RDS Abstract Book 2023

Oral Presentations

Session I:

Dermatomyositis

A NEW OUTCOME MEASURE FOR DERMATOMYOSITIS CLINICAL TRIALS: THE DERMATOMYOSITIS OUTCOMES FOR MUSCLE AND SKIN (DMOMS)

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The Total Improvement Score (TIS), which is used as the primary efficacy measure in dermatomyositis (DM) clinical trials, lacks a skin-specific measure. However, skin is a defining feature of DM. This study evaluated a new composite outcome measure, the Dermatomyositis Outcomes for Muscle and Skin (DMOMS), which consists of improvement from baseline in Manual Muscle Testing (MMT), Physician Global Assessment (PGA) and Patient Global Assessment (PtGA), all weighted as in TIS except a 50% weight increase in PtGA, and the Cutaneous Dermatomyositis Disease Area and Severity Index-Activity (CDASI-A), weighted equally to MMT. Each component was scored on a point-based scale as indicated in Table 1. All component scores were collected at Baseline and Weeks 16-52 in the lenabasum phase 3 study. Patients that had ≥10-point improvement in MMT scores or ≥8-point improvement in CDASI-A scores at each timepoint from Baseline were considered responders. The study population consisted of 174 DM patients with 81% female and 75% Caucasian. Mean (SD) age was 51.9 (12.2) years. Mean change at each timepoint in DMOMS and TIS for both skin and muscle responders and non-responders is depicted in Figure 1. Compared to TIS, DMOMS captures greater improvement in both muscle and skin response, without any increase in score in non-responders. DMOMS may perform well as an outcome measure in DM trials that include patients with both muscle and skin involvement.

Abstract Category: Dermatomyositis

DYSREGULATED PATHWAYS AND POTENTIAL BIOMARKERS IN DERMATOMYOSITIS PLASMA-DERIVED EXTRACELLULAR VESICLES

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Plasma-derived DNA-containing EVs have been shown to induce STING-mediated inflammation in dermatomyositis (DM), but their protein content is not well characterized. We collected EVs from plasma of 17 DM patients and 5 controls and analyzed their content by mass-spectrometry. Sixty-seven proteins were uniquely detected in the patient cohort. Thirty-five were differentially expressed, of which 13 were upregulated and 22 downregulated. Over-representation analysis found unique and upregulated proteins enriched for myeloid mediated immunity, glutathione metabolism, nucleic acid synthesis and vesicle transport pathways. Downregulated proteins were enriched for the classical and lectin complement pathways. The diminution of complement components in vesicles may reflect its abundance in target tissues but may also reflect host inability to circulate these molecules to damaged tissue, which in a chronic stage of disease may have a protective role. Using machine learning (random forest algorithm) 15 proteins were identified as biomarkers that distinguish patients with DM from controls. Of these, the following were validated by ELISA in a separate cohort: The antioxidant enzyme glutathione peroxidase 3 (GPX3) was significantly less abundant in patients' EVs ($p = 0.04$) suggesting DM patients may be susceptible to oxidative stress due to defective transport of GPX3 by EVs. Two complement proteins, Ficolin-2 (FCN2) and SERPING1 were significantly less abundant in patients' EVs ($p = 0.007$ and 0.006 respectively). Finally, surfactant protein B (SFTPB) was expressed almost exclusively in patients with lung disease, rendering it a possible marker for pulmonary involvement. Its assessment in plasma of DM patients with ILD revealed significantly higher abundance than in plasma of both healthy controls and DM patients without pulmonary disease ($p<0.0001$). In conclusion, our findings indicate GPX3, FCN2 and SERPING1 as biomarkers of disease in DM. SFTPB is a potential biomarker for pulmonary involvement in DM.

Teaching point: These findings, along with a growing body of evidence, suggest roles for EVs as disease biomarkers and prompts further mechanistic studies to elucidate their role not only in plasma, but also in muscle and skin.

Category: Dermatomyositis.

RAPID IMPROVEMENT IN RECALCITRANT CUTANEOUS JUVENILE DERMATOMYOSITIS WITH ANIFROLUMAB

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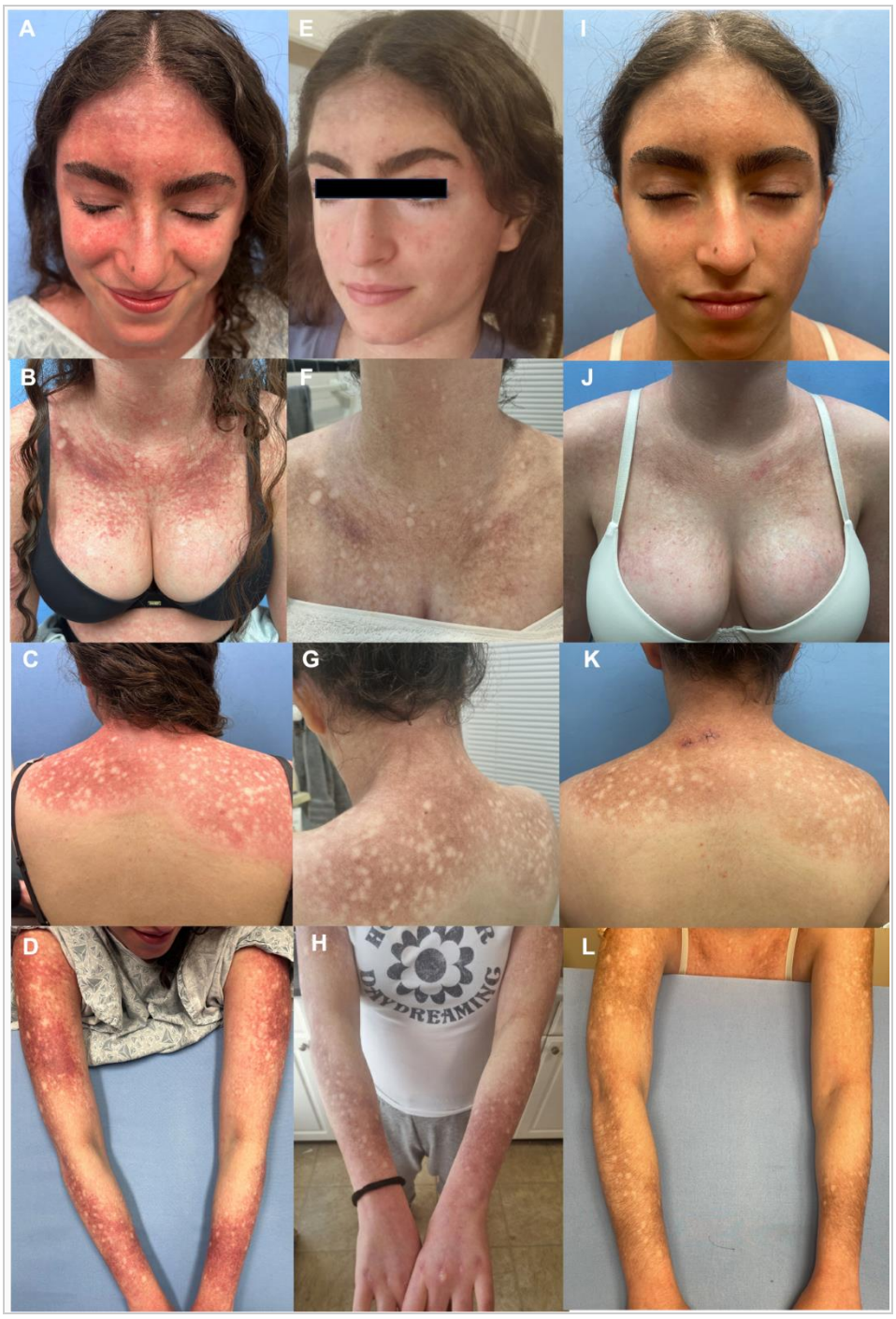
Juvenile dermatomyositis (JDM) is an idiopathic inflammatory myopathy of childhood that manifests with proximal muscle weakness and varying degrees of extramuscular pathology. While muscle disease is often responsive to first-line systemic corticosteroids and traditional steroid-sparing immunosuppressants, cutaneous involvement in JDM may persist, precluding complete disease remission. Recent transcriptomic analyses have demonstrated striking upregulation of type I IFN-stimulated genes in the peripheral blood, muscle, and lesional skin of JDM patients, with higher IFN scores corresponding to increased disease severity. As such, type I IFN has increasingly emerged as an attractive therapeutic target for both adult and juvenile DM patients, although FDA-approved therapies are currently lacking. Herein, we describe the case of a 14-year-old female who presented to our pediatric Rheumatology-Dermatology Program at Boston Children's Hospital with a six-year history of severe, refractory anti-TIF-1γ JDM. Despite adequate trials of systemic steroids, hydroxychloroquine, methotrexate, mycophenolate mofetil, cyclosporine, tacrolimus, tofacitinib, rituximab, and intravenous immunoglobulin (IVIg), she reported minimal improvement in her cutaneous disease (Figure 1, A-D). Given the patient's elevated serum IFN-beta levels (8 pg/mL, normal <=2 pg/mL), a trial of anifrolumab, a monoclonal antibody targeting type I IFN receptor subunit 1, was considered. After potential risks were reviewed, the patient and her family opted to pursue treatment. Within 72 hours of undergoing her first infusion of anifrolumab, the patient noted dramatic symptomatic improvement in her eruption and provided home photos demonstrating brisk resolution of erythema (Figure 1, E-H). Upon follow-up in clinic 56 days later, further improvement in erythema was noted, as codified by a significant reduction in the Cutaneous Dermatomyositis Disease Area and Severity Index Activity Score (CDASI-A) from 36 to 8 (Figure 2, I-L). To our knowledge, this is the first report of a case of refractory cutaneous DM treated with anifrolumab. The selection of anifrolumab was motivated by the patient's severe, disabling, and recalcitrant disease (including to JAK inhibition) and serologic evidence of elevated IFN-beta. Not only did the patient demonstrate significant clinical

improvement with just one infusion of anifrolumab (including a 28-point reduction in CDASI score where a reduction in 4-5 points is considered clinically meaningful), but the rapidity of clinical improvement within a matter of days was striking. We therefore aim to highlight the importance of the type I IFN axis in refractory cutaneous DM and highlight anifrolumab as a viable therapeutic option for those patients with contraindications to standard therapies.
Teaching point: Anifrolumab may be a promising therapeutic option for recalcitrant cutaneous dermatomyositis, particularly in those patients with contraindications to standard therapies.
Category: Dermatomyositis

Figure 1: Rapid improvement in cutaneous juvenile dermatomyositis disease activity with anifrolumab initiation

A 14-year-old girl with a six-year history of severe, refractory anti-TIF-1γ JDM presented with a diffuse photosensitive eruption and proximal muscle weakness. After an adequate five-month trial of tofacitinib (10mg twice daily) and IVIg (2mg/kg every four weeks), the patient experienced improvement in muscle strength and radiographic resolution of myositis, but continued to experience severe cutaneous disease activity as exemplified by persistent, deep red erythema and poikiloderma on her face (A), chest (B), abdomen, upper back (C), extensor arms (D) and anterolateral legs. Within 72 hours of receiving anifrolumab, the patient experienced dramatic improvement in erythema, as captured by patient-provided photos (E-H), which was sustained at clinic follow-up 56 days later (I-L).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CHARACTERIZATION OF SCALP INVOLVEMENT IN DERMATOMYOSITIS BASED ON MYOSITIS SPECIFIC ANTIBODY SUBSETS

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Category: Dermatomyositis

Word Count: 300/300

Myositis specific antibodies (MSA) have emerged as biomarkers in characterizing clinical phenotypes associated with subsets of dermatomyositis (DM). While scalp involvement is recognized as a relatively common clinical manifestation of DM, no studies to date have correlated it with MSA subsets.

In order to identify the prevalence of scalp DM in different MSA subsets, our institution's electronic medical records were screened to retrospectively identify patients diagnosed with DM between 2013 and 2023 using ICD-10 code M33.x. Patients with a diagnosis verified by the positive identification of an MSA were included for review. Dermatomyositis subsets were categorized into the following MSAs: NXP2, TIF1, Mi2, MDA5, SAE, ARS (including Jo1, PL-7, PL-12, EJ, OJ), and SRP. The presence of scalp involvement and its clinical features were then noted from patient charts.

A total of 91 patients with dermatomyositis and one MSA each were identified (17 M, 74F; mean age, [SD] 54.5y, [16]). Scalp involvement was reported in 60% of these patients (9M, 46F; mean age 56.5y), with clinical manifestations reported as erythema (58%), alopecia (42%), scaling (24%), and/or pruritis (36%). The highest prevalence of scalp dermatomyositis was seen in SAE (100%, [7/7]), SRP (100% [1/1]), TIF1 (85%, [11/13]) and NXP2 (74%, 14/19). A relatively lower prevalence of scalp DM, though still significant proportion, was observed in MDA5 (54%, [7/13]), Mi2 (40%, [6/15]), and ARS (45%, [10/22]).

In this study, we confirmed scalp involvement as a common manifestation of DM, occurring in 60% of DM patients. Our results are in line with previous estimates of 63%-82%. Limitations of our study design include small sample, dependence on physician assessment/documentation, and known variability in sensitivities of different myositis panels. Overall, our findings suggest that scalp involvement may be more likely to present in certain MSA subsets, though larger studies are needed to confirm this observation.

DETERMING THE PATHOGENICITY OF IL-21 AND CD8 T CELLS IN DERMATOMYOSITIS

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Aside from characteristic skin and muscle pathology, dermatomyositis may feature significant morbidity and mortality from inflammatory lung disease[1–4]. Recent research suggests CD4 T cell-derived IL-21 may be a driver of dermatomyositis disease[5–7]. IL-21 is best known as a product of follicular helper CD4 T cells stimulating B cells to promote antibody class-switching and affinity maturation[8–10]. However, CD8 T cells can express the IL-21 receptor (IL21R)[10], and IL-21 has been identified CD4 T cell-derived driver of CD8 T cell differentiation to tissue resident memory cells (T_{RM})[11]. T_{RM}, named for their abilities to be maintained independent of the circulation in non-lymphoid tissues, rapidly release effector molecules during antigen re-encounter[12–17]. Meanwhile, IL-21-producing CD4 T cells have been isolated from dermatomyositis patients with higher population correlating with increased disease activity[7]. In a mouse model of interstitial lung disease, IL-21 has been shown to induce CD8 T cell differentiation into effector cells driving pulmonary fibrosis.[5] This suggests IL-21-driven CD8 T cell differentiation may be an important, CD4 T Cell-dependent step in the overall pathogenesis of interstitial lung disease in dermatomyositis. Using single-cell RNAseq data from the lungs of a dermatomyositis patient[18], we show lung CD8 T cells highly express IL21R compared to CD8 T cells from the lungs of healthy controls. We also performed gene set enrichment analyses (GSEA) using these data, finding significant enhancement in the expression of T_{RM} genes in the CD8 T cells from the dermatomyositis lung when compared to healthy controls. These data suggest IL-21 could be an important, yet understudied driver of interstitial lung disease in dermatomyositis, and a potential therapeutic target. Specifically, IL-21 may act on CD8 T cells to drive differentiation into long-lived T_{RM} in the tissues of dermatomyositis, likely contributing to tissue destruction and clinical pathology.

Abstract Category: Dermatomyositis

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HOSPITALIZATION CHARACTERISTICS OF A U.S. MDA-5 DERMATOMYOSITIS COHORT: A RETROSPECTIVE SINGLE-INSTITUTION DESCRIPTIVE ANALYSIS

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Melanoma-differentiation associated-gene-5 (MDA-5) dermatomyositis (DM) is a heterogenous disorder that most characteristically presents with limited, if any, myositis, the potential for rapidly progressive interstitial lung disease (RP-ILD) and cutaneous ulcerations. This single-center pilot analysis characterizes initial presenting symptoms, hospitalization rates, admission indications, and interdisciplinary involvement among seventeen MDA-5-DM patients. Over 50% of patients presented initially to their primary care provider and the remainder to a rheumatologist (18%), dermatologist (12%), pulmonologist (6%), or the emergency room (12%). Median delay in diagnosis was 204 days (interquartile range: 360). Seventy percent of patients were hospitalized due to DM-related symptoms at least once, and on average 1.3 times (SD: 1.21). While laboratory-confirmed myositis was present in 41% of patients, weakness was among the most common indications for hospitalization (73%), followed by DM-related cutaneous eruption (55%) and pulmonary symptoms (41%). Eighty-three percent of first hospitalizations due to DM-related symptoms occurred prior to serology-confirmed MDA-5 diagnosis. Of this group, 58% were on immunosuppressants (corticosteroids in all but one patient on mycophenolate mofetil (MMF)) for suspected autoimmune disease other than MDA-5 DM, and median time from initial presentation to first hospitalization was 19 weeks (versus 2.9 weeks for those not on immunosuppressants). Twenty-seven percent of hospitalizations occurred in patients already diagnosed with MDA-5-DM; these were due to DM-related cutaneous eruption (50%), pulmonary symptoms (50%), and weakness (16.7%). Death occurred in 2 patients due to RP-ILD. All patients were given corticosteroids at some point during their disease course (median duration:19 mos). Other treatments included hydroxychloroquine (53%), intravenous immunoglobulin (47%), MMF (47%), and vascular directed agents (calcium channel blockers, phosphodiesterase-5 inhibitors, and botulinum toxin) (35%). This pilot study highlights the high hospitalization rate, long diagnostic delay and duration of corticosteroid exposure in MDA-5-DM, emphasizing the need for earlier recognition of MDA5. Future studies are needed to determine whether earlier diagnosis and initiation of steroid-sparing therapy may mitigate hospitalization rates.

Category: Dermatomyositis

OVERLAPPING CLINICAL FEATURES OF ANTI-SYNTHETASE SYNDROME AND DERMATOMYOSITIS

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Anti-synthetase syndrome (ASSD) commonly presents with positive anti-synthetase antibodies and a triad of symptoms consisting of interstitial lung disease (ILD), arthritis, and myositis [1]. However, defining classification criteria for ASSD remains an ongoing challenge. The debate centers around whether ASSD should be considered a distinct entity or a subset of dermatomyositis (DM) within the myositis spectrum. DM is characterized by classic cutaneous manifestations and can occur with or without muscle pathology. Both conditions share an elevated risk of ILD, arthritis, and Raynaud's phenomenon [2]. In a retrospective chart review, we identified eight patients exhibiting positive anti-synthetase antibodies and classic DM cutaneous patterns, ranging from mild to severe. These cases defied straightforward classification as DM or ASSD. The patients, ranging from 43-77 years old, included five Caucasians, two African Americans, and one Asian individual. All serologies were found to be positive for at least one of the following: Jo-1, PL-7, PL-12, U1RNP, OJ, Jo-1, RNP, and PM-Scl-75. Myositis was present in all, with ILD in four, arthritis in five, and mechanic's hands in one. Raynaud’s phenomenon was prevalent in six cases, and characteristic DM dermatological hallmarks – malar rash, Gottron's sign, V-sign, and heliotrope rash – were uniformly observed. A previous study revealed differences in the IFN signature between DM and ASSD when examining muscle pathology and select skin biopsies from mechanic’s hands [3]. Consequently, some experts consider ASSD a distinct entity separate from DM. However, a subsequent study on ASSD patients exhibiting DM-specific skin manifestations revealed that the skin biopsies displayed similarities in type 1 IFN, cytokine, and JAK-STAT pathways to pure DM patients [4]. This suggests an overlap between these conditions, particularly in ASSD patients with DM-specific rashes. These cases underscore the challenge of categorizing ASSD and DM as separate entities and emphasize the overlap between these diseases.

Teaching point: It is difficult to decipher a diagnosis for patients with overlapping clinical features of dermatomyositis and anti-synthetase syndrome suggesting these diseases may lie on a spectrum instead of existing as separate entities.

