Lupus

1. DEVELOPMENT OF SYSTEMIC LUPUS IN PATIENTS WITH CUTANEOUS LUPUS: A COMPARISON OF THREE CLASSIFICATION CRITERIA

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Studies investigating the progression of patients from cutaneous lupus (CLE) to systemic lupus (SLE) have used the American College of Rheumatology (ACR) diagnostic criteria more than newer criteria including the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) criteria or the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria. Our study aimed to compare frequency of progression from CLE to SLE with each criteria set in a cohort of CLE patients. We also identified baseline risk factors associated with CLE to SLE progression under the EULAR/ACR criteria. We conducted a retrospective, single-center chart review study of CLE patients seen in the outpatient dermatology clinics at University of Texas Southwestern Medical Center and Parkland Memorial Hospital between December 2008 to July 2021. Patients were included if they had a diagnosis of CLE, were age ≥18 years, and had ≥6 months of follow up. Patients were excluded if they were diagnosed with SLE at or within 6 months of their initial visit. 7.8% (6/77) of patients progressed from CLE to SLE using the EULAR/ACR criteria (median time: 2.4 years). 15.6% (12/77) and 16.9% (13/77) CLE patients progressed to SLE under the SLICC criteria (3.65 years) and ACR criteria (5.45 years), respectively. Baseline risk factors for SLE progression under the EULAR/ACR criteria included ANA titer >1:80 ($p=0.0065$), proteinuria ($p=0.0051$), and positive dsDNA antibodies ($p=0.0148$). Patients most frequently developed low complements (2 patients) and joint involvement (2 patients) that led to SLE diagnosis using the EULAR/ACR criteria. Decreased CLE to SLE progression under the EULAR/ACR criteria may be due to the hierarchal design allowing one criterion to count for each domain and positive ANA designated as an entry criterion. This lower rate of progression under the EULAR/ACR criteria may better reflect the general trend of CLE patients developing mild SLE disease.

2. COMPARATIVE RESPONSIVENESS OF CUTANEOUS LUPUS ERYTHEMATOSUS PATIENTS TO METHOTREXATE AND MYCOPENOLATE MOFETIL: A COHORT STUDY

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For patients with antimalarial-refractory cutaneous lupus erythematosus (CLE), methotrexate (MTX) and mycophenolate mofetil (MMF) are frequently used. Although surveys show providers have medication preference by CLE subtype which includes acute, subacute (SCLE), and discoid (DLE), there is a lack of evidence-based research comparing response between these medications across subtypes. In this retrospective study of our prospectively collected data, we examined response rates to methotrexate and mycophenolate mofetil, the most commonly used immunosuppressive medications in our cohort, stratified by subtype. Response or non-response was determined by 50% improvement or lack thereof in skin activity measured by the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), a previously established definition, or chart abstraction, and analyzed using Fisher's exact test. Discontinuations due to side effects were analyzed separately. Twenty-eight SCLE and 45 DLE patients identified took at least one of these medications, including 34 with concomitant SLE; the other subtypes were not powered for analysis. Mean response rate was 71.5% (95% CI 70.5-72.5%) for SCLE and 58% (95% CI 34.5-81.5%) for DLE. No statistically significant difference was found in rate of response to MTX or MMF when comparing SCLE vs DLE (72% vs 46% for MTX, 71% vs 70% for MMF; $p > 0.05$). Our results suggested that MMF may be more effective in DLE than MTX, but our sample was not powered to show this difference (70% vs 46%, $p=0.175$). Difference in response rate overall for MTX vs MMF was also not significantly different ($p=0.446$), showing comparable response rates in this cohort. These findings suggest similar efficacies for MTX and MMF between subtypes, but further studies are needed to assess whether MMF may work better than MTX in DLE. Clinicians may then use other factors to guide medication choice, such as side effect profile and comorbid conditions.

