prolonged sweating, and 1 with oral herpes outbreaks. Among the 16 patients in our cohort, 8 patients (50%) discontinued anifrolumab, 4 (25%) of which due to AEs. Other reasons for discontinuation were logistical difficulties (6%), loss of health insurance (6%), inadequate effect (6%), and pregnancy (6%).

Our results demonstrate a lower proportion of patients experiencing AEs from anifrolumab – but a higher proportion discontinuing the medication due to AEs – as compared to the MUSE, TULIP-1, and TULIP-2 trials.[3,4,5] We postulate that these differences may be related to characteristics of our patient population, such as complex comorbidities, number of concomitant systemic medications, and socioeconomic factors. Additional studies on AEs associated with anifrolumab are warranted.

Category: Lupus

References:

1. Loncharich MF, Anderson CW. Interferon Inhibition for Lupus with Anifrolumab:
2. Tummala R, Abreu G, Pineda L, et al. Safety profile of anifrolumab in patients with active SLE: an integrated analysis of phase II and III trials. *Lupus Sci Med*. 2021;8(1):e000464. doi:10.1136/lupus-2020-000464
3. Furie R, Khamashta M, Merrill JT, et al. Anifrolumab, an Anti-Interferon-α Receptor Monoclonal Antibody, in Moderate-to-Severe Systemic Lupus Erythematosus. *Arthritis Rheumatol*. 2017;69(2):376-386. doi:10.1002/art.39962
4. Furie RA, Morand EF, Bruce IN, et al. Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomised, controlled, phase 3 trial. *Lancet Rheumatol*. 2019;1(4):e208-e219. doi:10.1016/S2665-9913(19)30076-1
5. Morand EF, Furie R, Tanaka Y, et al. Trial of Anifrolumab in Active Systemic Lupus Erythematosus. *N Engl J Med*. 2020;382(3):211-221. doi:10.1056/NEJMoa1912196
Critical Appraisal of the Evidence Leading to FDA Approval. *ACR Open Rheumatol*. 2022;4(6):486-491. doi:10.1002/acr2.11414

ASSESSING PGY-4 DERMATOLOGY RESIDENT COMFORT WITH ORDERING AND MANAGING INFUSION THERAPIES

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Intravenous immunoglobulin (IVIG), methylprednisolone, infliximab, rituximab, and anifrolumab infusions are commonly used to treat rheumatologic-dermatologic conditions including lupus erythematosus, psoriasis and psoriatic arthritis, dermatomyositis, vasculitis, and others. However, many of these medications have potentially severe side effects and managing infusion orders requires a particular set of knowledge. To better assess the comfort level of dermatology residents with ordering and managing infusions and to identify a potential gap in knowledge, we developed a 10-question survey for PGY-4 dermatology residents that was distributed to dermatology residency programs across the United States. Participants were asked to include the number of times they ordered infusions in residency, whether they sign or pend orders, their comfort level ordering infusions and managing infusion side effects, which medications they felt most comfortable and least comfortable ordering and managing, and which medications, if any, they plan to utilize in future practice. Based on our survey results, we found that on a scale from 1 to 10 (1 indicating not comfortable at all and 10 indicating completely comfortable), the average comfort level of residents ordering infusions was 4.85 and the average comfort level managing infusion therapies was 4.45. Less than 10% (5/53, 9.43%) of participants felt completely comfortable ordering infusions, and less than 2% (1/53, 1.89%) felt completely comfortable managing side effects from infusions. If a resident reported they had placed at least one infusion order during residency, the reported comfort level increased by 3.58 points. Notably, we found that while residents generally report they are not comfortable ordering and managing infusions, over 90% (48/53, 90.6%) indicated that they plan to order infusions in their future practice. The results of this survey suggest a gap in PGY-4 dermatology resident knowledge which could be addressed by increasing resident involvement in placing infusion orders and managing patients with complex dermatologic disease.
Teaching Point: N/A (clinical cases only)