Abstract category: Dermatomyositis

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DERMATOMYOSITIS INDUCED CARDIOMYOPATHY: A RARE MANIFESTATION OF DISEASE

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Abstract category: Dermatomyositis

A 55-year-old female patient with past medical history of dermatomyositis with positive p155/140 antibodies, intermediary factor 1-gamma (TIF1-γ) secondary to stage IV diffuse large B cell lymphoma (DLBCL) and heart failure with recovered ejection fraction due to cardiotoxic cardiomyopathy consistent with chloroquine exposure (biopsy proven), presented to the emergency department with 1 week of worsening dyspnea on exertion, shortness of breath and lower extremity edema in the setting of a skin flare

Transthoracic echocardiogram was performed at the time of the admission and was shown to have a significant reduced left ventricular ejection fraction (LVEF) that decreased from 55 % (patient's baseline) to 20%, moderate to severe increase wall thickness and severely depressed systolic function, grade III diastolic dysfunction, dilated right ventricle, pro-B type natriuretic peptide (proBNP) found to be elevated 16,138 pg/mL (baseline between 1,000-2,000) as well as creatinine kinase (CK) 217 U/L, aldolase 29 U/L and troponin 28 ng/L. Whole body FGD-PET was performed without evidence of malignant disease, given history of DLBCL.

Patient was subsequently started on a 10-day course of dexamethasone with mycophenolate taper for treatment of dermatomyositis flare involving the cardiac muscle as well as furosemide drip due to significant symptomatic decompensation and volume overload. Several of the guideline directed medical therapy for heart failure had to be held due to acute kidney injury.

Dyspnea is the most prevalent symptoms in dermatomyositis patients with myocardial involvement. Unfortunately, there are no available guidelines for treating cardiac involvement in myositis, there are only care reported in the literature who recovered after treatment with either pulse-dose corticosteroids followed by oral prednisone, methotrexate, intravenous immunoglobulin, rituximab, and use of biological agents.

Teaching point:
Cardiac involvement is one of the organs damages whose prevalence is underestimated in dermatomyositis and a significant marker of poor disease prognosis leading to increase morbidity and mortality.

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SESSION II:

Sclerosing and Other Connective Tissue Diseases

EVIDENCE FOR INFLAMMATORY CELL DEATH, RECOGNITION OF SELF DNA AND INCREASED JAK/STAT SIGNALING IN EOSINOPHILIC FASCIITIS AND MORPHEA

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The pathobiology of eosinophilic fasciitis (EF) is poorly understood. We transcriptionally profiled 6 EF, 10 morphea and eight healthy skin (HS) biopsies. 67 differentially expressed genes (DEG) distinguished EF from HS (FDR<-.1). EF had signatures of immunogenic cell death, recognition of self DNA, CGAS/STING activation, induction of type I, II, and III IFN signaling, and fibrosis. There was increased NF-κB, JAK/STAT, type 2 (IL-4,9,13,33), type 1 (IFNG) and type 17 (IL-17,22,23) cytokine signaling and increased eosinophil attracting/activating factor signaling (GM-CSF, IL-13, IL-33). EF gene expression changes had many similarities to those observed in morphea. 53/67 DEG, 79/99 canonical pathways and 41/49 upstream regulators were shared in EF and morphea. EF had increased GM-CSF, PI3K/AKT and T cell exhaustion signaling and morphea had increased evidence of T cell signaling and activation, NK and cytotoxic T cell mediated killing, alternative macrophage activation and costimulation. JAK1 signaling was markedly enhanced in both disorders and immunostaining for pJAK1 and pSTAT1 demonstrated activated JAK1 and STAT1 signaling in T cells, dendritic cells, and macrophages in both EF and morphea. In summary, there is evidence of necroptosis, an immunogenic form of cell death, in both disorders that leads to recognition of self-DNA, leading to CGAS/STING activation, and production of type I, II, III interferons, and downstream production of multiple type 1, 2 and 17 inflammatory cytokines. There were surprisingly robust T cell inflammatory and cytotoxic signatures in both disorders, despite its pauci-inflammatory histologic appearance, suggesting small numbers of T cells may continue to drive injury and inflammation. There was evidence of robust JAK/STAT activation, particularly JAK1, and immunostaining confirmed active JAK1 and STAT1 signaling in key immune cell types in both disorders. These finding demonstrate strong pathophysiologic similarities between EF and morphea and support the use of JAK/STAT inhibitors in both conditions.

Category – sclerotic skin disease

RACE AND ETHNICITY IN CLINICAL TRIALS FOR AUTOIMMUNE CONNECTIVE TISSUE DISEASE THERAPEUTIC AGENTS: A SCOPING REVIEW

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Black, Indigenous, and People of Color (BIPOC) experience greater morbidity and mortality from autoimmune connective tissue diseases (AICTDs); thus, equitable access to randomized controlled trials (RCTs) for AICTDs is a scientific and ethical imperative. Drug safety and efficacy may not be optimized until participants reflect the disease epidemiology. This scoping review examines race and ethnicity in RCTs investigating biologic and small molecule agents for AICTDs. A search was conducted in August 2022 across six databases for English-language RCTs involving biologics or new small molecule drugs for lupus erythematosus (LE), dermatomyositis, and systemic sclerosis (SSc). Three independent reviewers performed screening followed by eligibility assessment, with inclusion dependent on consensus by two reviewers. Data was extracted and then verified by two independent reviewers. Ninety-two RCTs were included. Across AICTDs, patients who identified as White were the most frequently included (55.5%), followed by Asian (18.9%), Hispanic (16.3%), and Black/African American (11.9%). For each diagnosis, BIPOC patients were underrepresented, with the exception of patients who identified as Asian in LE and SSc trials. Chi-squared testing revealed that inclusion of BIPOC in RCTs on AITCDs has not changed significantly in the last five years ($X^2 = 3.26$, $p = 0.07$). Our data show that inclusivity in RCTs for AICTDs remains problematic. This comes despite recent pushes for greater diversity in RCT participants. The lack of diversity in trials serves to exacerbate disparities in outcomes for patients who identify as BIPOC and are diagnosed with AICTDs.

Abstract Category: E. Miscellaneous Rheumatic Skin Disease

USE OF 3-DIMENSIONAL STEREOPHOTOGRAMMETRY TO DETECT DISEASE PROGRESSION IN CRANIOFACIAL MORPHEA

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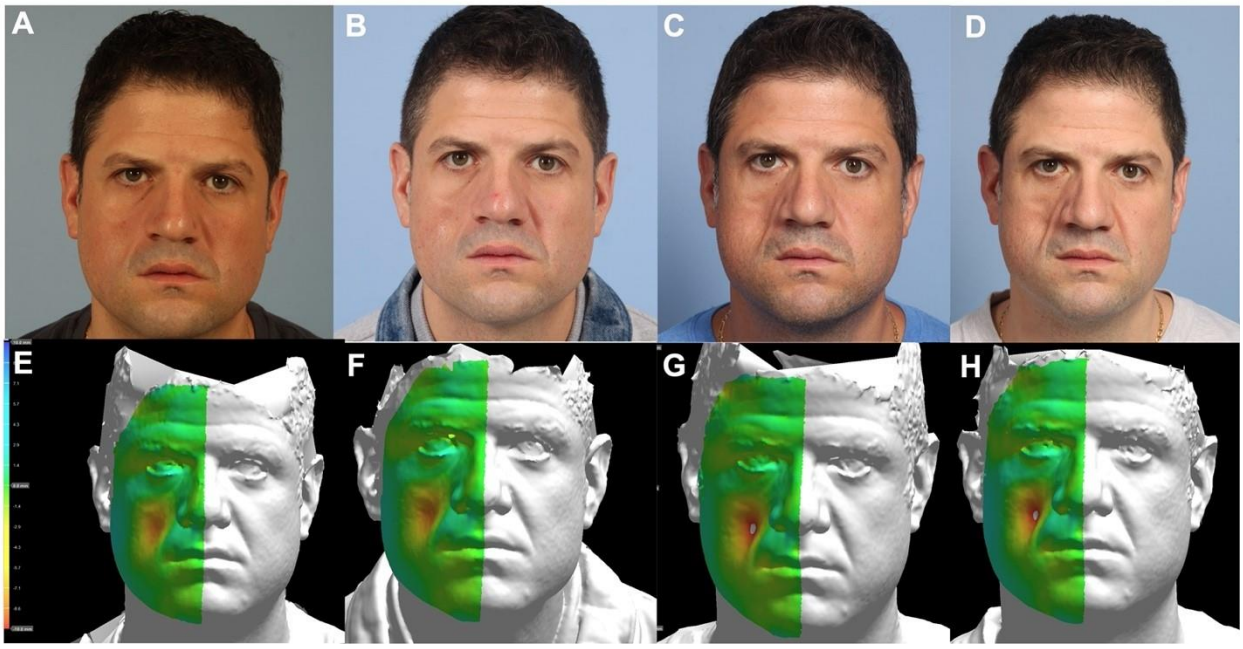
Craniofacial morphea (CM) is an autoimmune disorder characterized by inflammation and subsequent atrophy of the skin and underlying soft tissue. To avoid significant cosmetic and functional sequelae, timely initiation of systemic immunosuppression is key. Even with appropriate treatment, risk for disease recurrence persists. Unfortunately, determining disease progression in CM remains challenging as clinical findings of disease activity are often lacking. Existing tools including two-dimensional (2D) photography, clinical documentation, and provider/patient recall are all limited in their ability to detect subtle evolving facial atrophy. As such, a critical need for more sensitive methods to monitor patients with CM longitudinally persists. Three-dimensional (3D) stereophotogrammetry is a non-invasive, radiation-free imaging modality that has emerged as a potential tool for detecting and quantifying asymmetry in CM. A recent pilot study (Abbas *et al*, JAAD 2023) demonstrated the ability of 3D stereophotogrammetry to detect pathologic asymmetry in patients with CM, including occult asymmetry not appreciable on clinical examination alone. While the aforementioned study did not follow patients longitudinally, we hypothesized that tracking 3D stereophotogrammetry-generated facial heat maps over time could illustrate clinically meaningful disease progression in patients with CM. Thus, we performed a prospective study of 27 consecutive CM patients seen at Boston Children's Hospital and Brigham & Women's Hospital outpatient rheumatology-dermatology clinics from April 2019 to March 2023. Clinical and 3D-stereophotogrammetry assessments were performed

at 2- to 12-month time intervals, depending on the clinical context. Electronic health records (EHR) were reviewed for demographics, treatment data, and documentation of disease progression. A board-certified dermatologist and board-certified plastic surgeon, both blinded to the clinical outcomes of patients, independently reviewed sequentially-taken 3D stereophotogrammetry images to assess for progressive facial asymmetry. Statistical significance was assessed with kappa coefficients calculated for interrater reliability in R, version 4.2.0. Of 27 patients with CM (19 female; median age 14 years [range 5-40]) and 3D-stereophotogrammetry images obtained from a minimum of two time points (median, 4 images [range 2-10]) spaced 2-12 months apart (median, 3 [range, 2-12]), 10 experienced disease progression based on clinical assessments. In all cases where clinical progression was favored, blinded qualitative assessment of 3D-stereophotogrammetry images also favored progression with high interrater reliability (kappa = 0.8 [95% CI: 0.61-0.99]; **Figure 1**). Furthermore, review of 3D-stereophotogrammetry detected occult progression of asymmetry not noted on clinical examination in 3 additional patients. Taken together, we found that 3D stereophotogrammetry not only corroborated clinical impressions of disease progression but also identified occult progression of facial asymmetry not appreciable on clinical examination alone. 3D-stereophotogrammetry may thus serve as a valuable adjunctive tool for detecting disease progression in CM patients over time. Further studies are necessary to validate this measure in a larger cohort and guide its incorporation into medical decision-making for patients with CM.

Abstract Category: Sclerotic skin disease

Figure 1: Representative 2D and 3D Images of Progression in Craniofacial Morphea

A man in his 40s with a history of adult-onset hemifacial atrophy. Frontal 2D (A-D) and 3D (E-H) photographs are shown at 4 time points. In the 3D images, *yellow* indicates minor and *red* indicates greater volume deficiency on the heat map side compared to the contralateral side. Atrophy and contour change on the R cheek, extending from the medial tear trough to the medial cheek with flattening of the nasolabial fold, were noted on baseline imaging (A, E) before the initiation of treatment with pulse-dose steroids and mycophenolate mofetil. Follow-up imaging at 9, 18 and 23 months (B-D, F-H) are shown. Disease progression was noted on the R medial cheek both in 2D and 3D imaging at 18- and 23-month follow-up (C-D and G-H, respectively). Given that the patient had already received first-line treatment with pulsed intravenous methylprednisolone and nearly two years of mycophenolate mofetil, the decision was made to transition from mycophenolate mofetil to oral Janus kinase inhibitor therapy to mitigate further disease activity.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USE OF HYDROXYCHLOROQUINE AND CARDIAC ADVERSE EVENTS IN AUTOIMMUNE CONNECTIVE TISSUE DISEASE

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Anti-malarial agents, especially hydroxychloroquine (HCQ), have a long history of use as anti-rheumatic agents for a variety of autoimmune connective tissue diseases[1]. Observations during the COVID-19 pandemic when hydroxychloroquine was widely used as therapy for SARS-COV disease has raised concern for significantly increased risk of cardiac toxicity[2]. However, the true cardiac risk among patients receiving HCQ for autoimmune disease is still unclear. We conducted a retrospective cohort study analyzing rates of cardiac adverse events (development of a new diagnosis of cardiomyopathy, ventricular arrhythmia, congestive heart failure or myocardial infarction) utilizing the Centrus database[3], a curated data repository of electronic health records from the Kansas City metro area. We identified 2487 patients who had a diagnosis of systemic lupus erythematosus (ICD-10 M32.9, N = 2282), dermatomyositis (M33.1, N = 40) or morphea (L94.0, N = 165) and were further propensity score matched based on gender, ethnicity, race, age and marital status. Of these, 106 individuals exposed to HCQ had a cardiac event while 723 exposed did not. 363 un-exposed had a cardiac event while 1295 un-exposed did not for an Odds ratio of 0.5280 (95% CI = 0.4178 to 0.6672, $P < 0.0001$) suggesting an association between HCQ and a cardioprotective effect in individuals with these conditions rather than toxicity. Limitations of this study include inability to control for other comorbid risk factors for cardiac disease or autoimmune disease severity. Further large population studies are needed to add clarification to the cardiac risk/benefit of HCQ in autoimmune disease.

Category: Miscellaneous rheumatic skin disease

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A RETROSPECTIVE STUDY IDENTIFYING AN ASSOCIATION BETWEEN IGA VASCULITIS AND COVID-19 INFECTION AND VACCINATION

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IgA vasculitis, a rare form of leukocytoclastic vasculitis in adults, is usually associated with infection. A novel infectious threat, SARS-CoV-2, was encountered by the global community during the COVID-19 pandemic. COVID-19 is primarily a respiratory disease, but recent literature has described various cutaneous manifestations/reactions, including vasculitis. We therefore sought to characterize the presentation of COVID-19-associated vasculitis. We identified and confirmed 183 cases of vasculitis in the UCI Health system from January 2000 to October 2022 from electronic health records based on ICD-9/10 codes. We identified 7 cases associated with COVID-19 infection or vaccination. Four of seven were females; average age at diagnosis was 33 (range 12-65) years. Six of seven patients underwent skin biopsy. Of these, 5/6 had a positive direct immunofluorescence (DIF) for IgA. Three of seven patients exhibited blistering disease, and 3/7 developed rash beyond bilateral lower extremities (BLE) (2/7 with BLE and upper extremities; 1/7 with widespread involvement); 4/7 cases were limited to BLE. Systemic manifestations included constitutional (3/7), renal (3/7), joint (3/7), and gastrointestinal disease (2/7). Six patients received extensive autoimmune workup, of which one patient returned positive for c-ANCA and RF. One patient was found to have elevated total serum IgA. Two patients tested positive for respiratory pathogens in addition to COVID-19: influenza B and group A streptococcus. All patients received systemic corticosteroids, with varying degrees of efficacy. Our study suggests that COVID-associated vasculitis is more likely to blister, extend beyond BLE, and be attributed to IgA vasculitis with increased possibility of renal disease. Clinicians should strongly consider conducting DIF studies when vasculitis is suspected in the context of COVID-19, as IgA vasculitis warrants prolonged monitoring for renal disease. Future studies are needed to expand our understanding of COVID-associated vasculitis and guide patient management.

Category: Vasculitis

RACIAL AND ETHNIC DISPARITIES IN HEALTHCARE ACCESS AND UTILIZATION AMONG US ADULTS WITH AUTOIMMUNE CONNECTIVE TISSUE DISEASES

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Understanding the effects of race/ethnicity on healthcare access and utilization in patients with autoimmune connective tissue diseases (AiCTD) is paramount to addressing the known healthcare disparities that exist within this population. We performed a cross-sectional analysis of data among adults with AiCTDs in the NIH's *All of Us* Research Program who completed the Healthcare Access and Utilization Survey and had complete baseline demographic information available. Multivariable logistic regression was used to analyze the relationship between race/ethnicity and healthcare access/utilization (reference group: White patients). Regression models accounted for age>65, biological sex, geographic region, insurance, income, and educational level. Participants with missing data were excluded from regression models. We identified 2,185 adults (332 non-Hispanic Black, 258 Hispanic, 128 non-Hispanic Other, and 1,467 non-Hispanic White) with the following non-mutually exclusive distribution of AiCTDs: 62.6% Systemic Lupus Erythematosus, 25% Morphea, 15.6% Cutaneous Lupus Erythematosus, 13.8% Systemic Sclerosis, 5.3% Dermatomyositis. We found that Black patients were more likely to seek care in an emergency room or urgent/minute clinic in comparison to a doctor's office/clinic or health center ($p<0.001$). Black patients were also less likely to see a general health provider due to financial constraints ($p=0.006$). Hispanic patients were more likely to forgo prescription medications ($p=0.03$) and were more likely to not take medications as prescribed ($p<0.001$) to save money. Both Black and Hispanic patients were less likely to have spoken with a mental health professional in the past year (Black $p<0.001$; Hispanic $p<0.001$). Black, Hispanic, and Other patients were all more likely to place importance on seeing a provider from the same background (Black $p<0.001$; Hispanic $p<0.001$; Other $p=0.01$) and were also more likely to report never being able to see such a provider (Black $p<0.001$; Hispanic $p<0.001$; Other $p=0.004$). Although this study is limited by survey responses that are not specific to AiCTD care, we provide important specific insights on disproportionate healthcare usage among racial/ethnic groups that may help with focused programming to progress towards health equity.

Category: Miscellaneous Rheumatic Skin Disease

RAPIDLY PROGRESSIVE EOSINOPHILIC FASCIITIS FOLLOWING COVID-19 INFECTION RESPONDING TO MULTIMODAL THERAPY

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A woman in her 30s with a history of asthma presented with a 10-month history of skin tightening with progressive impairment of mobility within 2 weeks of her primary COVID infection, associated with new muscle pain and profound eosinophilia. Left upper arm skin biopsy demonstrated thickened collagen bundles, with clefts containing fibrin, lymphocytes and occasional eosinophils in the deep reticular dermis and subcutaneous septa, indicative of early deep sclerosing dermatosis. Initial treatment included pulse oral dexamethasone and methotrexate(MTX) with early improvement; however, symptoms recurred with initiation of steroid taper and were exacerbated following COVID bivalent vaccination. Over the following months, she received a total of 12 g of IV methylprednisolone, MTX, IVIG and mepolizumab. However, her disease continued to progress, with particularly concerning features involving her trunk, including newly restrictive pulmonary function tests and a deep plaque compressing tracheal soft tissue; CT imaging confirmed normal chest fields. Ruxolitinib was administered, but given persistent rapid truncal progression, cyclosporine(CSA) was added for rapid stabilization; MTX was changed to MMF and mepolizumab to dupilumab. Over the following weeks, the patient's disease stabilized, with gradual improvement and skin softening. She recently received a rituximab(RTX) dose, and successfully tapered off CSA, MMF, and systemic steroids, with sustained improvement near her prior baseline function. Notably, SARS-CoV2NP immunostaining of her original skin biopsy specimen was negative. However, COVID remains a potential trigger due to timing of eosinophilia onset, clinical progression, and disease exacerbation following vaccination. Furthermore, the upregulation of Th2-drive immune modulations and pro-inflammatory cytokine release, observed in COVID-related bullous pemphigoid, supports the unique role of Ruxolitinib and Dupilimab as antifibrotic therapies in EF[1-7]. Furthermore, truncal involvement may serve as a valuable prognostic marker for the development of severe, steroid-resistant disease[8-9]. This case emphasizes a stratified, multimodal approach for immunosuppressive therapy in particularly refractory and life-altering disease.