3. DISCOID LUPUS ERYTHEMATOSUS SKIN LESION DISTRIBUTION AND CHARACTERISTICS IN BLACK PATIENTS: A RETROSPECTIVE COHORT STUDY

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Epidemiological studies have shown that discoid lupus erythematosus (DLE) has a higher incidence and prevalence in racial/ethnic minority groups, particularly Black individuals. The objectives of this retrospective cohort study were to identify the differences in DLE lesion distribution and characteristics in Black patients. A total of 183 DLE patients (112 Black patients and 71 non-Black patients) with a reported race/ethnicity and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) scores were included in this retrospective cohort study. Univariate analysis was performed to determine significant differences in demographic data, clinical characteristics, DLE lesion distribution and DLE lesion characteristics in Black and non-Black DLE patients. Multivariable logistic regression was performed to determine significant predictors of DLE lesion location and characteristics. Black patients with DLE had worse baseline CLASI damage scores compared to non-Black patients with DLE [median=10.0 (IQR: 6.0-14.5) vs. 6.0 (3.0-10.0), $p<0.001$)]. Multivariable analyses showed that Black patients had 2.54 greater odds of having scalp involvement [95% CI (1.20-5.37), p=0.015] and 1.97 greater odds of having ear involvement [95% CI (1.06-3.68), p=0.032] compared to non-Black patients. Black patients also had greater odds of dyspigmentation in any anatomical location (OR=48.9, 95% CI (5.82-411.77), $p<0.001$), scalp dyspigmentation (OR=5.85, 95% CI (2.94-11.61), $p<0.001$), ear dyspigmentation (OR=2.89, 95% CI (1.50-5.54), p=0.001), and scarring alopecia (OR=3.00, 95% CI (1.56-5.78), p=0.001). Limitations include single-center design and small sample size. This study provides important information on clinical differences in patients with DLE and emphasizes that disease damage may be more of a significant issue in Black DLE patients. Recognizing differences in clinical presentations of DLE among Black patients can assist future efforts with understanding biological, cultural, psychosocial and systemic factors that influence DLE presentation and outcomes in Black patients and may guide clinicians when counseling Black patients.

4. METABOLOMIC PROFILING OF CUTANEOUS LUPUS ERYTHEMATOSUS

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Metabolic reprogramming plays a critical role in modulating the innate and adaptive immune response (in vitro and in animal models), but its role in specific diseases is less well-studied. An improved understanding of the metabolic changes occurring in cutaneous lupus erythematosus (CLE) could improve our understanding of disease pathogenesis, identify potential biomarkers, and introduce novel treatment targets. Here, untargeted liquid chromatography–mass spectrometry metabolomics was used to characterize the skin and serum of CLE patients. CLE patients were recruited from outpatient dermatology clinics at University of Texas Southwestern and Parkland Hospital in Dallas, TX. Statistical analysis was performed using R. Unpaired t-tests were performed to compare disease samples to controls, and p-values were corrected for multiple comparisons. 14 serum samples (9 CLE vs 6 control) were compared, as were 13 skin samples (5 CLE vs 8 control). No patients had concurrent systemic lupus erythematosus (SLE), and most were off systemic medications (86% of samples). CLE patients were found to have 11 differentially expressed metabolites in the skin, but only 2 differentially expressed metabolites in the serum. Metabolites of interest in CLE skin included the up-regulation of citrulline (fold change (FC)=1.15, p=0.02) and uracil (FC=1.79, p=0.04), in which similar trends have been seen in other autoimmune disorders, and the down-regulation of cyclic adenosine diphosphate (cADP) (FC=0.83, 0=0.04), nicotinamide mononucleotide (NMN) (FC=0.75, p=0.016), and nicotinamide adenine dinucleotide (NAD+) (FC=0.86, p=0.016). Notably, derangements in nicotinamide metabolism have recently been implicated in development of SLE, and treatments targeting this pathway have shown some success in SLE patients. We have identified metabolite candidates that may eventually provide novel insight into the pathogenesis of CLE and will be examined for their biomarker potential. Future directions will include confirmatory assays and repeat studies with larger, heterogenous samples.