ASSESSING HOW AUTOIMMUNE CONNECTIVE TISSUE DISEASE DIAGNOSES AND TREATMENTS AFFECT REPRODUCTIVE DECISIONS

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Connective tissue diseases (CTDs) are chronic, systemic disorders that disproportionately affect women, often present in the third and fourth decade[1], and can require treatments that may impact reproductive health, posing challenges for women of childbearing age.[2,3] These patients face not only the physical and emotional burdens of their diseases but also uncertainties about pregnancy and the potential teratogenic effects of treatments. There is a paucity of dermatology literature examining the impact of CTDs on women's reproductive decisions. We therefore conducted an IRB-approved, anonymous survey study at an academic dermatology clinic. In our initial cohort of twenty-seven biological females ages 19-45 with dermatomyositis, scleroderma, lupus, morphea, eosinophilic fasciitis, lichen sclerosus, or vasculitis, we found that nearly half (44%, N=12) reported that their diagnosis directly influenced their decision to have children, while 48% (N=13) said it did not and 7% (N =2) were unsure. Similarly, 48% (N=13) indicated that their treatments influenced this decision. When asked what the most influential factor was regarding the decision to pursue pregnancy, 37% (N=10) cited concerns that the therapy/therapies they were on could affect their pregnancy or baby. While most patients (82%, N=22) felt their questions regarding fertility and pregnancy were satisfactorily answered, only 33% (N=9) were seen by a high-risk obstetrician, and over a quarter (26%, N=7) reported they did not currently have an obstetric provider. Out of all participants, 19% (N =5) said they received pregnancy information from their dermatologist. These results highlight the profound impact both diagnosis and treatment of CTDs have on women's reproductive decisions. Concerns about active disease symptoms, heritability, and treatment safety all influence these decisions. Our findings underscore the need for open patient-dermatologist communication on these issues, including referrals to obstetricians where appropriate, and additional data on the use of newer biologic therapies in pregnancy.

Category: Miscellaneous rheumatic skin disease

References:

1. M. Gaubitz, Epidemiology of connective tissue disorders, *Rheumatology*, Volume 45, Issue suppl_3, October 2006, Pages iii3–iii4, https://doi.org/10.1093/rheumatology/kel282
2. Ateka-Barrutia O, Nelson-Piercy C. Connective tissue disease in pregnancy. *Clin Med (Lond)*. 2013;13(6):580-584. doi:10.7861/clinmedicine.13-6-580
3. Silva CA, Bonfa E, Østensen M. Maintenance of fertility in patients with rheumatic diseases needing antiinflammatory and immunosuppressive drugs. *Arthritis Care Res (Hoboken)*. 2010;62(12):1682-1690. doi:10.1002/acr.20323

A SYSTEMATIC SCOPING REVIEW TO IDENTIFY IMMUNOSTIMULATORY HERBAL SUPPLEMENTS THAT MAY FLARE AUTOIMMUNE SKIN DISEASE

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Autoimmune skin diseases are often exacerbated by external factors, including immunostimulatory herbal supplements (IHS). This risk is not widely known by the public, and there is an increased prevalence of IHS use among patients with autoimmune skin diseases compared to healthy controls. Moreover, the sales volumes and variety of commercially available IHS have continued to grow since the COVID-19 pandemic. For this reason, we conducted a systematic scoping review in accordance with PRISMA-ScR guidelines to generate a comprehensive list of IHS that may trigger or exacerbate autoimmune skin disease. A standardized string structured as [Immune Terms] AND [Herbal Supplement Terms] AND ([Autoimmune Terms] OR [Skin Terms]) was used to search PubMed, yielding 8,715 abstracts. After initial screening, 153 full-text articles were reviewed in detail. 97 studies were included in the final analysis. In addition to well-known IHS including spirulina, elderberry, ashwagandha, echinacea, chlorella, and alfalfa, this systematic scoping review expanded the list to 49 different herbal supplements that have the potential to exacerbate autoimmune skin diseases based on in vitro, animal, or clinical data. The reviewed articles also demonstrated that patients often take herbal supplements without complete knowledge of their contents. This may occur because many supplements are contaminated with unlisted ingredients, marketed as blends, or named according to their intended effects without specifying their composition. Future work will focus on developing updated educational materials that incorporate this expanded list of potentially harmful supplements to help educate patients on what to avoid. Further in vitro studies are needed to elucidate the specific biological effects of these supplements on patients with autoimmune skin diseases.