Teaching points: This case of severely recalcitrant EF suggests that COVID-19 may be a potential trigger for disease development, highlights the unique role of Ruxolitinib and Dupilimab as anti-fibrotic therapy, and emphasizes the significance of layered, multimodal immunosuppressive treatment in the setting of refractory, life-altering disease.

Category: Clinical Case

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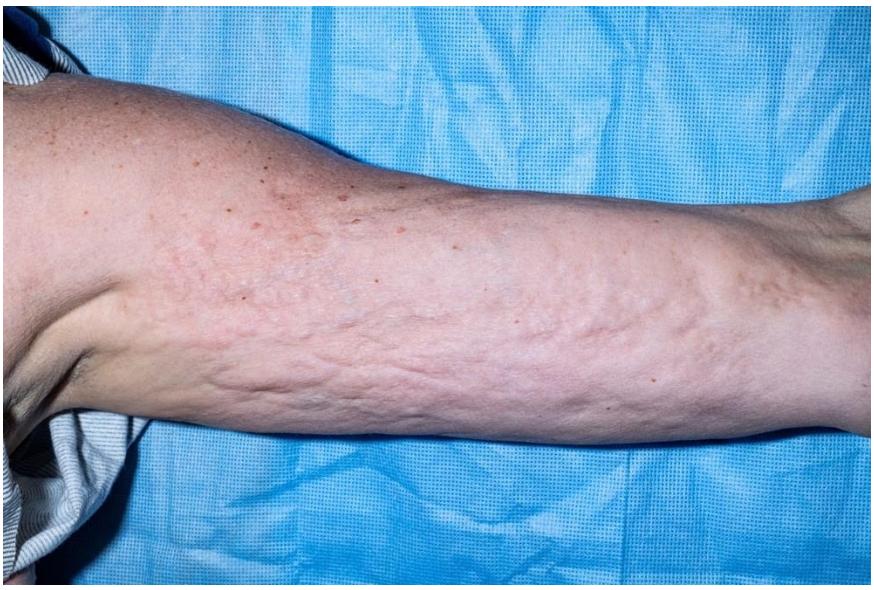
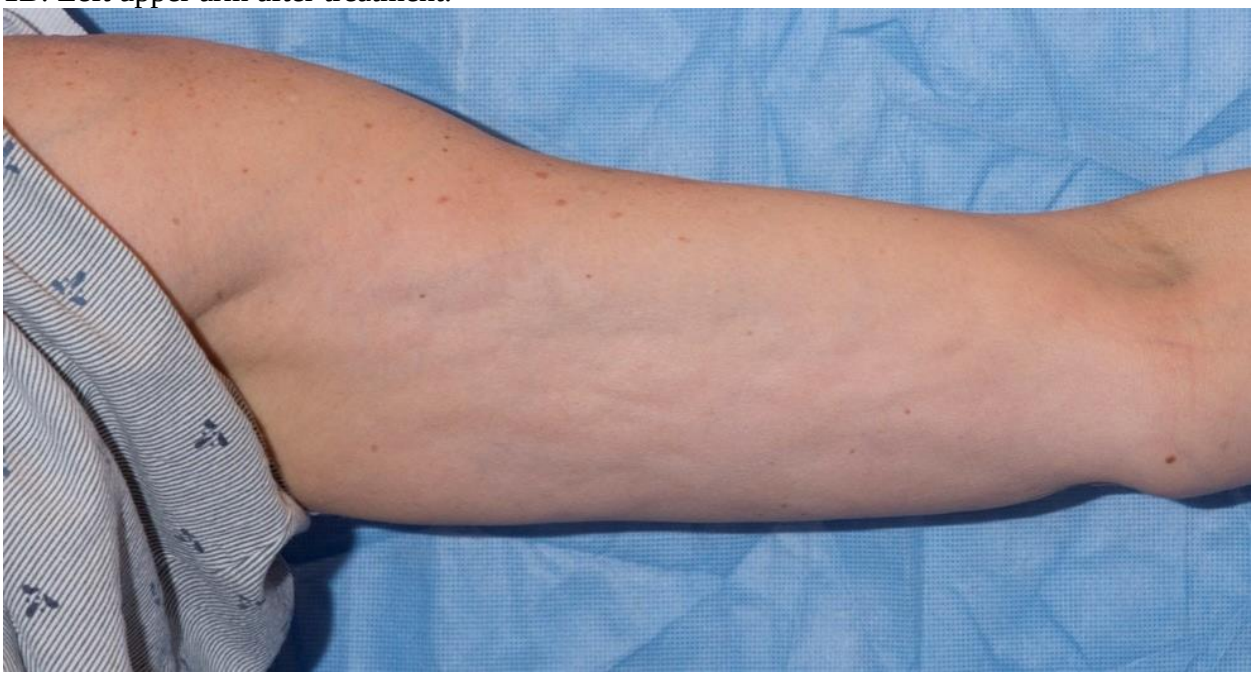
Figures:

Figure 1A:Left upper arm prior to treatment.



1B: Left upper arm after treatment.



SESSION III:

Lupus Erythematosus

PATIENTS WITH AUTOIMMUNE SKIN DISEASES ARE AT INCREASED RISK OF ADVERSE PREGNANCY OUTCOMES

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Increased adverse pregnancy outcomes (APOs) have been associated with rheumatologic diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). However, little is known about APOs in patients with autoimmune skin diseases (ASDs). We aimed to determine the frequency of APOs in patients with ASDs.

This was a case-control study using the TriNetX U.S. Collaborative Network. Pregnant patients aged 15-44 years between January 2016 and December 2021 were included. Participants with ASDs (e.g. cutaneous lupus, morphea, amyopathic dermatomyositis, vitiligo) were matched to healthy controls and SLE or RA disease controls. Patients with other autoimmune diseases or hidradenitis suppurativa were excluded. Primary outcomes were APOs defined as spontaneous abortion, gestational hypertension, preeclampsia/eclampsia, gestational diabetes, intrauterine growth restriction (IUGR), preterm premature rupture of membranes, preterm birth, and stillbirth. Patients with ASDs and controls were 1:1 propensity score matched by demographics and comorbidities. Odds ratio (OR) with a 95% confidence interval (CI) was calculated.

2,788 patients with ASDs were matched to 2,788 controls. Patients with ASDs had a higher risk of spontaneous abortions than controls (OR, 1.54; 95% CI, 1.36-1.75; P<0.001). Specifically, patients with cutaneous lupus (OR, 2.41; 95% CI, 1.86-3.13; P<0.001) or vitiligo (OR, 1.3; 95% CI, 1.03-1.64; P=0.03) were more likely to have spontaneous abortions. Compared to SLE group, patients with ASDs were at lower risk of having infants with IUGR (OR, 0.59; 95% CI, 0.4-0.87; P=0.01), preterm birth (OR, 0.68; 95% CI, 0.47-0.98; P=0.04), and stillbirth (OR, 0.50; 95% CI, 0.25-0.97; P=0.04). Differences in APOs between ASD and RA groups were not statistically significant.

Patients with ASDs had increased rates of APOs versus controls and were similar in risk to RA. These patients may benefit from multidisciplinary care with maternal-fetal medicine specialists. Further studies will be helpful to identify mechanisms behind increased risk of APOs in patients with ASDs.

Category: Lupus

ITEM REDUCTION AND VALIDATION OF THE CUTANEOUS LUPUS ERYTHEMATOSUS QUALITY OF LIFE QUESTIONNAIRE

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The 37-item Cutaneous Lupus Erythematous quality of life (CLEQoL) instrument is a disease-specific patient-reported outcome measure (PROM) for CLE. A brief version could reduce respondent burden and increase clinical utility. Thus, we performed an item reduction study of CLEQoL while maintaining clinical relevance and psychometric properties. This retrospective cohort study analyzed data from 185 CLE patients recruited in outpatient dermatology clinics at University of Texas Southwestern Medical Center and Parkland Health from June 2016 to November 2022. Patients completed the CLEQoL, Short-Form-36 (SF-36), and visual analogue scale (VAS). Item reduction was conducted by evaluating each item's response distribution and inter-item correlations. Internal consistency was assessed using Cronbach's alpha. Structural validity was examined via exploratory factor analysis. Convergent validity was determined via Spearman correlations between CLEQoL, SF-36, VAS, and Cutaneous Lupus Erythematosus Disease Area and Severity (CLASI) scores. Data were analyzed using SPSS version 29.0; significance set at $p<0.05$. Thirteen items were removed, resulting in a 24-item scale. Internal consistency was satisfactory (Cronbach's alpha: 0.842-0.939). Exploratory factor analysis identified three domains: *"Emotions and Social Interactions," "Symptoms and Functioning," and "Lupus Specific Questions*." The brief CLEQoL demonstrated convergent validity with the SF-36 (*r* range: -0.243 to -0.172) and VAS (0.348 – 0.671). There was no convergent validity with CLASI activity or damage scores. The brief 24-item CLEQoL was found to be a valid and reliable PROM for assessing CLE patients' quality of life, and establishing its psychometric properties is crucial for its use in outpatient clinics and clinical trials. The nonconvergence between the brief CLEQoL and CLASI can be attributed to their measurement of different properties: subjective patient experiences versus physician assessment of disease severity. Integrating information from both allows for comprehensive patient assessments. We plan to prospectively administer the brief CLEQoL to a larger CLE cohort for further evaluation of psychometric properties.

Category: Lupus

ANIFROLUMAB FOR THE TREATMENT OF REFRACTORY CUTANEOUS LUPUS ERYTHEMATOSUS: INTERIM ANALYSIS OF REAL-WORLD OUTCOMES

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Category: Lupus

Reliable and effective treatments for refractory cutaneous lupus erythematosus (CLE) have remained elusive. Anifrolumab, a human monoclonal antibody targeting the type I interferon receptor, was recently approved for the treatment of moderate-to-severe systemic lupus erythematosus (SLE) and has since yielded encouraging results in CLE as demonstrated by isolated case reports and small case series. However, anifrolumab use outside of clinical trial settings remains poorly studied, particularly in those SLE patients with severe or refractory CLE. Thus, we aimed to characterize the real-world efficacy and tolerability of anifrolumab in CLE patients using validated disease activity instruments. This single-center, prospective observational cohort study includes SLE patients with severe or refractory CLE who have received ≥ 1 dose of anifrolumab. Cutaneous disease activity is assessed periodically at 2, 6, 9, 12, and 18 months using the Cutaneous Lupus Disease Area and Severity Index (CLASI). Adverse events and concurrent treatments are also routinely evaluated. To date, 22 patients have been enrolled, with 6-month follow-up data available for 15. At the time of anifrolumab initiation, 95% of participants had discoid LE (DLE), 60% had mucosal DLE, and 13% had subacute CLE. A Friedman test showed statistically significant changes over time in CLASI activity score (CLASI-A) (χ^2 (2) =20, p<0.0001) (Figure 1) and CLASI damage score (CLASI-D) (χ^2 (2) =9.5789, p=0.0083) (Figure 2). To estimate effect sizes, we employed linear mixed models, which demonstrated statistically significant reductions in the CLASI-A score from baseline by an average of 14 points at 2 months (p<0.001) and 18 points at 6 months (p<0.001); notably, a reduction in CLASI-A of 4 is considered clinically meaningful. The decrease in CLASI-D scores was significant only at 6 months (average reduction of 1.4, p=0.007). At 2 months, 20% of patients experienced a 50% or more reduction in CLASI, which increased to 60% of patients at 6 months. For those patients on systemic corticosteroids (SCS) at the time of anifrolumab initiation (n=4), all were able to either discontinue or taper their SCS. Four adverse events were noted with anifrolumab, including herpes zoster (n=1), bronchitis (n=1), upper respiratory tract infection (n=1), and infusion reaction (n=1), none of which resulted in treatment discontinuation. To our knowledge, this represents the largest

single-center cohort of CLE patients treated with anifrolumab to date. Taken together, our results suggest that anifrolumab is a promising, effective, and well-tolerated therapeutic option for patients with severe or refractory CLE with benefits observed as early as 2 months after treatment initiation.

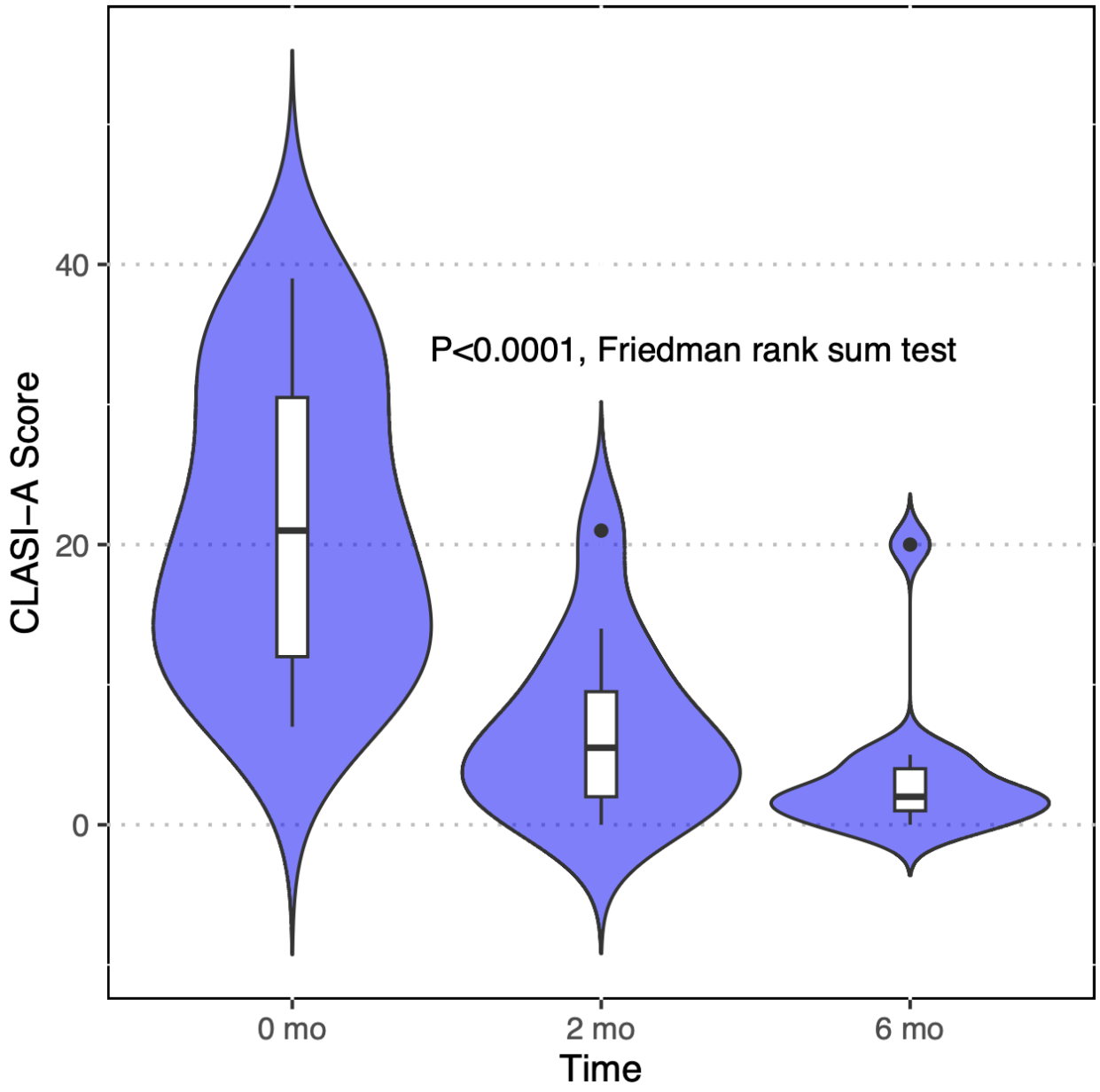

Fig. 1. Violin plot depicting the CLASI-A scores at 0, 2, and 6 months.

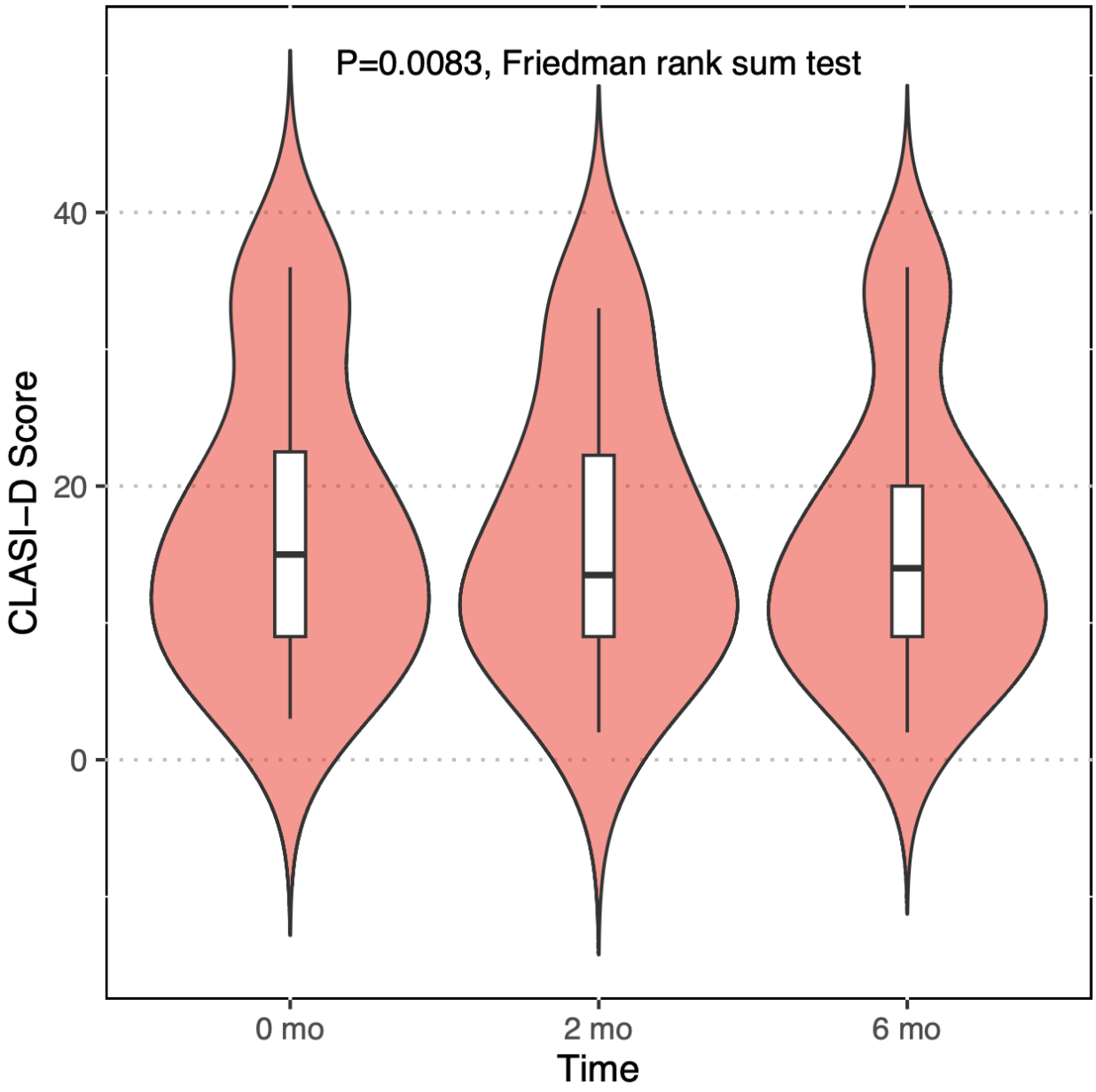

Fig. 2. Violin plot depicting the CLASI-D scores at 0, 2, and 6 months.