5. LATE-ONSET CUTANEOUS LUPUS ERYTHEMATOSUS PATIENTS HAVE DISTINCTIVE CLINICAL FEATURES AND DEMOGRAPHICS VERSUS EARLY-ONSET PATIENTS

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Cutaneous lupus erythematosus (CLE) has been thought to occur between 20-40 years of age. CLE can also present later in life, but the frequency and risk factors associated with late-onset CLE are not well characterized. This cross-sectional study compares demographic and disease characteristics of patients with early and late-onset CLE in a cohort of 291 CLE patients seen in the outpatient dermatology clinics at University of Texas Southwestern and Parkland Health and Hospital System in Dallas, TX. Early-onset and late-onset CLE were defined as onset younger than 50 years and 50 years and older, respectively. Univariate and multivariable logistic regression analyses were performed to identify significant factors distinguishing the groups. The early-onset group comprised the majority of CLE patients versus the late-onset cohort (79.0% vs. 21.0%, P<0.001). Univariate analyses showed that early-onset group had higher occurrence of systemic lupus erythematosus (SLE) (53.5% vs. 29.5%, p=0.001). Late-onset cohort was associated with Caucasian race (50.8% vs. 26.1%, p<0.001) and drug-induced CLE (13.1% vs. 1.7%, p=0.001). Chronic CLE (CCLE) (79.1% vs. 63.9%) and acute CLE (10.9% vs. 1.6%) were more frequent in the early-onset group, while subacute CLE appeared less often in the early-onset group (10.0% vs. 34.4%) (p<0.001). Multivariable analysis found that Caucasian race (odds ratio (OR): 2.23 (95% confidence interval (CI): 1.19-4.19), p=0.013), CLE subtypes other than CCLE (OR: 2.18 (1.02-4.65), p=0.044), absence of oral ulcers (OR: 3.58 (1.46-8.78), p=0.005), absence of renal disorder (OR: 4.02 (1.10-14.71), p=0.036) and drug-induced CLE (OR: 4.65 (1.18-18.24), p=0.028) were significantly associated with late-onset CLE patients. In summary, late-onset CLE patients have higher proportions of Caucasians and are more associated with drug-induced CLE and CLE subtypes other than CCLE. Providers can be more mindful of CLE in older patients presenting with photosensitive rashes by checking their medication histories and performing thorough histories and physicals.

6. SPATIAL TRANSCRIPTOMICS OF CUTANEOUS LUPUS ERYTHEMATOSUS

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Cutaneous lupus erythematosus (CLE) is mainly categorized into acute (ACLE), subacute (SCLE), and chronic (CCLE) subtypes. Although CLE subtypes are distinct on clinical examination, the histopathological and transcriptomic signatures are very similar. Further, the immune cells' composition and localization within skin architecture is not well-established in CLE. We performed spatial transcriptomics using digital spatial profiling (DSP) technology on skin samples of ACLE, SCLE, and DLE, the most common variant of CCLE, as well as healthy controls. We identified differentially expressed genes (DEGs) between CLE subtypes and regions of interest (ROIs), revealing differences in specific cellular compartments in different disease subtypes. GSEA pathway analysis confirmed the association of type I IFN signaling in CLE. We further identified 150 and 170 DEGs between deep dermal versus superficial dermal CD3+ cells and CD45+CD3- cells of CLE skin, respectively. GSEA pathway analysis showed upregulation of apoptotic cleavage of cellular proteins, epigenetic regulations, and the Notch pathway in superficially located $CD3^{+}$-cells versus those deeper in the dermis. We also found the upregulation of neutrophil degranulation, and Notch pathways in superficially located $CD45^{+}CD3^{-}$-cells versus deep dermis-located cells. Moreover, comparing involved versus uninvolved epidermis revealed upregulation of inflammatory response genes in areas near interface dermatitis, including *AIM2*. Accordingly, we found an increase in protein levels of IL-18, the final product of AIM2 activation, and IL-18 receptors in CLE samples. The DSP data also elucidated the source of several chemokines detected in Olink data and the expression of cognate receptors on cells in multiple discrete areas of the skin and different sources of interferons. In summary, a spatial approach to study skin cells in lupus identifies additional mechanisms contributing to their response.