Abstract Category: Miscellaneous rheumatic skin disease

DYSTROPHIC CALCINOSIS CUTIS COMPLICATING MORPHEA: A CASE SERIES

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We present a series of 4 patients with morphea complicated by dystrophic calcinosis cutis, a rare manifestation of disease damage. We performed a retrospective review of patients at UCSF via de-identified search (EMERSE)(1), using morphea and calcinosis-related terms. 412 charts were screened leading to confirmation of 72 patients with morphea (32 pediatric and 40 adult onset), with identification of 4 cases of morphea complicated by calcinosis cutis (2 male, 2 female). Average age of morphea onset in calcinosis-affected cases was 47.5 years, with one case of pediatric onset. Average latency between morphea and calcinosis was 6 years amongst patients with adult onset morphea; latency was not available for the patient with pediatric onset. Affected morphea subtypes included 2 cases of linear morphea (one involving upper only and one involving upper and lower extremities), 1 case of morphea profunda involving upper and lower extremities, and 1 case of unknown subtype; calcinosis affected lower extremities in 3 cases and the upper extremity in 1 case. All 4 patients had a history of smoking and two had a history of local trauma. Three cases were complicated by all of the following: ulceration, secondary infection, and pain; status of the remaining case is unknown. Three patients were treated with surgical excision with resolution, one patient with minocycline with no response, and one patient with topical sodium thiosulfate with partial improvement. The favorable response to excision in this series aligns with prior observations (2). The overall prevalence of dystrophic calcinosis in the present morphea population was 5.6% and tended to occur in deep/severe variants; when present the calcinosis also tended to be symptomatic. These findings suggest dystrophic calcinosis may be more common and impactful in morphea than previously recognized and prompts us to expand study to affiliate sites in the future.

TEACHING POINT: Calcinosis cutis is considered a rare complication of morphea but was present in 5.6% of the current patient series.

CATEGORY: SCLEROTIC SKIN DISEASE

References:

1. Hanauer DA, Mei Q, Law J, Khanna R, Zheng K. Supporting information retrieval from electronic health records: A report of University of Michigan's nine-year experience in developing and using the Electronic Medical Record Search Engine (EMERSE). J Biomed Inform. 2015 Jun;55:290-300. PMID: 25979153.
2. Brockman R, Wills A, Greiling TM, Leitenberger S, Fett N. Calcinosis cutis arising in morphea: a case series. Dermatol Online J. 2020 Jun 15;26(6):13030/qt26c9m00s. PMID: 32815688.

CARDIOVASCULAR AND RENAL COMPLICATIONS IN SYSTEMIC SCLEROSIS: FINDINGS FROM A LARGE DATABASE-DRIVEN COHORT STUDY

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Systemic sclerosis (SSc) is a rare autoimmune disease with multi-system complications, but prior studies on its cardiac, renal, and vascular impacts have been limited by a lack of comprehensive longitudinal data. This study thus aims to assess the incidence of complications such as myocardial infarction (MI), atrial fibrillation (AF), pulmonary embolism (PE), and chronic kidney disease (CKD) in patients with SSc compared to controls without SSc. Using the TriNetX database, we analyzed patient records records from January 2014 to April 2024. Patients with an ICD-10 code for SSc were matched with controls based on age, sex, hypertension, diabetes, smoking, hyperlipidemia, and malignancy history. After matching, 136,727 patients were included in both the SSc and control cohorts. 5-year, 10-year, and lifetime risk differences (RD) and relative risks (RR) with 95% confidence intervals (CIs) were calculated using logistic regression. Patients with SSc had significantly higher risks of all complications compared to controls for all time periods. For myocardial infarction, the 10-year relative risk was 2.19 (95% CI 2.08–2.30), while the risk of atrial fibrillation was increased by 1.59 times (95% CI 1.55–1.63). The lifetime incidence of CKD in the SSc cohort was also higher (RR 1.86; 95% CI 1.81–1.92). Additionally, patients with SSc were more than twice as likely to develop pulmonary embolism (RR 2.56; 95% CI 2.38–2.75) within 5 years. The most common complications in the SSc cohort were atrial fibrillation (lifetime risk 10.6%) and CKD (lifetime risk 10.1%). Our results demonstrate patients with SSc face significantly elevated risks of developing MI, AF, stroke, PE, VTE, and CKD compared to controls. These findings underscore the need for careful long-term monitoring and management of cardiovascular and renal complications in patients with SSc.