ANIFROLUMAB IN ADOLESCENT DISCOID LUPUS ERYTHEMATOSUS: A RETROSPECTIVE STUDY FROM THREE ACADEMIC MEDICAL CENTERS

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Anifrolumab, a human monoclonal antibody targeting type I interferon receptor subunit 1, has recently emerged as an efficacious agent for adult systemic lupus erythematosus (SLE) patients with refractory cutaneous disease (particularly, discoid lupus [DLE]). While a phase III trial designed to evaluate the efficacy of anifrolumab in pediatric SLE patients is forthcoming, to our knowledge, no reports exist describing the real-world outcomes of adolescent SLE patients with refractory DLE treated with anifrolumab. Thus, we performed a multicenter retrospective study utilizing the electronic health records (EHR) of adolescent patients treated with anifrolumab at Boston Children's Hospital, NYU Hassenfeld Children's Hospital, and the University of Wisconsin Hospital. Inclusion criteria were adolescent SLE patients (AAP criteria, ages 11-21) with recalcitrant DLE seen between August 2022 and June 2023 who received ≥1 dose anifrolumab. EHR was reviewed for patient demographics, treatment data, and adverse events. Seven adolescent SLE patients (6 female; median age, 17 years [range, 14-20]) treated with anifrolumab (300mg administered intravenously every 4 weeks; median 6 doses [range 3-8]) were identified. All had DLE recalcitrant to standard therapies at time of anifrolumab initiation. The primary outcomes were improvement in the validated Cutaneous Lupus Erythematosus Disease Area and Severity Index score (CLASI) and SLE Disease Activity Index-2K score (SLEDAI-2K). All patients demonstrated substantial improvement in cutaneous disease activity after initiating anifrolumab (**Figure 1A, 2**). Mean decrease [SD] and mean percentage decrease [SD] in CLASI-A scores were 18.0 [8.9] and 72.1% [9.4] after one dose of anifrolumab, respectively (p=0.014,

Mann-Whitney U test); this effect was sustained at six-month follow-up in those patients who had received at least 5 doses of anifrolumab (p=0.012). Additionally, mean decrease [SD] in SLEDAI-2K score at last follow-up was 7.0 [6.2], reflecting overall improvement in systemic SLE disease activity. No significant change in CLASI damage score, which quantifies scarring and dyspigmentation from antecedent DLE disease activity, was observed (**Figure 1B**). One (14.2%) patient experienced an adverse event (AE) in the form of recurrent herpes simplex 1 (HSV-1) reactivation. Although limited by small sample size and retrospective design, our findings suggest that anifrolumab mediates rapid and sustained improvement of recalcitrant DLE in adolescent SLE patients. The rapidity of clinical response (within one month) is particularly noteworthy given the potential for DLE to cause irreversible scarring and disfigurement in cosmetically sensitive areas that may impact self-esteem and psychosocial functioning, particularly in adolescent patients. Larger prospective studies of anifrolumab are necessary to guide its incorporation into the therapeutic armamentarium for children and adolescents with lupus.

Teaching point: Anifrolumab may be a promising therapeutic option for adolescent SLE patients, particularly those with severe or recalcitrant DLE.
Category: Lupus

Figure 1: CLASI activity and damage before and after anifrolumab initiation

Line graphs showing CLASI activity (A) and damage (B) scores in 7 patients before and at month 1, 3, and/or 6 of anifrolumab treatment. Blue solid circles represent individuals. The red line indicates mean CLASI-A (A) and CLASI-D (B) scores calculated at M0, M1, and M6. Patients with missing values at M6 (n=2) were excluded from mean calculation. Error bars indicate standard error. P values were calculated using the Mann-Whitney U test. $P<0.05$ was considered significant. Analyses were performed using R programming language (version 4.2.2). *CLASI-A*, Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity; *CLASI-D*, Cutaneous Lupus Erythematosus Disease Area and Severity Index Damage; *M*, month; *NS*, not significant.

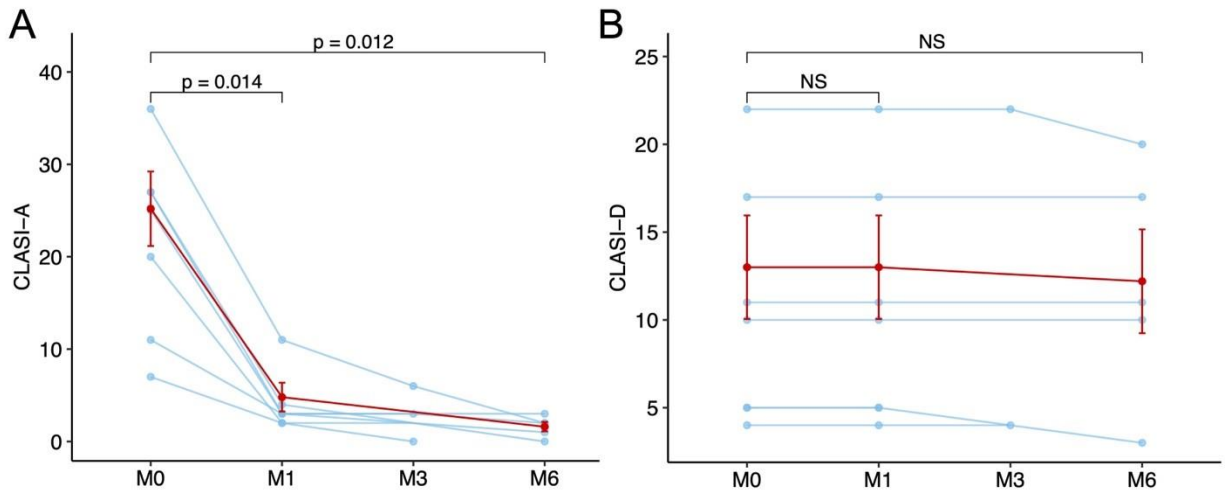
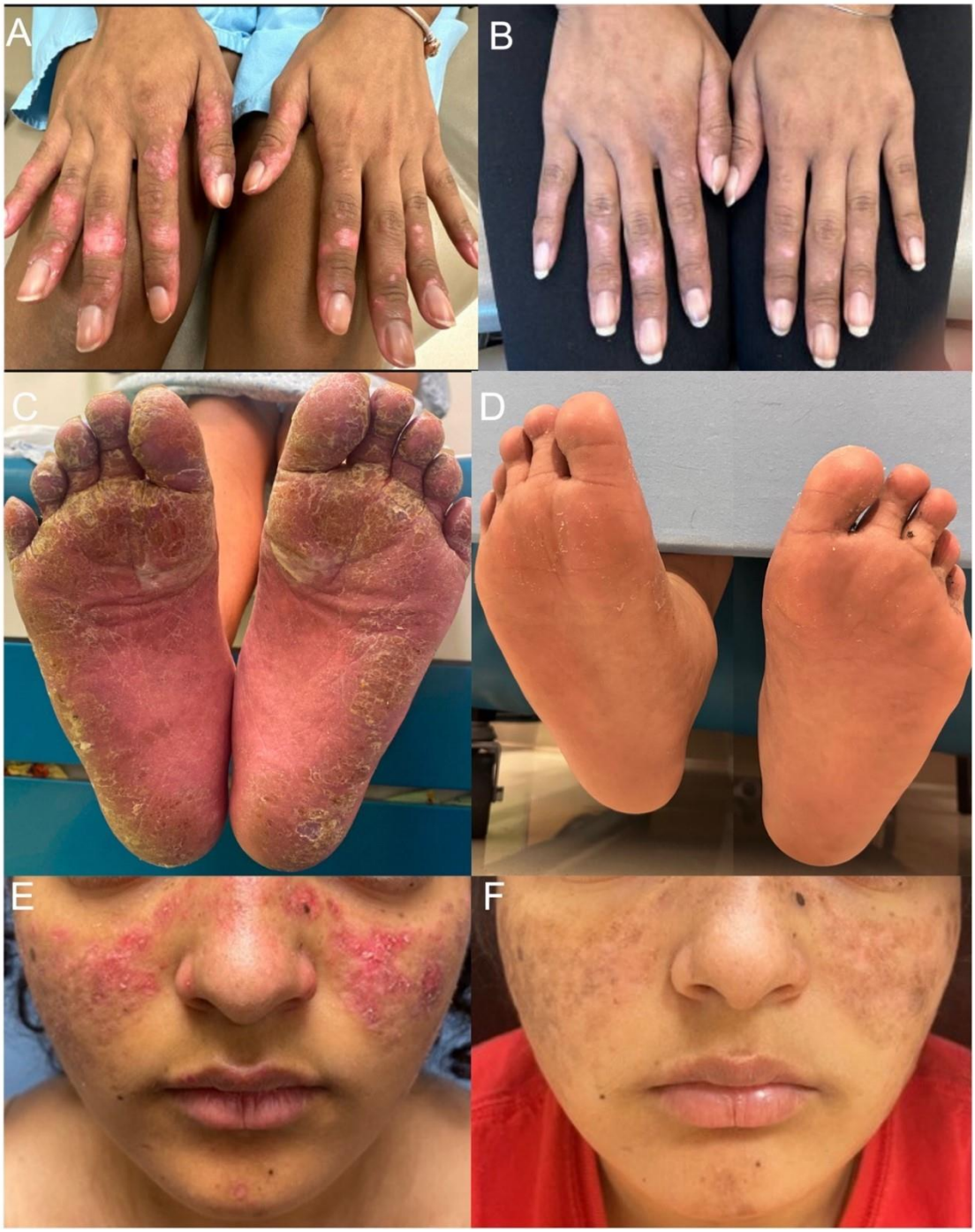


Figure 2: Clinical improvement of adolescent patients with recalcitrant DLE treated with anifrolumab

Representative photographs of three adolescent patients demonstrate dramatic improvement in discoid lesions on the hands (A), feet (C), and face (E) after 1 month (B), 2 months (D), and 3 months (F) of treatment with anifrolumab, respectively.


A
B
C
D
E
F

DISEASE SUBTYPE AND BASELINE DISEASE ACTIVITY ARE ASSOCIATED WITH DIFFERING DISEASE ACTIVITY TRENDS IN PATIENTS WITH CUTANEOUS LUPUS

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Retrospective studies evaluating the natural disease course of patients with CLE have been limited by irregular follow-up intervals and missing data. Thus, we conducted a six-month prospective study of CLE patients on standard-of-care therapies with regular two-month follow-up intervals to characterize their disease courses and identify patient characteristics associated with disease trends. Patients were recruited at 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 outcome variable was the average change score (ACS), or the mean of the differences in the Cutaneous Lupus Disease Area and Severity Index (CLASI) scores taken at the baseline visit and each follow-up visit. Predictive variables associated with disease activity and damage trends were analyzed using Mann-Whitney or Kruskal-Wallis tests for continuous variables and chi-squared or Fisher's exact tests for categorical variables. 106 of 133 CLE patients completed the study. 43 (40.6%) patients demonstrated stability in disease activity (-3<ACS<3), 40 (37.7%) showed improvement (ACS $\leq\leq$ -3) and 23 (21.7%) showed worsening (ACS $\geq\geq$ 3). 76.7% of patients with mild baseline disease activity remained stable whereas most patients with moderate (60.4%) and severe (53.6%) baseline activity demonstrated improvement ($p<0.001$). In terms of CLE subtype and disease activity, localized discoid lupus erythematosus (DLE) had the greatest proportion of stability (18, 62.1%), generalized DLE had the greatest proportion of worsening (10, 21.3%), and subacute and acute CLE had the greatest proportion of improvement (14, 60.9%) ($p=0.03$). While providing important historical control data for clinical trials, these results indicate that baseline disease activity and CLE subtype can predispose patients to different clinical outcomes. The data also underscores the need to expand the armamentarium of CLE therapies, given the significant percentage of patients experiencing disease worsening.

Category: Lupus

EFFECTS OF VITAMIN D DEFICIENCY ON CARDIOVASCULAR OUTCOMES IN PATIENTS WITH DISCOID LUPUS ERYTHEMATOSUS

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Discoid lupus erythematosus (DLE) is the most common form of cutaneous lupus erythematosus (CLE), typically occurring in the absence of concurrent systemic lupus erythematosus (SLE). However, DLE is associated with systemic effects, including chronic inflammation, immune system dysregulation, and endothelial dysfunction.[1]These processes may contribute to atherosclerosis and plaque formation, potentially elevating the risk of adverse cardiovascular disease (CVD) outcomes in DLE patients.[2] Additionally, vitamin D deficiency – a condition linked to exacerbated cardiovascular outcomes – is highly prevalent in DLE patients.[3] This retrospective chart review seeks to address a crucial research gap by exploring whether vitamin D deficiency serves as an indicator of heightened CVD risk in DLE patients. We identified 67 (51.5%) vitamin D deficient patients, and 63 (48.5%) patients with healthy levels of vitamin D, with a mean age of 45.3 years. All patients were diagnosed with DLE at Johns Hopkins Hospital prior to June 1st, 2018, and had documented vitamin D statuses in the 5 years following diagnosis. After adjusting for age, sex, race, smoking, hyperlipidemia (HLD), hypertension (HTN) and type 2 diabetes mellitus (T2DM), multivariable analyses showed that vitamin D deficient patients were more likely to experience coronary artery disease (p=.013, OR 9.21, 95% CI 1.89-72.27) or angina (p=.013, OR 9.90, 95% CI 1.94-83.03), in the five years following DLE diagnosis. Vitamin D deficient patients were similarly more likely to be diagnosed with HTN (p=.0025, OR 4.14, 95% CI 1.69-10.82), HLD (p=.000016, OR 8.58, 95% CI 3.40-24.28), or T2DM (p=.031, OR 6.67, 95% CI 1.51-71.62), than non-deficient patients. Our study identified no significant differences relating to risk of experiencing stroke, congestive heart failure, myocardial infarction, pulmonary embolism, or deep vein thrombosis. These findings shed light on the intricate interplay between DLE and CVD and underscore the importance of monitoring and managing vitamin D levels in DLE patients.

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Category: Lupus

UTILIZING 3D-STEREOPHOTOGRAMMETRY TO DETECT FACIAL ASYMMETRY AND DISEASE PROGRESSION IN PATIENTS WITH LUPUS PANNICULITIS

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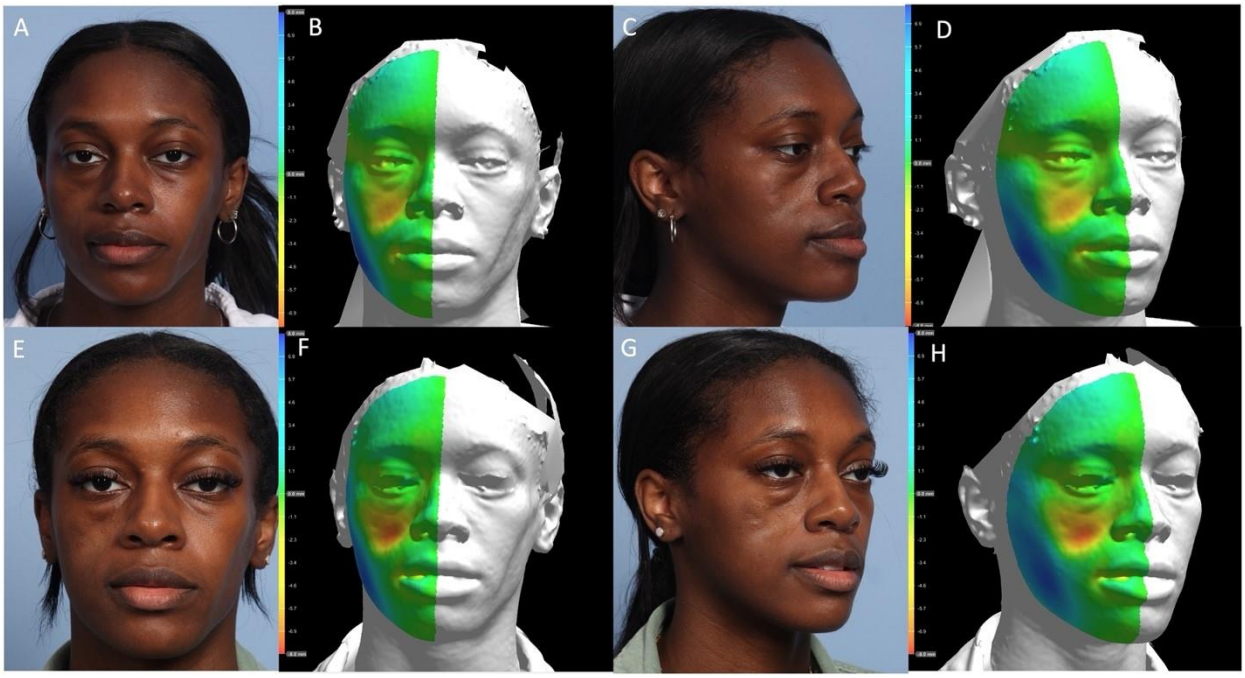
Lupus erythematosus panniculitis (LEP) is a rare variant of chronic cutaneous lupus erythematosus (CCLE) distinguished by its potential to cause irreversible scarring, lipoatrophy, and disfigurement. Due to its variable association with SLE (with rates of 20-62% reported in the literature), diagnosis is often delayed. Moreover, LEP often follows a relapsing and remitting course, with tender subcutaneous nodules and plaques (most commonly on the proximal arms, buttocks, and face) giving way to substantial ensuing lipoatrophy. Systemic immunosuppressive and/or immunomodulatory therapy is critical to abrogate disease activity to avoid significant cosmetic sequelae. And yet, even in those patients with a known diagnosis of LEP, monitoring for ongoing disease activity can be challenging as evolving subcutaneous nodularity and/or atrophy can be subtle. Existing tools including two-dimensional (2D) photography, clinical documentation, and provider/patient recall are all limited in their ability to detect subtle contour change, particularly on the face. As such, a critical need for more sensitive methods to monitor patients with LEP for progression longitudinally persists. 3D-stereophotogrammetry is a non-invasive, radiation-free imaging modality that recently emerged as an effective tool for detecting evolving facial asymmetry in patients with craniofacial morphea. Thus, we hypothesized that 3D-stereophotogrammetry could similarly be utilized in patients with facial LEP to identify evolving contour change. Herein, we report the case of a 23-year-old female with biopsy-proven, refractory facial LEP monitored longitudinally with 3D-stereophotogrammetry. Initially diagnosed with LEP in 2017 after developing painful subcutaneous nodules on her cheeks and proximal arms, she initially achieved disease stability with combination hydroxychloroquine and mycophenolate mofetil (MMF). Baseline facial 3D-stereophotogrammetry images were obtained in September 2022 and were notable for atrophy and contour change on the right malar cheek (Figure 1, A-D). The patient was subsequently lost to follow-up before re-presenting to care in August 2023. She endorsed self-discontinuation of MMF several months prior. Repeat 3D-stereophotogrammetry demonstrated progressive volume loss on the R malar cheek (Figure 1, F&H), and MMF was reinitiated due to concern for ongoing LEP disease activity. To our knowledge, this is the first report of 3D-stereophotogrammetry being utilized to monitor disease progression in LEP. Given that unrecognized and untreated LEP can lead to the accrual of permanent damage in cosmetically

sensitive areas, 3D-stereophotogrammetry may serve as a valuable adjunctive tool for monitoring patients with facial LEP over time.