7. IMPACT OF RACE/ETHNICITY AND SKIN TYPE ON ILLNESS PERCEPTIONS AND QUALITY OF LIFE IN PATIENTS WITH DISCOID LUPUS ERYTHEMATOSUS

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Discoid lupus erythematosus (DLE) is a chronic dermatologic condition with the potential for permanent disfigurement and hair loss. Long-term sequelae including scarring and post-inflammatory pigmentary change may especially affect patients with darker skin types. While some studies investigated illness perceptions and quality of life in patients with DLE, none have evaluated the influence of patient skin type or race/ethnicity on these measures. We sought to understand whether skin type and race/ethnicity impact illness perceptions and quality of life for patients with DLE. Dermatology providers at Brigham and Women's Hospital identified patients with DLE. Researchers reached out to all eligible patients and offered previously-validated Brief Illness Perception Questionnaire and Skindex-16 questionnaires to be completed online or over the phone. Chart review was also performed. Response rate was 60.33% (73/121 patients). Patients with Fitzpatrick type VI reported greater level of concern about their DLE than patients with Fitzpatrick type I (mean difference=4.190, 95%CI, 0.008-8.373, p=0.049 after Tukey correction). Hispanic patients reported greater emotional impact from their DLE than White (mean difference=3.673, 95%CI 0.355-6.991, p=0.024 after correction) and Black patients (mean difference=4.092, 95%CI, 0.431-7.752, p=0.022 after correction). Hispanic patients reported greater impact on quality of life in the domains of symptoms, function, and emotion, as well as overall compared to all other racial/ethnic groups ($p<0.05$ after Tukey correction). In conclusion, patients with darker skin types had higher levels of illness concern and Hispanic patients had greater emotional impact and quality of life impairment than other racial/ethnic groups.

8. MANAGEMENT OF THE HEIGHTENED RISK FOR CLINICAL EVENTS FROM ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) IN AN ESTABLISHED COHORT OF LUPUS ERYTHEMATOSUS PATIENTS

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Lupus erythematosus (LE) patients, including those with systemic or cutaneous LE, are at heightened risk of clinical events, chiefly heart attacks and strokes, caused by atherosclerotic cardiovascular disease (ASCVD). Here, we performed a single-center study of all 370 patients with systemic or cutaneous LE in an established longitudinal cohort within the University of Pennsylvania Health System. Our focus was to assess management of conventional ASCVD risk factors, including hyperlipidemia, hypertension, smoking, and diabetes mellitus. We found that 45.83% of this cohort had plasma low-density lipoprotein cholesterol concentrations (LDLc) >100 mg/dL, a standard threshold for initiating treatment in high-risk patients. 65.8% of LE patients with LDLc >100 mg/dL were not prescribed a statin, and 21.2% of LE patients previously prescribed a statin still had LDLc >100 mg/dL. Regarding blood pressure, 52.9% of the cohort had hypertension, recently re-defined as ≥130/80 mm Hg. 38.8% of patients with hypertension were not on anti-hypertensive medications, and 55.3% of patients already on anti-hypertensive medication were not at goal. 27.3% of the cohort had diabetes or prediabetes, with 9.9% of these patients having inadequately managed diabetes with a hemoglobin A_{1c} > 6.5% and 39.6% of these patients having inadequately managed prediabetes of hemoglobin A_{1c} between 5.7-6.4% defined as no subsequent medication or lifestyle modifications. While 45.9% of the cohort were former or current smokers, 16.4% of these patients did not receive smoking cessation counseling. Using categorizations for levels of ASCVD event risk that we recently proposed for LE patients, 88.9% of patients in this LE cohort who would now be classified at high-risk were not on lipid-lowering medications, 73.5% of patients at very high risk were not on lipid-lowering medications, and 39.1% of patients at extreme risk were not on lipid-lowering medications. From 1990 to the present, 25.8% of patients in our LE cohort experienced an ASCVD-related event/diagnosis, which included myocardial infarction, ischemic stroke, newly symptomatic peripheral vascular disease, ischemic heart disease, heart failure, or hospitalization for chest pain, shortness of breath, or palpitations with suspicion of ischemic origin which is higher than the age-adjusted prevalence of all types of heart disease was 10.6% across the general population. We conclude that lupus patients are inadequately treated for conventional risk factors for ASCVD events. Efforts to improve prevention and management of ASCVD event risk in LE patients are underway.