Abstract Category: Sclerotic skin disease

DISEASE ACTIVITY IN RELATION TO SERUM CXCL9 LEVELS IN A PATIENT WITH GENERALIZED MORPHEA/EXTRAGENITAL LICHEN SCLEROSUS OVERLAP

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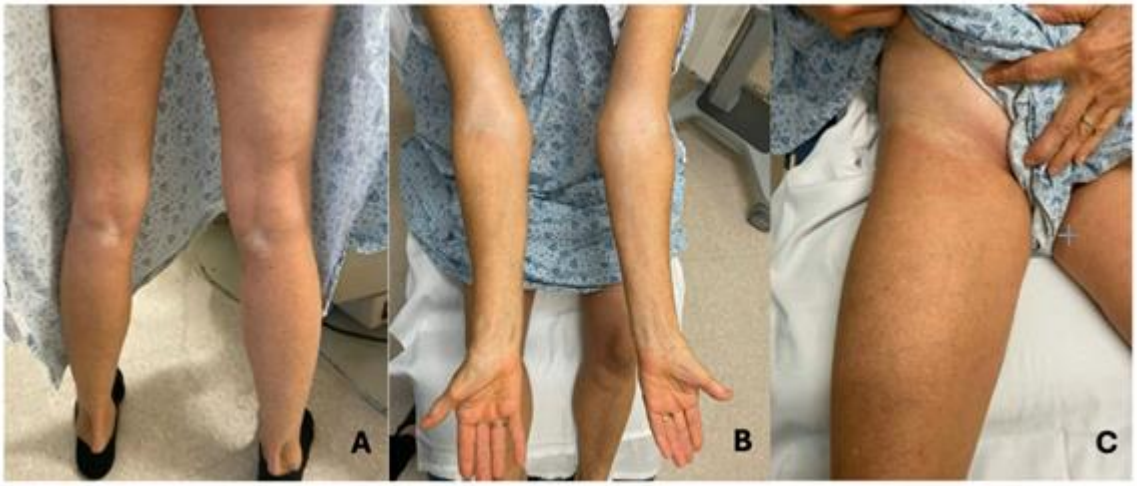
Morphea is a fibrosing autoimmune condition in which initial inflammation can lead to permanent damage. It can be difficult to discern disease activity from physical examination at a single point in time, making treatment decisions challenging. CXCL9, a cytokine involved in chemotaxis, leukocyte differentiation, and tissue extravasation has emerged as a potential biomarker for disease activity. We describe a 65-year-old woman with a two-year history of skin changes with associated pruritus and burning sensation. Physical examination demonstrated shiny, white-pink plaques on her neck and back; ivory white plaques on her axillae, breasts, medial thighs, antecubital fossae, popliteal fossae, and hip girdle, with variable induration and pink inflammatory border (Figure 1). Punch biopsy was consistent with morphea, and clinical examination demonstrated generalized morphea/extragenital lichen sclerosus overlap phenotype. Systemic treatment was initiated with subcutaneous methotrexate (25 mg weekly) and oral dexamethasone (4 mg given two days/week), but during her first two months of therapy, the patient experienced worsening dysesthesia and developed contracture. A serum CXCL9 level from this timepoint was elevated to 2,376 pg/ml (normal < 647 pg/ml). Pulsed dexamethasone was replaced with an oral prednisone taper, with daily dosing starting at 1.2 mg/kg, while methotrexate was continued. One month later, the patient reported notable improvement with decreased itch and increased range of motion. Nevertheless, CXCL9 level was paradoxically higher at 5,301 pg/ml. With two more months of treatment, the patient had continued clinical improvement, and CXCL9 decreased to 1,625 pg/ml. This case demonstrates that severe, generalized morphea can be associated with very high levels of CXCL9, that this serum cytokine can decrease as a patient improves, but serum levels may lag clinical fluctuations. Until more data is collected, this test should not be relied upon to inform treatment decisions. Clinical assessment and close monitoring remain the gold standard for morphea assessment.