Teaching point: 3D-stereophotogrammetry is a noninvasive imaging modality that may serve as a valuable adjunctive tool for quantifying facial asymmetry and detecting disease progression in patients with facial lupus panniculitis over time.

Category: Clinical Case

Figure 1: Representative 2D and 3D Images of Progressive Contour Change in a Patient with Facial Lupus Panniculitis A woman in her 20s with a history of LEP. Frontal and three-quarter views are shown at 2 time points. In the 3D-images, *yellow* indicates minor, and *red indicates* greater volume deficiency on the heat map side compared to the contralateral side. Atrophy and contour change on the R malar cheek are noted on baseline imaging (A-D). Follow-up imaging 11 months later is shown (E-H). While minimal change is appreciable in the 2D-images, progressive facial atrophy is notable on the R malar cheek in the 3D-images. Due to concern for progressive disease activity, the decision was made to restart therapy with mycophenolate mofetil.



SUCCESSFUL TREATMENT OF RECALCITRANT LUPUS ERYTHEMATOSUS TUMIDUS WITH DEUCRAVACITINIB

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A 51-year-old male active smoker with a family history of systemic lupus erythematosus was referred to our outpatient clinic for a recurrent, photosensitive, pruritic cutaneous eruption over several years. The rash was previously biopsied by an outside provider and consistent with tumid lupus erythematosus (TLE). The patient also reported diffuse joint pain, including some morning stiffness lasting 30-60 minutes. On physical exam, he was found to have erythematous, edematous papules and plaques in photodistributed areas (helices, face, extensor forearms, dorsal hands), as well as knees and abdomen. A subset of these, particularly on the lower extremities, were annular with central hyperpigmentation and raised borders (Figure 1 A-C). Joint exam did not reveal synovitis or inflammatory arthritis. Clinical presentation was most suggestive of TLE with a component of chillblains/perniosis to the knees, however, a granulomatous process remained as a differential diagnosis. Systemic autoimmune disease workup, including ANA, DsDNA, C3/C4, and RF, was negative. A repeat punch biopsy demonstrated prominent papillary dermal edema and “cuffed” perivascular and periadnexal lymphocytic infiltrates without granulomatous inflammation, consistent with TLE. Over the course of several years, the patient failed numerous therapies including: high potency topical steroids, topical tacrolimus, oral steroids, hydroxychloroquine, chloroquine, methotrexate, pentoxifylline, mycophenolate mofetil, and thalidomide. The patient also modified lifestyle behaviors such as photoprotection and smoking reduction. Given his treatment-refractory disease, the patient was started on deucravacitinib, an oral tyrosine kinase 2 (Tyk2) inhibitor, while continuing chloroquine 250 mg daily. At his three month follow-up, the patient reported noticeable improvement of his symptoms and rash, with minimal induration and only some violaceous changes remaining (Figure 1 D-F). He tolerated the medication well with no side effects.

Teaching point: Deucravacitinib, a Tyk2 inhibitor, is a promising therapy for recalcitrant tumid lupus erythematosus and may be an effective treatment option for other types of cutaneous lupus due to its downstream effect on type I interferon signaling. A subset of early phase II clinical trial data demonstrated that deucravacitinib achieved significant reduction in cutaneous lupus symptoms compared to placebo (CLASI-50 response 69.6% versus 16.7%; $p<0.001$).[1]

Abstract Category: Clinical Case

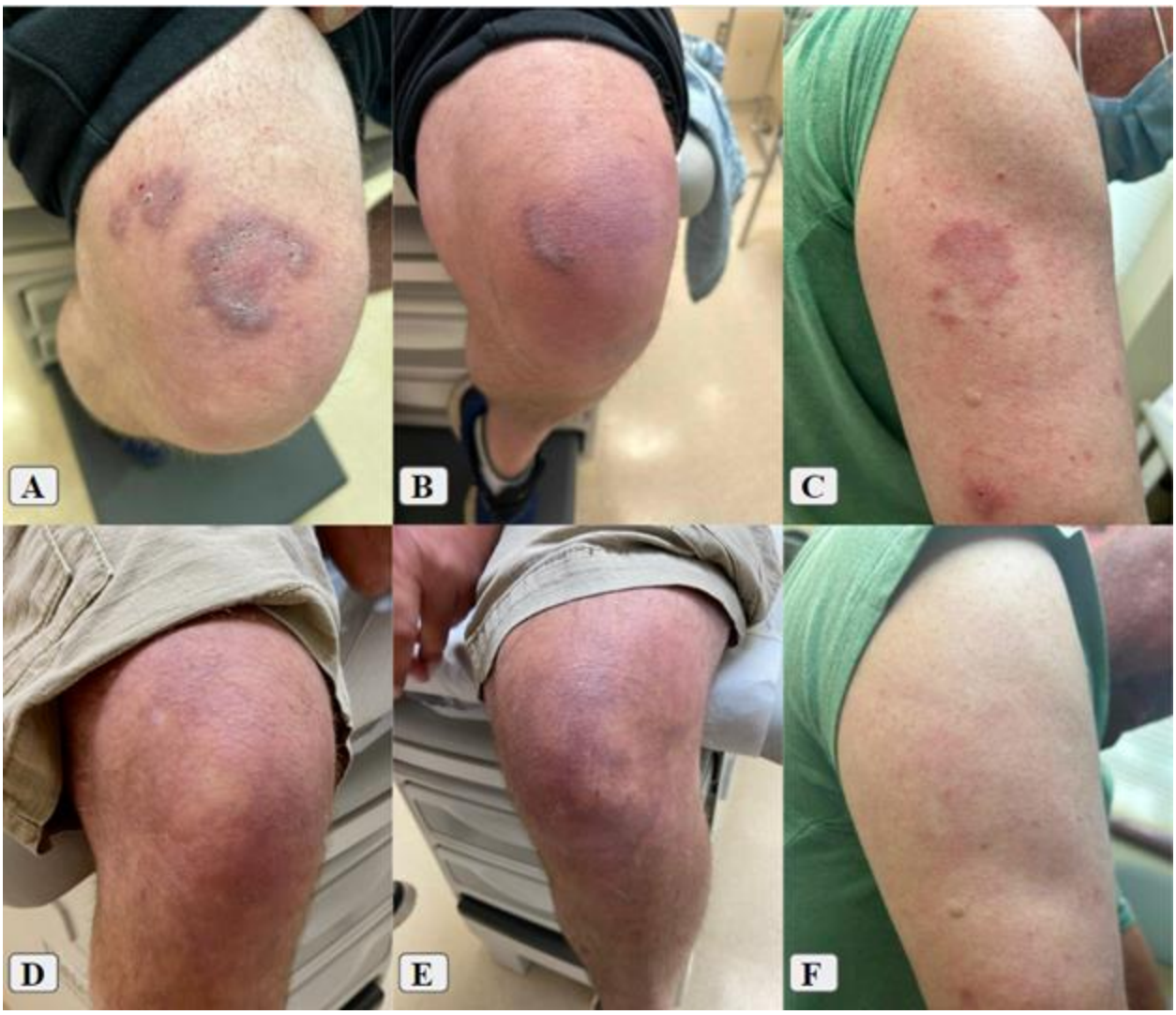

Figure 1. 51-year-old male pre- and post-treatment of tumid lupus erythematosus with deucravacitinib after four months. Right anterior lower extremity (A), left anterior lower extremity (B), and right upper extremity (C) with violaceous, indurated plaques prior to addition of deucravacitinib therapy. Right anterior lower extremity (D), left anterior lower extremity (E), and right upper extremity (F) three months after initiation of deucravacitinib therapy, with residual improved violaceous changes and minimal skin thickening at sites of previous plaques.

Clinical Cases of the Year

CEREBROSPINAL FLUID POSITIVITY IN RUBELLA VIRUS ASSOCIATED MULTISYSTEM GRANULOMATOUS DISEASE

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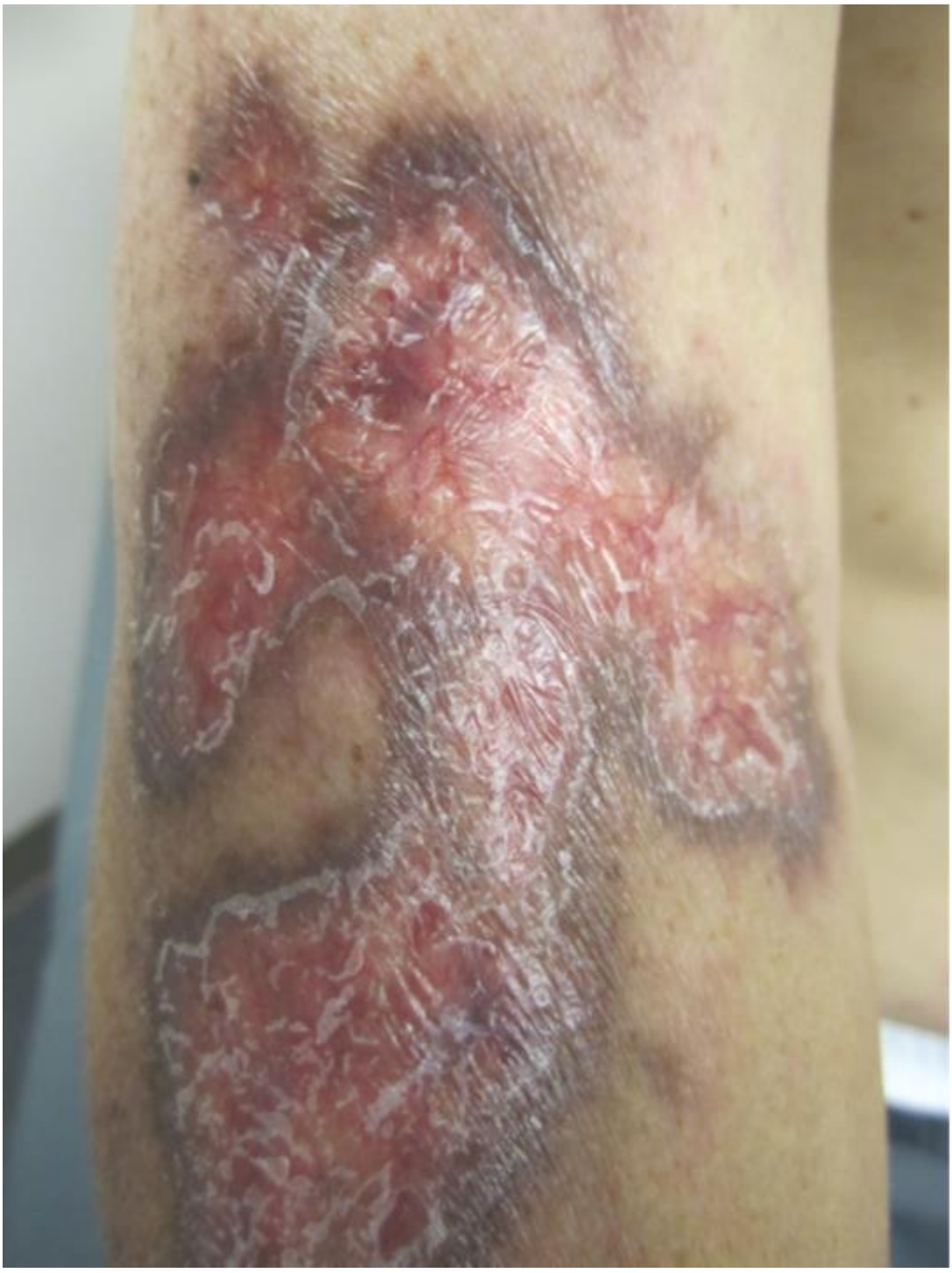
Rubella virus (RV) has been considered eliminated from the US since 2004, largely due to widespread implementation of the live-attenuated measles, mumps, rubella vaccine (MMR) vaccine. However, several recent cases document wild-type and vaccine-derived rubella virus (VDRV) detection within granulomata of systemic granulomatous disease with active viral shedding from nasopharyngeal secretions, skin lesions and urine. To our knowledge, VDRV detection in cerebrospinal fluid (CSF) has not been reported previously. We present a 41-year-old male with common variable immunodeficiency (CVID) first diagnosed during workup following the development of cutaneous granulomatous disease (CGD) in 2009. Over time his CGD became destructive and extensive, and he developed systemic involvement affecting his skin, eyes, liver, lungs, and central nervous system (CNS), alongside significant inflammatory arthritis. Disease activity stabilized with subcutaneous immunoglobulin, infliximab, methotrexate, hydroxychloroquine, and glucocorticoids. He experienced several years of good control. Unfortunately, following changes to his treatment regimen due to infections and somewhat fragmented care, the patient developed severe disease recurrence. Skin biopsy in 2020 was positive for RuV capsid protein on immunohistochemistry and reverse-transcription polymerase chain reaction (RT-PCR) confirmed VDRV. Despite resuming granuloma-directed therapy, the patient developed progressive skin, CNS and liver involvement and was hospitalized in 2022 following onset of blindness, severe hearing loss, anosmia, gait and balance issues. Active VDRV shedding was detected via RT-PCR from nasopharyngeal swab, and VDRV was detected in his CSF via metagenomic next-generation sequencing. Despite advancing immunomodulatory therapy with the addition of tofacitinib, and treatment with ribavirin and nitazoxanide, the patient expired in early 2023. Posthumously, the patient was found to have an inactivating mutation in IKZF3 (Aiolos). Both his mother and brother carried the same mutation but without CVID or CGD expression.

Teaching Point: VDRV and wild-type RV have been associated with granulomatous disease in a number of inborn errors of immunity, to our knowledge this is the first case of CNS detection of VDRV.

Abstract Category: Clinical Case



ALOPECIA SECONDARY TO SEVERE DISCOID LUPUS RESPONDING TO ANIFROLUMAB

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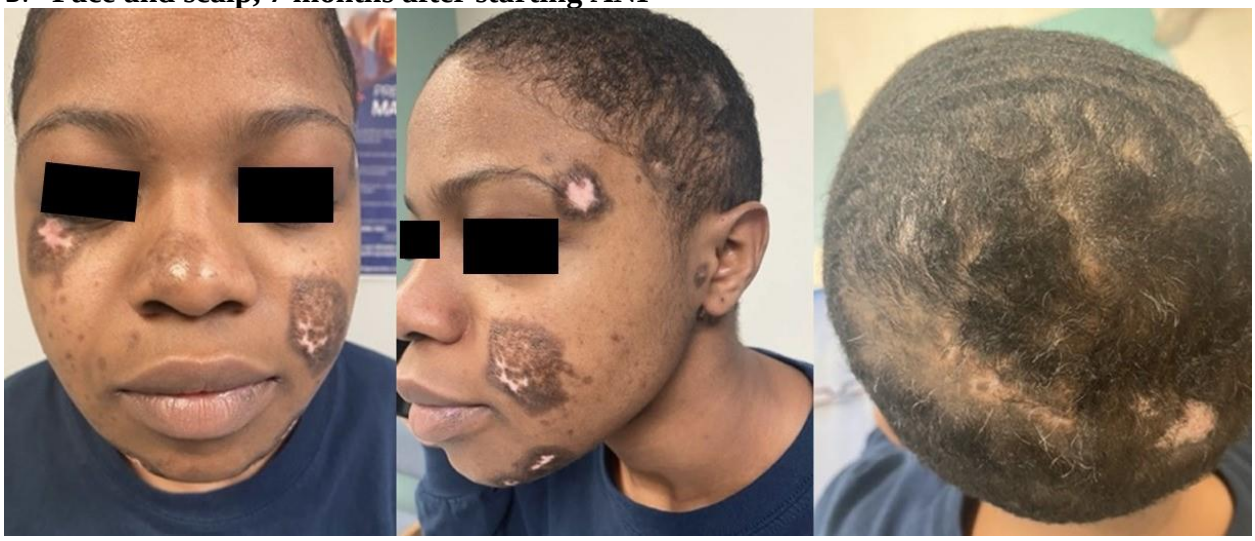
Discoid lupus erythematosus (DLE) is a subset of cutaneous lupus that can cause irreversible scarring and profoundly affect quality of life. Traditional therapies, including immunosuppressants, retinoids, antimalarials, and thalidomide have shown variable success for recalcitrant DLE. Anifrolumab (ANI), a human monoclonal antibody targeting type I interferon receptor subunit 1, was approved by the Food and Drug Administration (FDA) in 2021 for systemic lupus erythematosus (SLE). The hallmark phase 3 trial TULIP-2 studying ANI therapy in SLE showed a benefit in reduction of skin lesion severity, with 50% or more reduction in CLASI (Cutaneous Lupus Erythematosus Disease Area and Severity Index) activity score in 49% of patients treated with ANI versus 25% of patients in the placebo group. We present a case of a 21-year-old woman with a three-year history of a discoid rash and alopecia. Initial examination was notable for multiple erythematous atrophic patches with peripheral hyperpigmentation on the scalp, face, ears, and right upper chest within a tattoo, with significant alopecia of the scalp. Treatment with tacrolimus ointment, clobetasol ointment, and prednisone was initiated, with later addition of hydroxychloroquine and azathioprine. The patient had minimal response to the standard oral treatment options. Additionally, she had difficulty adhering to the treatment regimen, so the decision was made to stop azathioprine and to start ANI, with an infusion schedule of 300 mg every 4 weeks. At the one month follow-up visit, we observed significant improvement in appearance and size of cutaneous lesions, with impressive hair regrowth seen at seven months.

Figure 1. Face and Scalp of Patient at Baseline and 7 Months

A. **Face and scalp, prior to initiation of ANI**

B. **Face and scalp, 7 months after starting ANI**



Teaching Point: Prior evidence has shown significant benefit of Anifrolumab in patients with SLE, but there is minimal peer reviewed data regarding the efficacy in DLE. Anifrolumab is a therapeutic option that should be considered in patients with refractory or severe DLE. Its benefits include more favorable side effect profile and greater medication adherence.
Category: Clinical Case

WHEN TWO RARITIES MEET: SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA AND LUPUS PANNICULITIS IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOUSUS

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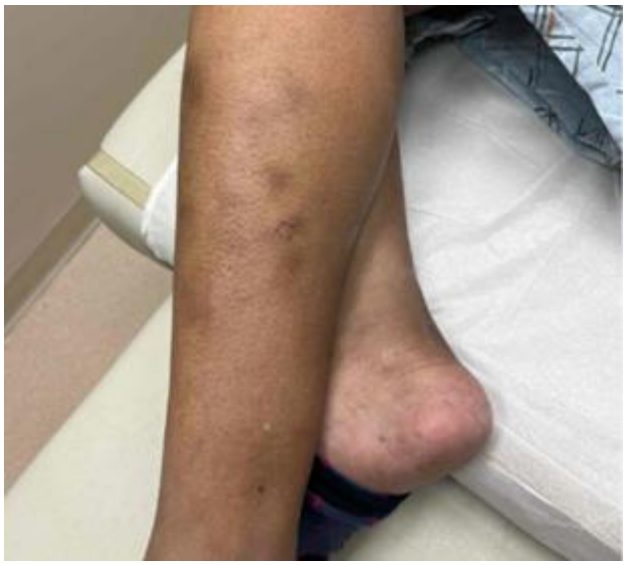
Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare cutaneous T-cell lymphoma often associated with autoimmune diseases, primarily systemic lupus erythematosus (SLE) (1,2). Approximately 37% of SPTCL patients may develop hemophagocytic lymphohistiocytosis (HLH), an immune hyperactivation syndrome that can result in multi-organ failure and death without timely detection (3). We present the case of a 52-year-old female with a history of SLE, rheumatoid arthritis, discoid lupus erythematosus, and lupus panniculitis (LEP) who presented with new tender nodules over her breast, arms, and particularly prominent on the distal lower legs. She was previously managed with methotrexate, but it was discontinued due to severe intolerance, leukopenia, and mucositis.