9. B CELL SIGNATURE DIFFERENTIATES DISCOID FROM SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

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While B cells account for a significant fraction of the lymphocytic infiltrate in discoid lupus erythematosus (DLE), whether they contribute to pathogenesis is unknown. This study compares the immune landscape of DLE to subacute cutaneous lupus erythematosus (SCLE) using transcriptomic and histologic analyses of lesional skin biopsies. Data from a modified Autoimmune Profiling Panel (NanoString) demonstrate that B cell-specific genes, including the canonical pan-B cell markers CD19, CD20, and CD79a, comprise the top nine most differentially expressed genes in DLE compared to SCLE skin. Among the 33 genes with at least 2-fold differential expression were many B cell-specific genes: immunoglobulins (IgM, IgD), all three B cell activating factor (BAFF) receptors (BAFF-R, BCMA, TACI), several Fc-receptor like (FCRL) family members, mature B cell marker CD22, B cell chemokine CXCR5, and B cell specific transcription factor Pax5. Relative cell type scoring revealed that B cells were preferentially present in DLE compared to SCLE, while relative abundance of other inflammatory cells was either roughly equivalent between DLE and SCLE, or more prevalent in SCLE. Many B cell-specific genes were exclusively upregulated in DLE as compared to normal skin, whereas markers of other inflammatory cells (CD4 and CD8 T cells, plasmacytoid dendritic cells, etc.) were upregulated in SCLE as well. Digital whole-image slide analysis (Visiopharm) of immunohistochemical staining for B cells (CD20), T cells (CD3), and plasma cells (CD138) supported the gene expression findings. Of note, quantitative analysis of CD20 by immunohistochemistry highly correlated to that by gene expression analysis ($R^2 = 0.8883$, $p < 0.0001$). These data provide evidence for a mixed B cell infiltrate, including naïve and memory B cells as well as plasma cells. Overall, this study identifies a novel B cell-predominant signature unique to DLE and establishes the need for future mechanistic studies of cutaneous B cells in DLE pathogenesis.

10. RISK OF INFECTION IN CUTANEOUS LUPUS PATIENTS

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High infection rates have been reported in patients with systemic lupus erythematosus (SLE), attributed to disease characteristics and treatments. Pneumonia, skin, and urinary tract infections are leading infections in patients with SLE, while sepsis and bacteremia contribute greatly to in-hospital mortality. We sought to characterize risk of infection in patients with cutaneous lupus erythematosus (CLE) via a retrospective cohort study. We analyzed CLE patients at one academic medical center between 6/1/2015-5/13/2019. Patients with a diagnosis of SLE were excluded. A total of 161 patients were eligible, of which 53 (32.9%) experienced an infection during the study period. We compared patients with infection to patients without infection. Demographics were similar between groups. Two deaths occurred in the study period with one attributed to infection. The annual incidence of infection was 229/1000 patient-years. A total of 106 infections occurred, with a breakdown of upper respiratory (38.7%), urinary tract (28.3%), pneumonia (13.2%), skin and soft tissue (9.4%), influenza (4.7%), sepsis/bacteremia (2.8%), opportunistic (1.9%) and herpes zoster (0.9%). Infections were most often viral (45.3%), followed by bacterial (44.3%), unknown (8.5%), and fungal (1.9%). Nearly half (45.3%) of patients with infections had one infection during the study period, whereas 54.7% of patients with infections had two or more. Patients with infections were treated in outpatient clinics (50.0%), inpatient (27.4%), and the emergency department (22.6%). Patients with infections were more likely to have been prescribed corticosteroids during the study period (34.0% vs. 9.3%, $p<.001$) and take corticosteroids at the time of infection (7.5% vs. 0.0%, $p=.011$). This study further characterizes infection risk in patients with CLE, which has not previously been well-described. More research is needed to determine whether patients with CLE have an elevated risk of infection compared to the general public, and what disease or treatment characteristics may predispose CLE patients to infection.