Teaching point: CXCL9 is a promising biomarker for tracking disease activity in morphea, but clinical examination remains the gold standard for assessment of disease activity until CXCL9 is better validated.

Category: Sclerotic skin disease

Figure 1: A 65-year-old female with a 2-year history of white, sclerotic plaques on her popliteal fossa, antecubital fossa, and hip girdle with inflammatory border (A, B, C).



EXPLORING NEUROLOGICAL MANIFESTATIONS AND MRI FINDINGS IN ADULT-ONSET EN COUP DE SABRE: A RETROSPECTIVE REVIEW OF 32 PATIENTS

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Abstract
Frontoparietal linear morphea, known as En Coup de Sabre (ECDS), is a rare form of localized scleroderma primarily affecting the face and scalp. Due to lesion location, neurologic manifestations can be associated and supported by neuroimaging.[1–6] Because ECDS is primarily diagnosed in childhood, existing literature focuses on pediatric ECDS.[1,3,7,8] Research on neuromanifestations in adults is scarce. Our study analyzes neurologic symptoms, neuroimaging findings, and neurologic care in an adult ECDS cohort. We identified 32 patients >=18-years-old with ECDS and brain MRI using the Mass General Brigham Research Patient Data Registry. Mean age was 50.94 years, with 28 out of 32 patients (88%) being women. Mean time between onset of symptoms noticed by the patient and clinical diagnosis was 95.4 months (7.96 years) with median time of 6 months. In total, 25 patients (78%) reported neurologic symptoms. Headache was the most reported neurologic symptom (65%), followed by seizures (19%) and dizziness (9%), with some patients reporting multiple symptoms. The three most common MRI findings were white matter hyperintensities in 15 patients (46%), no abnormal findings in 10 patients (31%), and vascular irregularities in 5 patients (15%). Despite the frequency of neurologic symptoms and MRI abnormalities, only 18 patients (56%) were evaluated by a neurologist. Neurology evaluation was prompted by imaging findings in 68% of patients and neurological symptoms in 78% of patients. Two patients evaluated by neurology had neither symptoms nor imaging abnormalities. Of 16 patients evaluated by a neurologist due to symptomatology or imaging abnormalities, neurology felt morphea was responsible for the patient's findings in 50% of cases. Additional studies are needed in larger patient populations. However, this study represents the largest cohort evaluating neurologic manifestations in adult-onset ECDS to date and lends insight into the role for multidisciplinary care in managing these patients.

Abstract Category: Sclerotic skin disease

1. Amaral TN, Marques Neto JF, Lapa AT, Peres FA, Guirau CR, Appenzeller S. Neurologic Involvement in Scleroderma en Coup de Sabre. Autoimmune Dis. 2012;2012(1). doi:10.1155/2012/719685
2. Fain ET, Mannion M, Pope E, Young DW, Laxer RM, Cron RQ. Brain cavernomas associated with en coup de sabre linear scleroderma: Two case reports. Pediatr Rheumatol Online J. 2011;9:18. doi:10.1186/1546-0096-9-18
3. Chiu YE, Vora S, Kwon EKM, Maheshwari M. A Significant Proportion of Children with Morphea En Coup De Sabre and Parry-Romberg Syndrome Have Neuroimaging Findings. *Pediatr Dermatol*. 2012;29(6):738-748. doi:10.1111/PDE.12001
4. Nguyen K, Atty C, Ree A. Linear scleroderma en coup de sabre presenting with seizures. *Radiol Case Rep*. 2020;15(11):2164-2170. doi:10.1016/J.RADCR.2020.08.011
5. Duman IE, Ekinci G. Neuroimaging and clinical findings in a case of linear scleroderma en coup de sabre. *Radiol Case Rep*. 2018;13(3):545-548. doi:10.1016/J.RADCR.2018.02.001
6. Pinho J, Rocha J, Sousa F, et al. Localized scleroderma en coup de sabre in the Neurology Clinic. *Mult Scler Relat Disord*. 2016;8:96-98. doi:10.1016/j.msard.2016.05.013
7. Holland KE, Steffes B, Nocton JJ, Schwabe MJ, Jacobson RD, Drolet BA. Linear scleroderma en coup de sabre with associated neurologic abnormalities. *Pediatrics*. 2006;117(1). doi:10.1542/PEDS.2005-0470
8. Zhuo X, Fang F, Gong S, et al. [Analysis of clinical and imaging features of 6 cases of linear scleroderma en coup de sabre with central nervous system involvement in children]. *Zhonghua Er Ke Za Zhi*. 2022;60(11):1147-1152. doi:10.3760/CMA.J.CN112140-20220429-00396