Despite her history of LEP, biopsies were taken to consider alternative diagnoses given that lower leg involvement[1] is not typical for LEP. Skin biopsies were remarkable for a prominent lymphoid infiltrate expressing alpha/beta T cell receptors, irregular peri-adipocyte rimming, prominent karyorrhexis, and coarse chromatin, suggesting a SPTCL diagnosis. PET scan results indicated FDG-avidity in subcutaneous tissue. The patient received oral cyclophosphamide, prednisone, and hydroxychloroquine for treatment, with some lesion reduction but ongoing lesion development. Ruxolitinib 10 mg BID was initiated (5/2023). Repeat PET scan (8/2023) found near complete resolution of subcutaneous FDG uptake and no new sites of FDG-avid disease.

SPTCL can closely resemble LEP and can also co-occur with LEP. SPTCL typically affects the distal extremities, compared to LEP, which tends to affect the scalp, face, and proximal extremities. Further differentiation requires histological, immunophenotypic, and molecular analysis. Treatment options include immunosuppressants, and refractory cases may necessitate radiation and bone marrow transplantation (4,5). Furthermore, HLH should be immediately suspected among patients with SPTCL who develop high fevers, a widespread maculopapular rash, cytopenias, and hepatic dysfunction. SPTCL patients are at risk of developing life-threatening HLH, emphasizing the importance of timely detection and intervention to improve outcomes.

Teaching point: SPTCL may clinically present similarly to LEP. Appropriate diagnosis and management are required to prevent development of HLH, multi-organ failure, and death.
Category: Clinical Case

1. 01/2023 
    a. Tender subcutaneous nodules on bilateral lower legs consistent with SPTCL.

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HISTIOCYTOID SWEET'S SYNDROME IN THE SETTING OF DERMATOMYOSITIS

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A 45-year-old man presented with a rash on the neck, dorsal hands, axillae, and lower extremities. He also noted one-month history of proximal lower extremity weakness. Physical examination revealed erythematous papules on the metacarpophalangeal joints, as well as erythema and poikiloderma of the upper chest, consistent with dermatomyositis. However, numerous coalescing 2-3 mm erythematous papules on the neck, axillae, suprapubic area, and posterior thighs were also seen, atypical of dermatomyositis. Punch biopsy of the latter eruption from the left thigh exhibited papillary dermal edema with dense collection of mononuclear cells staining positively for CD68 and myeloperoxidase, consistent with histiocytoid neutrophils. Increased dermal mucin was highlighted by colloidal iron stain. These histopathologic findings were most consistent with histiocytoid Sweet's syndrome (HSS). Though myositis antibody panel was negative, laboratory findings were notable for elevated CPK 300 mcg/L, ALT 1823 U/L, and AST 1518 U/L, and a normal bilirubin. MRI of bilateral femur also revealed symmetric high signal enhancement of bilateral iliopsoas musculature consistent with myositis, and muscle biopsy revealed perifascicular atrophy with perimysial lymphocytic infiltrate. Ultimately, the patient was diagnosed with HSS in the setting of dermatomyositis. In comparison to classic Sweet's syndrome, HSS carries a higher risk of associated hematologic malignancy; extensive hematologic-oncologic workup in this case returned negative. Our patient was treated with intravenous immunoglobulin and methylprednisolone followed by oral prednisone taper with improvement in muscle weakness and resolution of HSS. To our knowledge, classic Sweet's Syndrome in the setting of dermatomyositis has been reported in a handful of cases, but there are no cases of HSS in the setting of dermatomyositis. The atypical presentation of Sweet's in dermatomyositis may be due to adaptive tissue responses to noxious insults. We report this unique case of HSS in the setting of dermatomyositis to raise awareness of this rare association.

Teaching Point: Though classic Sweet's syndrome has seldom been associated with dermatomyositis, histiocytoid Sweet's syndrome (HSS) is an even rarer disease process to be described in the context of dermatomyositis and can present as small papules. It too responds well to systemic corticosteroids.

Abstract Category: Dermatomyositis, Clinical Case

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ELDERBERRY SUPPLEMENTS AND DERMATOMYOSITIS: A CASE SERIES

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Herbal supplement sales in the United States are a multi-billion dollar industry that experienced unprecedented growth during the COVID-19 pandemic for their purported immune benefit [1]. Elderberry (*sambucus spp*), the top selling herbal supplement ingredient of 2020 [2], has been shown to stimulate monocyte production of inflammatory cytokines IL-1β, TNF-α, IL-6, and IL-8 up to 45 fold that of LPS [3]. Furthermore, there are several reports of autoimmune disease onset or exacerbation coinciding with immunostimulatory herbal supplement use [4-6]. A systematic review of elderberry literature published before June 2020 found no apparent risk of immune overstimulation due to a lack of reported clinical outcomes [7]. However, here we describe 3 cases of dermatomyositis (DM) onset or exacerbation following elderberry use. Case 1: 71-year-old female with cardiovascular disease developed proximal muscle weakness and a characteristic DM rash in October 2020 following use of elderberry gummies. Laboratory analysis revealed elevated AST, CK, and positive TIF1-gamma antibodies. Skin biopsy was consistent with DM. She discontinued her elderberry supplement and her rash improved on hydroxychloroquine and prednisone. Case 2: 42-year-old female with anxiety and bipolar disorder was diagnosed with classic DM in December 2022. She began taking melatonin with elderberry in February 2023 with subsequent muscle weakness exacerbation and elevated ALP and ALT in March. She was advised to discontinue elderberry use. Case 3: Previously healthy 25-year-old female began taking elderberry supplements for an upper respiratory infection in July 2022. One month later, she developed a heliotrope rash, shawl sign, proximal muscle weakness, fevers, and arthritis. Hospitalization for persistent symptoms in August 2023 revealed elevated LFTs, CK, aldolase, ferritin, ESR, and CRP with bilateral thigh MRI enhancements, suggesting an autoimmune/autoinflammatory process with adult-onset Still's disease and DM as the leading differential diagnoses. These cases underscore the need for caution and further investigation regarding the immunostimulatory effects of elderberry supplements.

Teaching point: Those with a personal or family history of autoimmune disease should be cautioned against using elderberry or other immunostimulatory herbal supplements as they have the potential to induce or exacerbate autoimmune disease in susceptible individuals.
Category: Clinical case

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Poster Presentations

A DELAYED DIAGNOSIS OF A RARE AUTO-INFLAMMATORY DISEASE: SCHNITZLER SYDNROME

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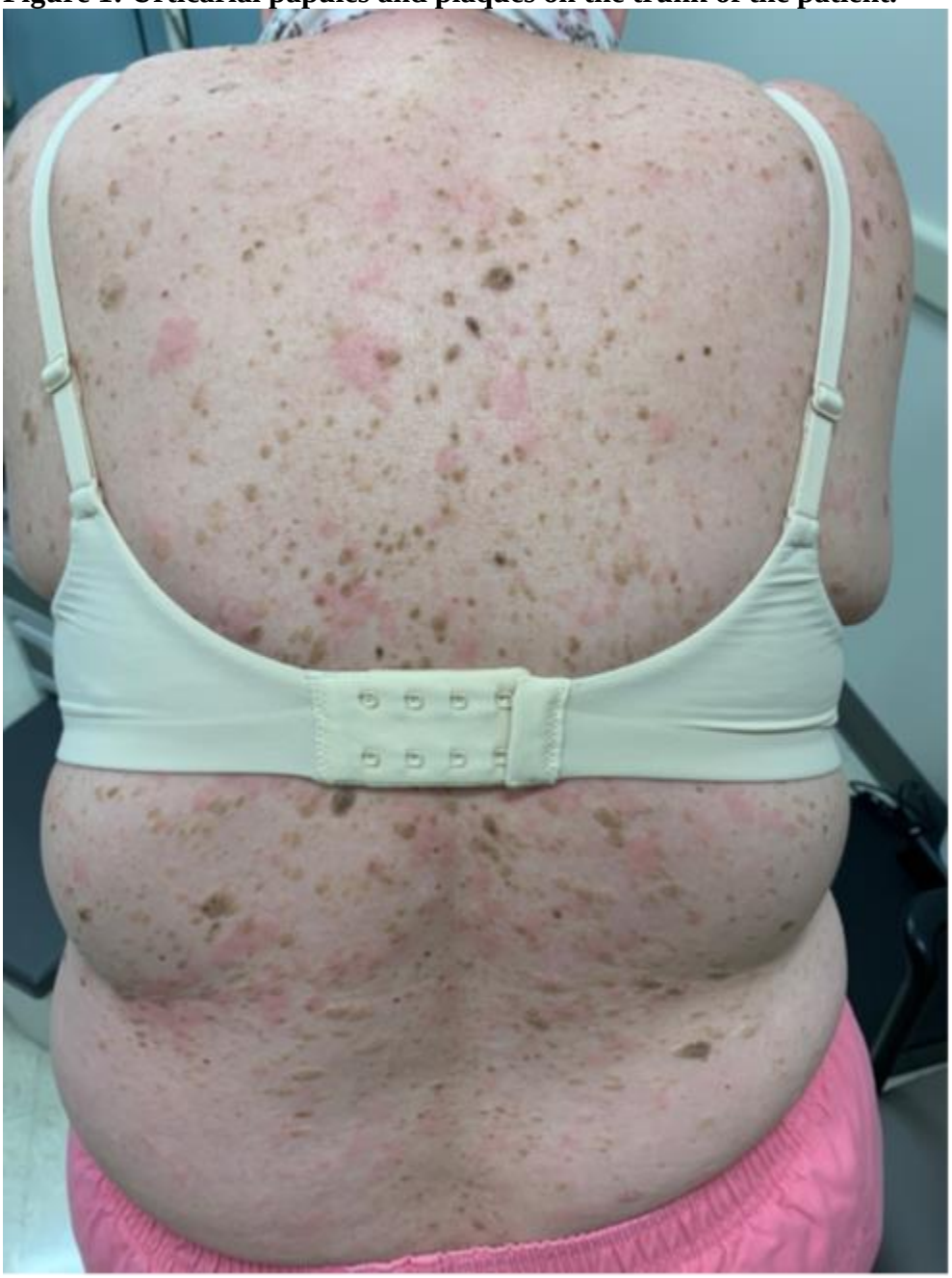
Abstract:
Schnitzler syndrome is a rare acquired/late onset auto-inflammatory disease associated with chronic urticarial rash that requires a monoclonal IgM component and at least two of the following signs for diagnosis: fever, joint and/or bone pain, lymphadenopathy, enlarged spleen and/or liver, increased erythrocyte sedimentation rate (ESR), increased neutrophil count, or abnormal bone imaging findings. This syndrome is often underdiagnosed or misdiagnosed, with a final diagnosis taking several years. We present the case of a 66-year-old female with a 15-year history of waxing and waning urticarial rash who required multiple subspecialist visits with dermatology, rheumatology, allergy/immunology and hematology/oncology for her ultimate diagnosis of Schnitzler syndrome. The patients' cutaneous manifestations included diffuse salmon-pink colored papules with coalescing plaques on her trunk, abdomen and extremities and was associated with a feeling of warmth, fatigue, chronic low back pain and arthralgias before abatement of her symptoms in 1-2 days. Further work up revealed elevated ESR/CRP, rheumatoid factor, ferritin, leukocytosis, and neutrophilia. Multiple biopsies showed urticarial dermatitis with a predominance of neutrophils, and she was initially diagnosed with chronic spontaneous/idiopathic urticaria. At first, she was treated with Allegra, montelukast, Pepcid, dapsone, systemic and topical steroids, with dapsone providing the most improvement. A trial of increasing doses of omalizumab showed minimal improvement followed by the addition of colchicine which remitted her rash and fatigue. A serum electrophoresis and immunofixation showed an elevated M-spike and IgM, meeting the Strasbourg criteria for Schnitzer's syndrome. Since around 20% of patients develop a lymphoproliferative disorder, a hematology referral for monoclonal gammopathy such as monoclonal gammopathy of undetermined significance (MGUS) or Waldenstrom's was made. Interleukin-1 (IL-1) blockers are the cornerstone of treatment for this disease, so canakinumab was started. This case provides additional clarity to the clinical course of Schnitzler syndrome and adds to the paucity of existing literature on this disease.

Teaching Point: Patients with Schnitzler syndrome are generally misdiagnosed and should be considered in the differential diagnosis of neutrophilic urticaria.

Category: Clinical Case

Figure 1: Urticarial papules and plaques on the trunk of the patient.



GRANULOMATOUS NODULES REVEAL ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA

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A 44-year-old male presented with a 4-month history of non-pruritic papules and nodules over his neck, bilateral arms, trunk, and face. Non-tender generalized lymphadenopathy was also appreciated. On review of systems, he endorsed subjective fevers, night sweats, and 30lb weight loss over the past 2 years. During this period, he was also diagnosed with a monoclonal IgG-λ gammopathy, hypothyroidism, and a peripheral neuropathy of unclear etiology.

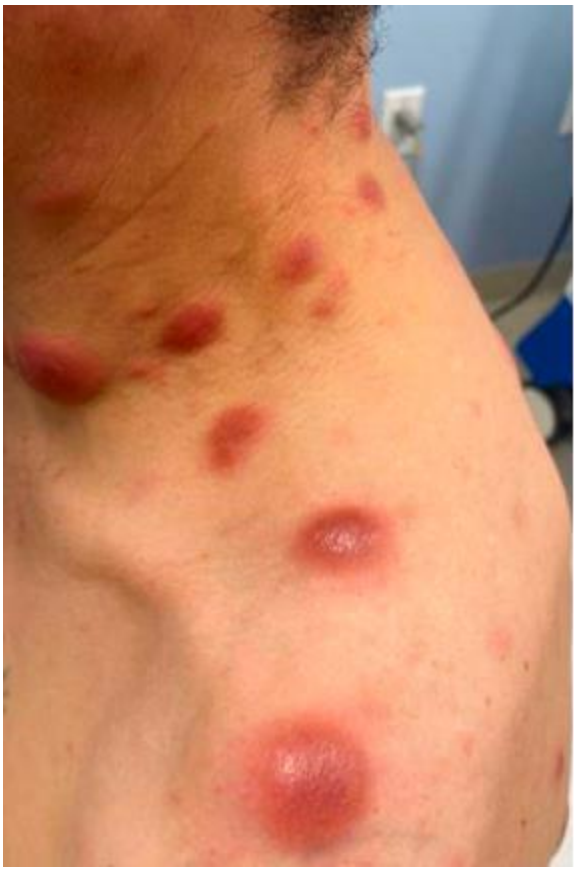
Given high suspicion for malignancy, two punch biopsies were obtained for H&E and was referred to hematology, where a core biopsy of the right inguinal lymph node was obtained. Notably, both skin and inguinal lymph nodes showed a mixed population of lymphocytes, histiocytes, eosinophils, and granulomas, but were non-diagnostic. CT of chest/abdomen/pelvis showed extensive, bulky lymphadenopathy and splenomegaly. A final, excisional biopsy of an inguinal lymph node revealed angioimmunoblastic T-cell lymphoma (AITL). Next-generation-sequencing detected TET2 mutations, which are particularly associated with AITL. PET/CT showed diffuse tumor infiltration throughout the body. The patient was initiated on chemotherapy with Romidepsin and Azacitadine.

AITL is a subtype of peripheral T-cell lymphoma (PTCL) with an aggressive course and poor prognosis. Approximately 50% of patients with AITL present with nonspecific cutaneous manifestations. It is also associated with hepatosplenomegaly, hypergammaglobulinemia, eosinophilia, autoimmune phenomena, and less commonly, neuropathy, which are all seen in this patient. Timely diagnosis may be challenging as it requires a constellation of clinical, laboratory, and histopathological findings.

Teaching Point: Angioimmunoblastic T-cell lymphoma (AITL) is a rare yet aggressive malignancy that often presents with cutaneous manifestations. Dermatologists should keep AITL in their differential for patients presenting with granulomatous nodules, particularly in the setting of systemic manifestations.

Category: Clinical Case

Clinical Photos:



PYODERMA GANGRENOSUM AFTER BREAST REDUCTION SURGERY

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Within 1-week of undergoing an uncomplicated bilateral breast reduction, a 61-year-old female presented with rapidly progressive ulcers, erythema, and severe pain on both breasts. Lesions began as tender vesicles along incision sites that quickly ulcerated and expanded in size. She also endorsed intermittent fever and chills.

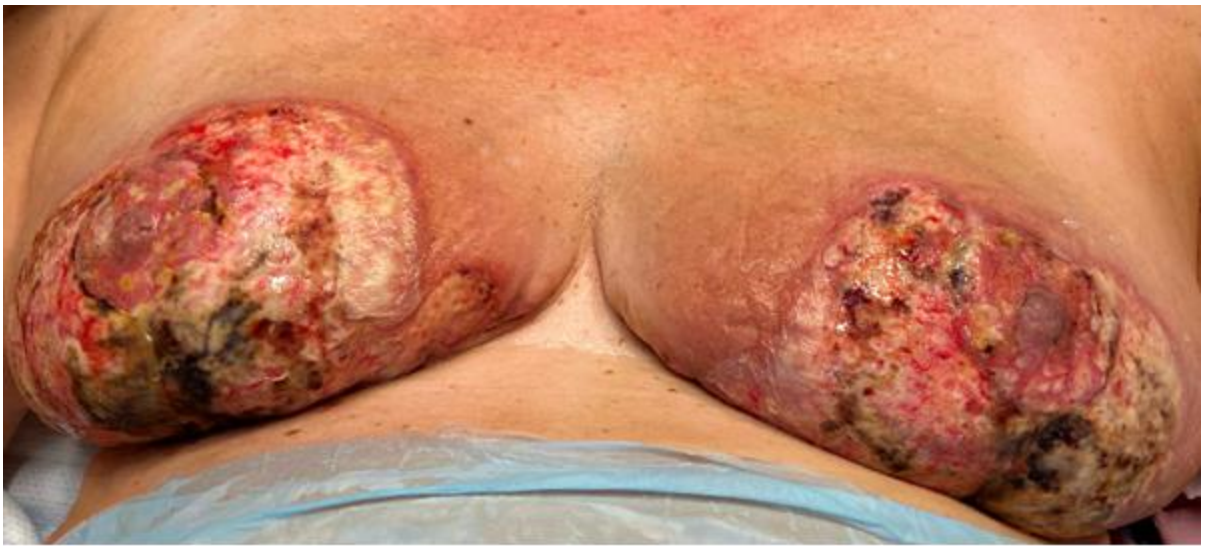
Physical examination showed two large, well-defined ulcerative plaques on bilateral breasts with overlying fibrinous and necrotic debris. Labs were remarkable for leukocytosis and elevated CRP. Antinuclear antibody, rheumatoid factor, and antineutrophil cytoplasmic antibodies were negative. Left breast punch biopsy revealed an ulcer with diffusely purulent neutrophilic infiltrate. Tissue culture returned negative for bacterial, fungal, and mycobacterial infections. Given her clinical presentation, tissue cultures, and biopsy findings, post-surgical pyoderma gangrenosum (PSPG) was diagnosed. She was initiated on adalimumab and a prednisone taper, which significantly improved her symptoms within 3 months.