11. IMMUNE MICROENVIRONMENT DEEP PROFILING OF CUTANEOUS LUPUS ERYTHEMATOSUS SKIN STRATIFIED BY PATIENT RESPONSE TO ANTIMALARIALS

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Lupus erythematous (LE) is a systemic autoimmune disease with a variety of cutaneous manifestations. Antimalarials are first-line systemic therapy, yet not all patients respond to hydroxychloroquine (HCQ), quinacrine (QC), or either (NR). Our group has previously shown that QC responders demonstrate increased conventional dendritic cells (cDC) and TNFα relative to HCQ responders. Here, we investigated the differences between these patients using Imaging Mass Cytometry (IMC), an unbiased multiplexed technique. 13 HCQ, 13 QC, and 22 NR treatment-naïve FFPE samples were stained with 37 metal conjugated antibodies and ablated on the Hyperion Imaging System (Fluidigm). Images were segmented using a nuclear app-based algorithm in Visiopharm and imported into histoCAT where single cell mean pixel intensity data was obtained to cluster cells using the Phenograph algorithm. One-way ANOVA, Kruskal-Wallis, and post-hoc Tukey/Dunn's tests (per data normality) were performed. Correlations were determined by Pearson's r. HCQ patients demonstrated increased CD4 T cells compared to QC ($p<0.05$). NR patients were found to have a decreased percentage of Tregs compared to QC responders ($p<0.05$). QC responders had a higher expression of pSTING and IFNκ compared to HCQ responders ($p<0.05$). The total expression of pSTING and IFNκ was found to positively correlate and colocalize in skin ($p<0.0001$, $r=0.676$). CD14+CD16+/CD68+ macrophages and cDCs were the predominant cell types found to express pSTING and IFNκ. These data may suggest a relative dysregulation in tolerance due to decreased Tregs in patients refractory to antimalarials. Our results show that activated STING correlated with IFNκ, suggesting co-regulation in macrophages and cDCs that may be responsive to QC. This analysis on treatment naïve biopsies may lead to further discovery of biomarkers that may predict patient response to therapy and direct targeted treatment.

12. THE BINDING MECHANISMS OF ANTIBODIES TO DNA FROM HEALTHY SUBJECTS AND PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: THE ROLE OF MONOGAMOUS BIVALENCY AND FC-DEPENDENCE

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Antibodies to DNA (anti-DNA) are a unique population of antibodies present in both typical and aberrant immunity. Scientists have historically studied anti-DNA in the context of systemic lupus erythematosus (SLE), a prototypic autoimmune disease in which these antibodies play a complex and critical role. Anti-DNA in individuals with SLE bind to a conserved antigenic determinant on DNA, most likely the phosphodiester backbone. In contrast, anti-DNA in otherwise healthy subjects (HS) has been shown to recognize specific motifs on certain bacterial and viral DNA. Previous work has demonstrated that anti-DNA in SLE bind by a mechanism termed Fc-dependent monogamous bivalency, in which stable binding requires the Fc region and that both Fab sites interact with the same extended DNA molecule. In this study, we aimed to determine whether the properties of monogamous bivalency and Fc-dependence also apply to the anti-DNA of HS. To do so, we compared the binding activity of intact IgG with Fab and $F(ab')_2$ fragments prepared from the plasmas of patients with and without SLE. Fab fragments from all plasmas tested demonstrated negligible binding to DNA compared to intact IgG. $F(ab')_2$ fragments showed consistently negligible binding to calf thymus DNA but showed variable reactivity to micrococcal DNA in SLE and HS. Our results indicate that anti-DNA binding is consistently monogamous bivalent in patients with and without SLE. Furthermore, our experiments suggest that individuals with SLE produce two populations of antibodies to DNA: one population resembling those found in otherwise healthy individuals with heterogenous Fc-dependence and another population that is homogenously Fc-dependent.