OUTSTANDING QUESTIONS IN URTICARIAL VASCULITIS

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Case: A 50-year-old male presented to the clinic with a 2-year history of itchy, painful hives on his arms, legs, and trunk, unresponsive to diphenhydramine, cetirizine, or loratadine and accompanied by polyarthritis, anemia, and widespread lymphadenopathy. A skin biopsy revealed neutrophilic inflammation, dermal edema, and vascular injury. Laboratory tests showed Coombs-positive autoimmune hemolytic anemia, low complement levels, and a positive lupus anticoagulant antibody. Diagnosed with hypocomplementemic urticarial vasculitis (UV), he was treated with colchicine and oral Prednisone (1 mg/kg), resulting in complete remission. **Background:** UV presents as urticarial lesions lasting over 24 hours, accompanied by leukocytoclastic vasculitis.[1] Due to its varying clinical appearance, a biopsy is often needed for diagnosis.[2] However, there is no consensus on UV dermatopathology, as its pathogenesis is poorly understood. UV is often mistaken for chronic spontaneous urticaria, resulting in delayed treatment and higher patient morbidity.[3] More research is needed to improve the understanding of biopsy findings in UV. **Objectives:** An international collaboration involving 9 university hospitals in Europe and the United States aims to identify UV patients' most common histological features and determine they correlate with clinical signs. **Methods:** Retrospective review of suspected or confirmed UV cases with available histopathology from the past ten years at each center. Cases showing only leukocytoclasis or neutrophilic urticarial dermatosis will be excluded. Two dermatopathologists will independently review the remaining sections. Clinical presentations, comorbidities, and treatments will also be analyzed. **Discussion:** UV may vary, appearing as fixed erythematous papules with post-inflammatory pigmentation or as purpuric or livedoid lesions. Also, it can present systemic symptoms and extracutaneous involvement. UV histopathology is not fully defined, and sometimes, frank vasculitis may not be evident. **Conclusion:** Further research and discussion on histopathological findings of UV are crucial to improving the accuracy and speed of diagnosis, leading to better patient treatment outcomes.

Teaching point:
No defined consensus exists for the dermatopathology of urticarial vasculitis (UV) since the pathogenesis of UV is poorly investigated and understood so an international multi-center collaboration is ongoing to answer the question: “What are the main histopathological features presented on a skin biopsy of a UV lesion?”

Category: Vasculitis and Clinical case

References:

1) Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The international EAACI/GA2LEN/EuroGuiDerm/APAAACI guidelinefor the definition, classification, diagnosis, and management of urticaria. Aller 2022;77:734-66.
2) Kolkhir P, Bonnekoh H, Kocatürk E, Hide M, Metz M, Sánchez-Borges M, et al. Management of urticarial vasculitis: A worldwide physician perspective. World Allergy Organ J 2020;13(3).
3. Bonnekoh H, Jelden-Thurm J, Allenova A, Chen Y, Cherrez-Ojeda I, Danilycheva I, Dorofeeva I, Jardim Criado RF, Criado PR, Gelincik Akkor A, Hawro T, Kocatürk E, Khoshkhui M, Metz M, Nasr I, Steć M, Zhao Z, Aulenbacher F, Salameh P, Altrichter S, Gonçalo M, Gimenez-Arnau A, Maurer M, Krause K, Kolkhir P. Urticarial Vasculitis Differs From Chronic Spontaneous Urticaria in Time to Diagnosis, Clinical Presentation, and Need for Anti-Inflammatory Treatment: An International Prospective UCARE Study. J Allergy Clin Immunol Pract. 2023 Sep;11(9):2900-2910.e21. doi: 10.1016/j.jaip.2023.06.030. Epub 2023 Jun 24. PMID: 37364667

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