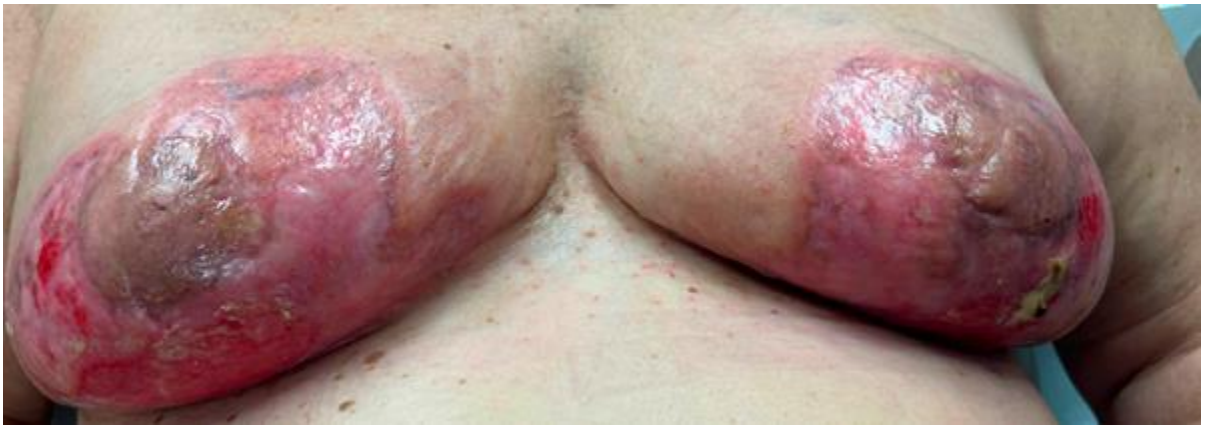
Pyoderma gangrenosum (PG) is an uncommon neutrophilic dermatosis that is characterized by painful, necrotic ulcers with undermined borders. Post-surgical pyoderma gangrenosum (PSPG) refers to the development of PG on surgical sites due to pathergy. Major risk factors of PSPG include a previous history of pyoderma gangrenosum, rheumatoid arthritis, inflammatory bowel disease, and hematologic malignancies. It is most associated with breast surgery, particularly reduction mammoplasty and breast reconstruction, accounting for 25% of all PSPG cases. Both cardiothoracic surgeries, particularly coronary artery bypasses, and abdominal surgeries, account for 14% of all PSPG cases. First-line treatment may involve systemic corticosteroids, cyclosporine, and immunomodulators.

Teaching Point: Post-operative pyoderma gangrenosum is an uncommon surgical complication that should be on dermatologists' differential when evaluating patients with ulcers on surgical sites, particularly after breast reduction mammoplasty and reconstruction. Additionally, biologic therapies should be considered as first-line treatment for patients with extensive and rapidly progressing disease.

Category: Clinical Case

Clinical Photos:





BYWATERS' LESIONS: A CASE OF CUTANEOUS RHEUMATOID VASCULITIS

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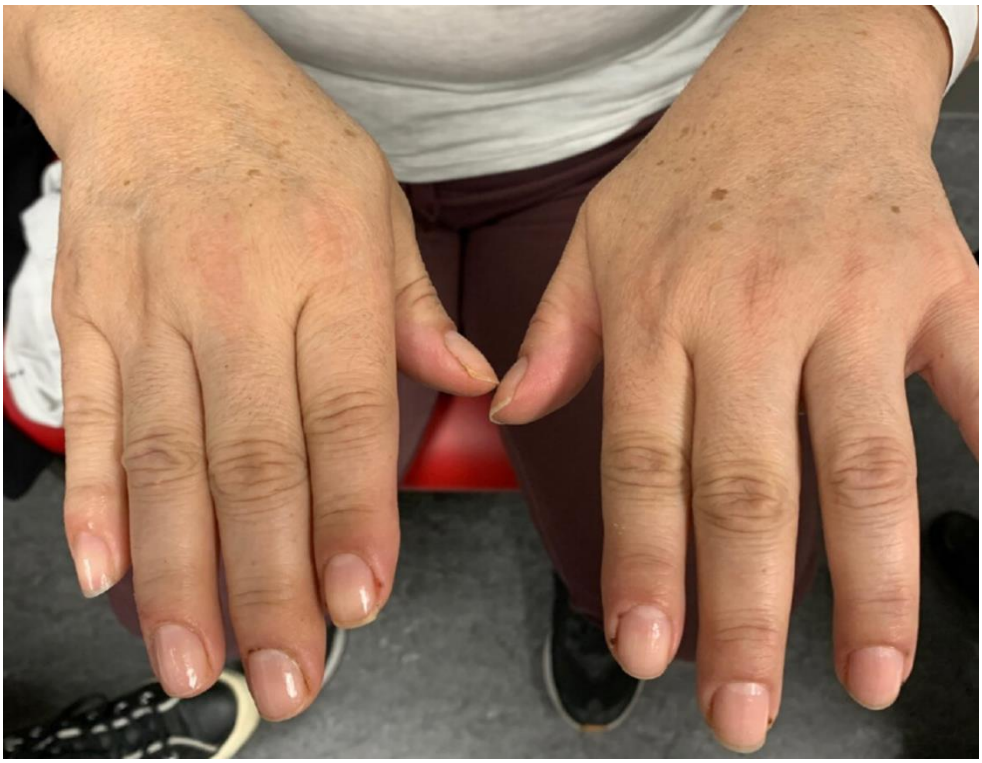
Rheumatoid vasculitis is a rare extra-articular manifestation of rheumatoid arthritis (RA) that can have systemic consequences. Rheumatoid vasculitis is typically seen in patients with long standing, seropositive, erosive disease. It can manifest with constitutional symptoms, neuropathy, cutaneous findings, ocular disease, and internal organ involvement. One subtype of rheumatoid vasculitis is isolated to the nail folds and termed Bywaters' Lesions. It is not associated with systemic organ involvement and generally responds well to treatment of the underlying RA. We present a 52-year-old woman with history of RA who presented to the rheumatology clinic with a 4-month history of painful lesions around several of her nails on both hands. Lesions initially appeared as red colored dots before turning darker and fading away. The patient had been treated with once weekly injection methotrexate and was recently started on etanercept for active RA. On exam, she had synovitis with 9 swollen and 14 tender joints. Several lesions were seen at the edge of the nailbeds on both hands. (Panel B, arrows). Subcutaneous nodules were palpated along the extensor surfaces of both forearms. Laboratory studies were notable for a positive rheumatoid factor of 60.9 IU/mL, CCP IgG antibody was greater than 250.0 units, C3 of 122 mg/dL (reference range 87-200), and C4 of 15 mg/dL (reference range 18-52). Additional studies revealed negative Anti Neutrophil Cytoplasmic Antibodies, negative hepatitis B core IgG and IgM antibodies, negative hepatitis B surface antigen, and negative hepatitis C antibody. Serum protein electrophoresis with immunofixation did not detect a monoclonal protein. A diagnosis of Bywaters' Lesions related to cutaneous rheumatoid vasculitis was made. The patient was started on treatment with a prednisone taper and was switched from etanercept to tocilizumab. At 3 month follow up, her nailbed lesions had resolved, and her joint pain and swelling had significant improved.

Teaching Point: Fingertip or nail bed lesions in a patient with active, seropositive RA should raise suspicion for Bywaters' lesions which are a rare cutaneous form of rheumatoid vasculitis that typically responds well to treatment of the underlying RA and has not been associated with internal organ involvement.

A



A: Bilateral hands with synovitis and nail bed lesions.

B: Closer look at nail bed lesions affecting several digits.

C: Complete resolution of nail bed lesions on 2 month follow up.

MORPHEA WITH UNDERLYING EOSINOPHILIC FASCIITIS

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A 79-year-old male was referred for bound-down plaques over the proximal extremities, trunk, and neck worsening for two years. Biopsy revealed an expanded dermis with hyalinized collagen bundles consistent with morphea. Autoantibody laboratory evaluation including RNA polymerase III, SSA/SSB, Scl-70, and ANA was negative; there was no absolute eosinophilia. An MRI of the thighs revealed bilateral medial and posterior thigh compartment fasciitis with mild muscle edema. The patient was diagnosed with eosinophilic fasciitis (EF) with overlying morphea, and he was started on methotrexate and continued on oral prednisone.

Another 59-year-old male patient was referred for hyperpigmented, firm plaques on the trunk and extremities with deep induration on the extremities, lower trunk, and buttocks and loss of joint mobility in the ankles, wrists, and hips. Two outside biopsies were consistent with morphea. CBC demonstrated absolute eosinophilia (927 cells/uL, range 15-500 cells/uL). He had been treated with oral methotrexate and oral prednisone with some improvement of the overlying plaques but no improvement of the deeper symptoms. MRI of the thighs showed nonspecific symmetric fasciitis and mild muscle edema. The patient was diagnosed with EF with overlying morphea. Due to refractory symptoms, he was switched to mycophenolate mofetil and recently started intravenous immunoglobulin.

EF and generalized morphea have overlapping features but have rarely been reported to coexist. MRI has shown to be a useful tool to confirm the diagnosis of EF when muscle biopsy is unavailable or nondiagnostic, and one systematic review showed 95% of patients with EF had an MRI finding suggestive of EF.

Teaching Point: Our cases highlight the importance of assessing for findings of eosinophilic fasciitis in cases of generalized or recalcitrant morphea, as well as emphasize the usefulness of MRI in diagnosing EF.

Category: Clinical Case

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Clinical Photo 1: 59-year-old male patient with hyperpigmented, firm plaque on the trunk with deep induration

Clinical Photo #2: 59-year-old patient with erythema, sclerosis, and induration of the lower extremities

A SINGLE CENTER RETROSPECTIVE ANALYSIS OF DERMATOLOGIC DIAGNOSES AND MISDIAGNOSES ASSOCIATED WITH DERMATMOYOSITIS

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Dermatomyositis (DM) is an idiopathic inflammatory myopathy with characteristic cutaneous findings. Accurately diagnosing cutaneous manifestations of DM is of paramount importance in ensuring prompt screening for potential comorbidities, notably interstitial lung disease and malignancy. However, the cutaneous manifestations of DM are frequently misdiagnosed due to their protean nature. Conversely, patients with DM may experience higher rates of other dermatologic conditions due to immunologic perturbations related to underlying autoimmune disease or systemic therapies. In pursuit of a comprehensive understanding of dermatologic manifestations in patients with DM, we aim to determine the prevalence of dermatologic diagnoses among individuals with DM and to characterize the misdiagnosis process, particularly concerning DM-mimicking diseases, including eczema, psoriasis, rosacea, among others. We identified a cohort of 178 DM patients who had ≥1 visit to a dermatologist and ≥1 relevant dermatological ICD-9/10 code (LXXX or skin cancer C44.XX). A correlating Epic™ diagnosis for each ICD code was assigned to a relevant dermatologic-disease grouping. 543 total dermatologic diagnoses were recorded, averaging 3.05 diagnoses per patient. The most prevalent diagnostic groupings were unspecified dermatitis (54 patients [30.3%]), pruritus (43 [24.1%]), pigmentation disorders (47 [26.4%]), infection (43 [21.9%]), and benign neoplasms (36 [20.2%]). After sub-categorization of primary inflammatory dermatologic diagnoses, the most frequent diagnosis were dermatitis (total: 72 [40.4%] – interface: 6 [3.4%], other: 12 [6.8%], unspecified: 54 [30.3%]), eczema (total: 60 [33.7%] – atopic: 9 [5.1%], contact: 18 [10.2%], unspecified eczema: 17 [9.5%], seborrheic: 16 [8.9%]), rosacea (17 [9.6%]), psoriasis/psoriasiform (15 [8.4%]), cutaneous lupus (7 [3.9%]), lichen planus/lichenoid (7 [3.9%]), and granulomatous disorders (5 [2.8%]). We are currently analyzing the data to determine the true prevalence of each diagnosis and the rate of misdiagnosis. Our ongoing analysis will contribute additional insights into the diverse cutaneous manifestations of DM, providing valuable clinical and diagnostic guidance to enhance patient care.

Category: Dermatomyositis

SUBTYPES OF DERMATOMYOSITIS (DM) AND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD): AN UPDATE AND COMPARISON TO CUTANEOUS LUPUS ERYTHEMATOSUS

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Category: Dermatomyositis
There has been increasing interest in the risk for atherosclerotic cardiovascular disease (ASCVD) in dermatomyositis (DM) and cutaneous lupus erythematosus (CLE). This study provides an update of ASCVD risk factor management and event risk in the UPenn DM-ASCVD cohort (n=238, 177 included, 61 excluded), and new comparisons between three DM subtypes (classic, amyopathic, hypomyopathic) and two LE groups (CLE with or without systemic LE) from the UPenn LE-ASCVD Cohort (n=370). By newly proposed guidelines (Keyes et al. 2021), 44.4% (n=12/27) were above goal for High Risk, 81.3% (n=104/128) above goal for Very High Risk and 68.2% (n=15/22) above goal for Extreme Risk. The number of patients categorized for each category was not significantly different between subtypes of DM and LE, $\chi^2(8, N=531) = 4.09$, p=0.85, nor the number of patients who were above goal LDL, $\chi^2(8, N=290) = 9.64$, p=0.29. Further, by American College of Cardiology's Risk Estimator Plus, there was no difference between the number experiencing 10-year estimated ASCVD event risks, $\chi^2(16, N=480)=21.36$, p=0.17, between LE and DM subtypes, nor between the number of patients who were not on LDL-lowering medication for each of those categories, $\chi^2(16, N=327)=11.00$, p=0.81. Of 118 DM patients with hypertension, 42.4% (n=50/118) were not on any anti-hypertensive medications, and another 41.5% (n=49/118) were undertreated. Diabetes management is adequate in DM and LE, and significantly fewer DM patients smoked compared to LE patients. 12.4% (n=22/177) experienced a major ASCVD event. Out of patients on LDL-lowering medications, DM patients were more likely to be on ezetimibe than LE patients, $\chi^2(1, N=167)=8.90$, p=0.0029, demonstrating a predilection for alternative LDL-lowering medications from statins in DM compared to LE. We conclude that ASCVD risk factors of hyperlipidemia and hypertension in DM still needs greater attention and that the management of these risk factors are comparable to that in LE. odel has good face validity and a simple structure that captures typical endpoints used in clinical trials. Further research and discussion of the model design will enable refinement and inform decisions in the evaluation of new therapies for CLE. Category: Lupus

CUTANEOUS VASCULITIS IN PATIENTS WITH ACTIVE VERSUS INACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS

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Cutaneous vasculitis (CV) is a rare manifestation of systemic lupus erythematosus (SLE). Raynaud's phenomenon and hematologic manifestations are predictors of CV. Hypocomplementemia, lupus nephritis, musculoskeletal manifestations, and Sjogren's syndrome are also reported to be associated with CV. About 61% of SLE patients with CV had inactive SLE during CV occurrence. To our knowledge, previous studies have not determined differences in characteristics of patients with active versus inactive SLE. A retrospective chart review was performed for patients with active SLE and with inactive SLE to determine demographics, clinical manifestations, lab and serologic findings, histologic results, and treatments. The patients with active SLE with CV have findings of systemic vasculitis involving the central nervous system, while CV in patients with inactive SLE is limited to the skin. Hypocomplementemia and cytopenia are present in the patients with active SLE but not in the patients with inactive SLE. CV in patients with active SLE presents near initial diagnosis of SLE and resolves with treatment of SLE, while CV in patients with inactive SLE tends to be more refractory and requires more targeted and intensive treatments. CV in patients with active SLE is associated with more systemic vasculitis compared to patients with inactive SLE. However, CV in patients with inactive SLE tends to be more severe compared to CV in active SLE patients and requires more intensive immunosuppression. Larger studies are needed to confirm these findings.

Category: Lupus

EFFICACY AND SAFETY OF LITIFILIMAB IN CUTANEOUS LUPUS ERYTHEMATOSUS: PHASE 2/3 AMETHYST STUDY DESIGN

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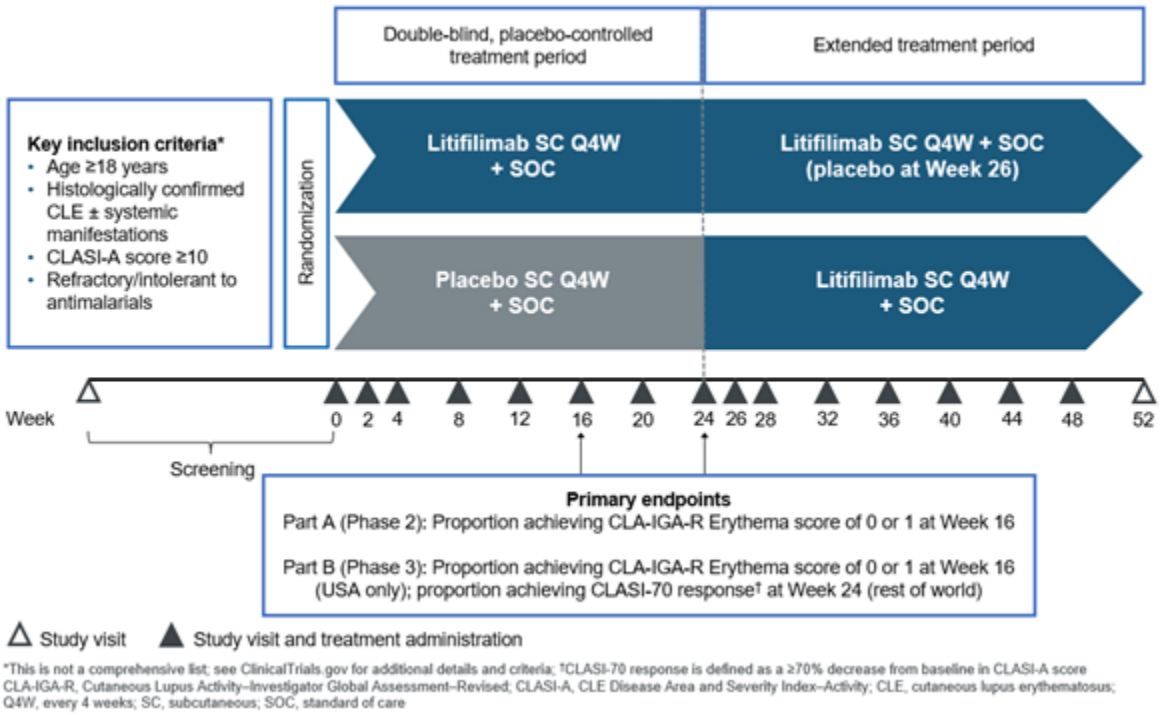
Abstract (300 words of 300 maximum)

Data from the Phase 2 LILAC study (NCT02847598) of litifilimab (BIIB059), a humanized immunoglobulin G1 (IgG1) monoclonal antibody targeting blood dendritic cell antigen 2 (BDCA2), supported its continued development in cutaneous lupus erythematosus (CLE) (Werth VP, et al. NEJM 2022;387:321–331). AMETHYST (NCT05531565), a global, multicenter, randomized, double-blind, placebo-controlled (DBPC), operationally seamless Phase 2/3 study of litifilimab, described here, is ongoing. AMETHYST will further evaluate litifilimab efficacy and safety in participants with active subacute or chronic CLE. Eligible participants are aged ≥18 years, with histologically confirmed diagnosis of subacute or chronic CLE (with or without systemic manifestations) that is refractory or intolerant to antimalarials, and a Cutaneous Lupus Erythematosus Disease Area and Severity Index–Activity (CLASI-A) score ≥10. Enrolled participants receive subcutaneous litifilimab or placebo once every 4 weeks (Q4W) during Weeks 0–20 and at Week 2; all participants receive litifilimab Q4W during Weeks 24–48 and placebo or litifilimab (respectively) at Week 26 to maintain blinding (Figure). Stable lupus background treatment is permitted. The primary endpoints are the proportion of participants achieving a Cutaneous Lupus Activity–Investigator Global Assessment–Revised (CLA-IGA-R) Erythema score of 0 or 1 at Week 16 (Phase 2 in all participating regions; Phase 3 in the USA only), or a ≥70% decrease from baseline in CLASI-A score (CLASI-70 response) at Week 24 (Phase 3 in the rest of the world). Secondary endpoints (including CLASI-50 response, change from baseline in CLASI-Damage score, further CLA-IGA-R analyses, and safety) will evaluate efficacy and safety during the DBPC and extended treatment periods. AMETHYST is recruiting; estimated enrollment is 474 participants. Data from AMETHYST will help further characterize the efficacy and safety of litifilimab in patients with subacute or chronic CLE. Funding: Biogen.

Medical writing: Selene Medical Communications, funded by Biogen. Abstract first presented at the ISID/ICCLE 2023 meetings.

Category: Lupus

Figure. AMETHYST study design



*This is not a comprehensive list; see ClinicalTrials.gov for additional details and criteria; †CLASI-70 response is defined as a ≥70% decrease from baseline in CLASI-A score
CLA-IGA-R, Cutaneous Lupus Activity–Investigator Global Assessment–Revised; CLASI-A, CLE Disease Area and Severity Index–Activity; CLE, cutaneous lupus erythematosus; Q4W, every 4 weeks; SC, subcutaneous; SOC, standard of care

INTERIM ANALYSIS OF COVID-19-RELATED OUTCOMES IN THE CONTEXT OF AUTOIMMUNE CONNECTIVE TISSUE DISEASE

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Coronavirus disease 2019 (COVID-19) is recognized as an immune-mediated disease, characterized by severe immune dysregulation in response to viral infection. Whether preexisting autoimmune disease results in more severe COVID-19 illness remains a subject of intense debate. Immunosuppressive and immunomodulatory (IS/IM) therapies used to treat autoimmune connective tissue diseases (AICTDs) have been used in the management of severe cases of COVID-19 with variable clinical benefit; the advantages and disadvantages of such therapies likewise remain controversial. A retrospective cohort study of patients seen in MHealth-Fairview clinics who have an AICTD diagnosed before 1/1/2020 with diagnostic confirmation in outpatient dermatology or rheumatology notes between 1/1/2010-6/30/2021 was performed. Data regarding COVID-19-related outcomes and timelines of IS/IM therapies were collected between 1/1/2020-6/30/2021. SARS-CoV-2 PCR and antibody results and rates of vaccination, hospitalization, intubation, and death were assessed. 1221 patients with AICTD were identified (80.6% female; mean age 56.7 years). The COVID-19 vaccination rate was 64.7%. 13.7% were diagnosed with COVID-19 during the study period and 21 (1.7%) participants were hospitalized due to complications from COVID-19. Most (81.0%) were not vaccinated for COVID-19 at the time of their hospitalization. One of the patients admitted with COVID-19 was intubated during their admission and there were five COVID-19-related deaths during the study window. Future analysis will evaluate COVID-19-related outcomes in patients with preexisting AICTD, stratified by demographics, IS/IM pharmacotherapy, and comorbid COVID-19-related risk factors. A complete analysis of these data may assist with assessment of the risks and benefits of IS/IM therapy for patients with AICTD during future COVID-19 outbreaks.

Abstract Category: E. Miscellaneous Rheumatic Skin Disease

COMPARING COMORBID CONDITIONS IN PALMOPLANTAR PUSTULAR PSORIASIS AND INTRINSIC HAND DERMATITIDES

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Palmoplantar pustular psoriasis (PPPP) is characterized by sterile pustules localized to the palms and soles. Commonly described comorbidities include inflammatory arthritis, thyroid dysfunction, contact sensitivities, and metabolic syndrome, though its psychiatric burden is poorly characterized.[1] Intrinsic hand dermatitides (IHD) are a group of frequently diagnosed, multifactorial conditions that result in skin barrier dysfunction of the hands. Individuals with IHD experience a higher prevalence of elevated body mass index, cardiovascular disease, and psychiatric disorders.[2,3] Although PPPP and IHD share clinical features, the prevalence and severity of associated systemic comorbidities differ and are primarily discussed separately in the literature without direct comparison.[1,4] We performed a retrospective analysis of adult patients with PPPP or IHD (confirmed by review of physician note) who were seen at MHealth Fairview Clinics between 1/1/2010-12/31/2019 to evaluate the prevalence of comorbid metabolic and psychiatric conditions. Data regarding metabolic and psychiatric conditions were collected using ICD-10 coding. Statistical significance was calculated using logistic regression analysis. We identified 258 patients with IHD and 76 with PPPP. Patients who identified as White made up the majority of both groups. Patients with PPPP tended to be older, heavier, and female, though these differences were not statistically significant. After adjusting for demographics, the odds of depression and diabetes in patients with PPPP were greater than those with IHD (OR 2.07 & OR 2.42; p=0.013 & p=0.016, respectively). There were no differences observed in the odds of anxiety, hypertension, hyperlipidemia, cardiovascular disease, or stroke between the groups. Our data suggest a greater need to screen patients diagnosed with PPPP compared to those diagnosed with IHD for depression and diabetes, facilitating prompt referrals to appropriate care to address these potential comorbidities.

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Abstract category: Miscellaneous rheumatic skin disease

PHOTOPROTECTIVE PRACTICES IN PATIENTS WITH AUTOIMMUNE DERMATOLOGIC DISEASES

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The American Academy of Dermatology strongly recommends that photoprotection be included in a daily skincare routine for all skin types. Patients with certain autoimmune diseases can have increased frequency and severity of disease flares in response to exposure to ultraviolet (UV) radiation. This study focused on understanding the photoprotective practices of patients with autoimmune skin diseases. A ten-question Qualtrics survey was offered to patients at general and rheumatology-dermatology clinics. One hundred patients completed the survey with 21 patients indicating that "autoimmune disease" was the primary reason for seeing a dermatologist. However, only 19% of autoimmune disease patients reported using sunscreen daily compared to 32% of the remaining patients. Interestingly, sunglasses were the leading form of photoprotection in both groups with 52% of autoimmune disease and 56% of general dermatology patients indicating that they wear sunglasses daily. Although twelve autoimmune disease patients selected using sunscreen with SPF 35 or higher, only five patients used a broad-spectrum sunscreen, seven used a water-resistant sunscreen and zero reported reapplying their sunscreen every two or four hours. Dermatology visits can serve as important opportunities to educate autoimmune disease patients about the importance of using sun protection daily, reapplying sunscreen, and selecting sunscreen with key properties. Increased education may reduce the incidence of autoimmune flares in susceptible patients.

Category: Miscellaneous rheumatic skin disease

EVALUATION OF PENTOXIFYLLINE IN THE TREATMENT OF NECROBIOSIS LIPOIDICA: OUTCOMES IN TEN PATIENTS

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Purpose: Necrobiosis lipoidica (NL) is a chronic granulomatous disease typically characterized by yellow-brown plaques with elevated violaceous rims involving the anterior pretibial region.[1] NL is associated with a poor cosmetic prognosis; high-quality treatment data are lacking. Although its etiology is not well characterized, NL may be associated with microangiopathy.[1] Pentoxifylline (PTX) is an anti-inflammatory vasodilator that has improved and completely reversed NL in case reports.[1-4]
Methods: PTX for the treatment of NL was evaluated via a 10-patient retrospective medical record review of NL patients treated with PTX between 2013-2020. Four total patients were lost to follow-up evaluation and were not included in the analysis. Outcomes were categorized as response (no new lesions and non-inflamed [brown] borders) and no response.
Results: Ten patients, primarily white (90%) females (80%) with a mean age of 36 $\pm$ 20 years, met the inclusion criteria. Seven patients had histories of diabetes mellitus (five type 1, two type 2) with a median hemoglobin A1c of 9.0 (range 5.1-15.3) upon initial presentation.[5] Other chronic conditions included dyslipidemia (5), hypertension (3), morbid obesity (body mass index > 40), sarcoidosis (2), and hypothyroidism (1).[5] All had lesions of the lower extremities. Eight were atrophic, while seven reported ulcerations and telangiectasias. Patients were diagnosed with NL a mean of four years before PTX initiation. Nine patients were naïve to systemic treatments; one had undergone prednisone therapy and experienced pain relief without change in size or appearance of their NL lesions. Seven patients were prescribed topical corticosteroid treatment before starting PTX.

All patients were prescribed PTX at 400 mg three times daily for a median of 12 months. Four patients achieved disease inactivity within a mean of 3.5 months, slower than previous reports (one month).[3] One patient with stabilization and symptomatic relief with PTX monotherapy experienced further subjective improvement with the addition of concomitant dapsone. Only one of five patients who underwent adjunctive therapy with 81 milligrams of aspirin daily and topical clobetasol achieved disease inactivity. No patient completely cleared, experienced malignant transformation, or developed ulcerations during PTX therapy. PTX was well-tolerated; two patients complained of nausea.

Implications: Managing NL is challenging. Despite a broad therapeutic armamentarium, NL has no well-defined therapeutic ladder.[1] While this study is limited by a small sample size and non-standardized outcome measures, PTX appears to be a well-tolerated, albeit not highly effective, treatment option to consider.
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Title: A NOVEL ASSOCIATION BETWEEN LIPODERMATOSCLEROSIS AND KEY VASCULAR OUTCOMES IN SYSTEMIC SCLEROSIS

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Lipodermatosclerosis (LDS) is a progressive condition linked to chronic venous insufficiency, presenting distinct changes in the lower extremities, such as an "inverted champagne bottle" appearance, skin hyperpigmentation, and occasional non-healing ulcers. Although not studied extensively alongside connective tissue diseases, it shares similar pathogenic pathways with systemic sclerosis (SSc), where vasculopathy leads to tissue hypoxia, inflammation, and subsequent fibrosis of the skin and subcutaneous tissues. This study estimated the prevalence of LDS in SSc, examined the demographic and SSc-related characteristics of patients with LDS, and estimated the association between LDS and major vascular outcomes in patients with SSc. We performed a retrospective cohort analysis of adult patients enrolled in our Autoimmune Skin Disease Registry between 2004-2023 and met ACR/EULAR 2013 classification criteria for SSc. While descriptive statistics were used to summarize data, logistic regression estimated prevalence odds ratios (pOR) and 95% confidence intervals of the association between LDS and a composite macrovascular outcome measure, including digital gangrene and/or renal crisis and/or pulmonary hypertension, adjusted for age and follow-up time. Among 586 SSc patients, 4% (N=25) had LDS. Baseline demographic and disease features were similar between the groups with the exception that patients with LDS had higher frequencies of cardiac arrhythmias, heart failure, and pulmonary hypertension (PH). Among patients with LDS, 36% were either discharged to hospice or died during a median follow-up time of 7.5 years, compared to 20.5% of patients without LDS followed for 5.6 years. LDS was associated with the composite vascular outcome in adjusted analysis with pOR =2.36 [1.02-5.45], but this was primarily driven by the association with PH. Sensitivity analysis confirmed an elevated pOR between LDS and pulmonary hypertension, with an adjusted pOR of 3.20 [1.37-7.49]. We conclude that LDS could portend severe vasculopathic manifestations in SSc, however temporality could not be determined by our analyses.

Teaching point: Clinicians should recognize the clinical features of LDS in SSc patients and closely monitor these patients for PH and other macrovascular complications.

Category: Sclerotic skin disease

ASSESSING COMPREHENSIVENESS, UNDERSTANDABILITY, ACTIONABILITY, AND READABILITY OF ONLINE HEALTH RESOURCES FOR MORPHEA

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This study assesses the quality of online patient health resources for morphea, focusing on their readability, understandability, and actionability. While prior research has investigated the readability of materials for various dermatologic conditions, our objective was to evaluate the alignment of online resources for morphea with patient concerns. We conducted a Google keyword search for "morphea," reviewed the first 30 webpages, and included 15 relevant resources after excluding journal articles and materials not intended for patient education. Future analysis will explore related terms such as “localized scleroderma,” “linear scleroderma,” and “en coup de Sabre.” Online resources underwent coding for themes derived from focus group interviews on morphea patients' quality of life, including descriptions of the disease experience, treatment, and differentiation from systemic sclerosis. We assessed readability using multiple established indices, including the Flesch-Kincaid Grade Level, before and after excluding unavoidable polysyllabic terms. Understandability and actionability were evaluated with the Patient Education Materials Assessment Tool (PEMAT), with a threshold of 70% for actionable or understandable resources. Initially, no materials met the American Medical Association's recommended readability standards, increasing to two (13.3%) after excluding complex terms. PEMAT scoring revealed that one source reached the threshold for understandability though none met the criteria for actionability. Content analysis illuminated critical gaps in these resources, including the absence of information on family planning, treatment costs, and the impact on personal relationships. Side effects of treatments were mentioned by 6.6% of sources and only 26.6% acknowledged impacts on self-esteem. Furthermore, only 40% of the resources addressed the incurability and non-contagious nature of morphea. These findings underscore the need for improved patient resources for morphea. Future efforts in patient education materials development should prioritize patient concerns and enhancing readability, understandability, and actionability.
Category: Sclerotic skin disease

POPULATION-LEVEL RETROSPECTIVE STUDY ASSOCIATING LICHEN SCLEROSUS WITH NUMEROUS AUTOIMMUNE DERMATOLOGIC AND RHEUMATOLOGIC CONDITIONS

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Abstract:

Lichen sclerosus (LS) is a chronic inflammatory mucocutaneous condition with a proposed T-cell mediated autoimmune pathogenesis. LS has been linked to several other autoimmune diseases, including thyroid disease, morphea, psoriasis, and primary biliary cirrhosis. Herein, we performed a population-level retrospective study to better evaluate the association between LS and other autoimmune conditions. We utilized TriNetX, a global health research network of over 95 million patients from the US, to retrospectively evaluate patients seen between June 2003-2023. International Classification of Diseases-10 (ICD-10) code L90.0, lichen sclerosus et atrophicus, was used to identify LS cases. Since LS most frequently affects the vulva, ICD-10 code N95, postmenopausal atrophic vaginitis, was used to identify the control cohort as this is a diagnosis without known autoimmune disease association. Cohorts were matched by age, sex, and race/ethnicity. Odds ratios with 95% confidence intervals were used to identify autoimmune diseases associated with LS. The LS cohort consisted of 81,787 patients with an equal number of matched controls. LS patients had an increased odds of the following conditions: morphea, systemic sclerosis, vitiligo, alopecia areata, psoriasis, psoriatic arthritis, systemic lupus erythematosus, discoid lupus erythematosus, other local lupus erythematosus, dermatomyositis, lichen planus, autoimmune thyroiditis, primary biliary cirrhosis, and Sjogren's syndrome. LS patients were found to have a decreased odds of myasthenia gravis and multiple sclerosis. LS was not associated with subacute cutaneous lupus erythematosus, reactive arthritis, type 1 diabetes, celiac disease, rheumatoid arthritis, inflammatory arthritis, or irritable bowel disease. Overall, our study found LS is associated with numerous autoimmune diseases, both systemic and cutaneous, confirming previously reported LS disease associations and finding new disease associations. Though further studies are warranted, these findings suggest LS may exist as part of a more systemic and complex autoimmune process and should not be considered an isolated anogenital skin disease.

Abstract Category: Sclerotic skin disease

THERAPEUTIC PROMISE OF HYALURONIDASE IN SYSTEMIC SCLEROSIS: A SYSTEMATIC REVIEW

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Systemic sclerosis (SSc), is a rare autoimmune condition characterized by skin and organ fibrosis, which can result in significant morbidity. Hyaluronidase, an enzyme that degrades hyaluronic acid in the extracellular matrix, presents a potential therapeutic option for scleroderma-induced microstomia. Therefore, we conducted a comprehensive systematic review initially on PubMed and Embase using the search terms “hyaluronidase” AND “scleroderma,” and "hyaluronidase” and “systemic sclerosis” yielding 213 articles. After screening the search results based on predetermined criteria, ten articles were included in our review. Our inclusion criteria comprised English articles published between 2013 to 2023. Articles not meeting the specified publication date range or published in other languages were excluded. Additionally, articles describing morphea, scleredema, scleromyxedema, or oral submucous fibrosis unrelated to underlying SSc were excluded. Our analysis consistently suggested an improvement in skin elasticity with simultaneous reductions in dermal thickness following hyaluronidase administration. A majority of studies reported a notable improvement in fibrotic manifestations of SSc: scleroderma-induced microstomia or and temporomandibular joint mobility as determined by MHISS (Mouth Handicap of Systemic Sclerosis) or direct mouth aperture measurement. The timing of symptom improvement varied depending on factors like disease severity and treatment protocols implemented. Two studies reported significant relief from microstomia-related symptoms at two weeks post-injection, while another two studies noted improvement after 3-5 months. Notably, no adverse side effects were documented with the exception of injection site bruising in two studies. The majority of articles focused on therapy for SSc-related microstomia, however, limited studies addressed its use in other SSc-related phenomenons such as Raynaud’s. Hyaluronidase has been shown to be effective in alleviating microstomia, a prominent and often distressing component of SSc. Our goal is to provide valuable insights into the clinical application of hyaluronidase in SSc treatment to ultimately advance evidence-based therapies to potentially enhance SSc patient outcomes and quality of life.

Category: Sclerotic skin disease (systemic sclerosis)

DEMOGRAPHIC CHARACTERISTICS AND COMORBIDITIES IN CUTANEOUS LUPUS ERYTHEMATOSUS PATIENTS OF HISPANIC ETHNICITY IN A LONGITUDINAL ELECTRONIC HEALTH RECORD DATABASE IN THE UNITED STATES

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Background: Cutaneous lupus erythematosus (CLE) is more common among African-Americans and Hispanics compared to non-Hispanic Whites, but there are limited published epidemiologic data on demographics and comorbidities among Hispanic CLE patients. The primary objective was to characterize demographic characteristics and frequencies of comorbidities among CLE patients of Hispanic ethnicity. *Methods:* This descriptive study utilized the Optum® de-identified Electronic Health Record dataset, which includes inpatient and ambulatory care records for ~103 million people in the US between 2007–2019. Adult CLE patients were defined as having ≥2 ICD-9 or ICD-10 codes for CLE during enrollment in the database. The date of the first CLE diagnostic code on record (index date) was considered the diagnosis date. Demographic characteristics and comorbidities were compared among the CLE patients by ethnicity. *Results:* Among 27,532 CLE patients, 4.8% (n=1,314) were Hispanic, 84.7% of which were female (F/M ratio = ~6/1). The mean age at CLE diagnosis (index date) was lower in Hispanic (46.5 years ± 14.4) compared to non-Hispanic (53.9 years ± 15.3) patients. A higher proportion of Hispanic CLE patients had a diagnosis in younger age categories compared to non-Hispanic patients; 14.7% vs 7.5% for the 18–30-year category and 33.9% vs 22.0% for the 31–45-year category. Common comorbidities among Hispanic CLE patients included non-traumatic joint disorders (62.7%) and connective tissue disease (60.8%), which was comparable to non-Hispanic patients (64.7% and 64.5%, respectively). The Hispanic CLE patients had a lower proportion (48.4%) of reported heart disease and hypertension (43.8%) compared to non-Hispanic CLE patients (56.1% with heart disease and 53.7% with hypertension). *Discussion*: Observations from this large EHR dataset suggest an earlier average age of diagnosis among Hispanic CLE patients compared to non-Hispanic patients and provide insight into the frequency of comorbidities that contribute to the disease burden in this patient population. *Funding:* Biogen.

Category: Lupus

CONCEPTUALIZING A MODEL TO ESTIMATE THE COST EFFECTIVENESS FOR TREATMENTS OF CUTANEOUS LUPUS ERYTHEMATOSUS

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No previously published economic models exist for cutaneous lupus erythematosus (CLE), a chronic autoimmune disease primarily affecting the skin. The purpose of this research was to conceptualize a cost-effectiveness model structure to evaluate new treatments for CLE. The model structure was based on desk-based literature research as well as clinician and health economist input. The model structure consists of two components: a decision tree capturing response to initial treatment, followed by a Markov model to extrapolate long-term outcomes. The Markov model includes health states for ‘remission’, ‘response without remission’, and ‘active CLE’ for non-responders who switch treatments. From the ‘active CLE’ state patients can transition to ‘remission’ or ‘response without remission’ while receiving subsequent treatment. Patients can transition between states over the lifetime horizon. Although clinical experts agreed that Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI)-50 could define ‘response’, it remains questionable how and when ‘remission’ should be defined. Some criticism of CLASI from a regulatory body was noted. Evidence gaps were observed for treatment discontinuation patterns after remission, treatment effect wearing off, and costs and benefits of subsequent lines of therapies. It was suggested to seek patient input on relevant assumptions. This is the first cost-effectiveness model structure for CLE. The model has good face validity and a simple structure that captures typical endpoints used in clinical trials. Further research and discussion of the model design will enable refinement and inform decisions in the evaluation of new therapies for CLE.

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