Dermatomyositis

13. MORTALITY IN PATIENTS WITH DERMATOMYOSITIS IN UNITED STATES

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Dermatomyositis (DM) is a rare idiopathic inflammatory myopathy (IIM) associated with extramuscular complications including respiratory disease and cancer. Prevalence of these complications is estimated at 46% for lung involvement and 25-30% for cancer. The mortality rate at 10 years was previously reported as 20% with the most common causes of death being cancer, and lung and cardiac complications. For this study, we aimed to better estimate the mortality of DM, prevalence of complications and how the presence of complications affects mortality rates. This is a retrospective observational study using data from TriNetX database. Patients were 18 years or older with at least 2 diagnosis codes of DM separated by a minimum of 6 months. Data were then queried for an additional diagnosis code of respiratory disease or cancer within 3 years of DM diagnosis. A total of 5,021 patients were identified of which 3,410 also had lung disease (67.9%), 1,518 with cancer (30.2%), and 875 with both cancer and lung disease (17.4%). The 10-year all-cause mortality for patients with DM was 5.4% and for patients with concomitant respiratory disease, cancer or both respiratory disease and cancer was 6.2% ($p=0.1$), 8.4% ($p<0.001$), and 9.3% ($p<0.0001$), respectively. The prevalence of complications was higher than expected with over two-thirds of patients being diagnosed with respiratory disease and over 30% developing cancer. In our cohort of patients with DM, mortality was elevated compared to the general population, but lower than previously reported values. This improvement in survival may represent the recent progress made in the diagnosis and treatment of DM. Clinicians should have high suspicion for respiratory disease and cancer in patients with dermatomyositis. The diagnosis of lung disease or cancer in patients with DM suggests a poorer prognosis and highlights an area of improvement for the screening and care of patients with DM.

14. LENABASUM, A CANNABINOID TYPE 2 RECEPTOR AGONIST, EXERTS ANTI-INFLAMMATORY EFFECTS IN DERMATOMYOSITIS IN TH1 CELLS

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Dermatomyositis (DM) is a chronic, systemic autoimmune disease that primarily affects the skin, muscle, and lungs. The decreased quality of life of DM patients combined with the inadequacy of current treatments highlight the therapeutic need for effective and safer treatment options. Lenabasum, a non-psychoactive cannabinoid type 2 receptor (CB2R) agonist, is currently being investigated as a potential non-immunosuppressive treatment option for DM. The activation of CB2R has been shown to reduce several key pro-inflammatory cytokines implicated in DM. Our lab has demonstrated via immunohistochemistry (IHC) decreased CD4, IFNβ, IFNγ and IL31 expression in lenabasum-treated subjects' skin at 12 weeks ($p<0.05$), with no differences in IL4 compared to placebo ($p>0.05$). We utilized multiplexed flow cytometry of leukocytes eluted from DM skin to further analyze the expression of CB2R on 12 cell lineages. When evaluating cell lineages, CD4 T helper (Th) subsets were gated on CD4+ IFNγ+ Th1 and CD4+IL4+ Th2. There was a significantly higher frequency of parent percentage ($p<0.05$) of CB2R in Th1 (61.05% n=6) versus Th2 cells (25.5% n=6). Among myeloid cell lineages, there was greater frequency of parent of CB2R in M2 macrophages (CD68+CD163+), CD14++CD16++ macrophages, and monocyte derived dendritic cells (moDCs; CD11c+CD14+). With 15□mol of Lenabasum, there was a trend towards a decrease of TNFα in M2 macrophages, IFNγ and IFNβ in CD4+ Tcells, IFNβ in CD16+ cells and IL31 in Th1 cells, CD14++CD16+ macrophages and M2 macrophages. There was also a significance decrease in moDCs secreting IL31 with Lenabasum ($p<0.01$). Imaging mass cytometry of DM skin demonstrated the highest IL31 MPI in moDCs. IL31 was also elevated to a lesser extent in other myeloid cell lineages. These data suggest Lenabasum may exert specific anti-inflammatory effects in DM, particularly on Th1 cells and Th1-derived IL31.

15. REMISSION IN DERMATOMYOSITIS: HOW LONG DO PATIENTS NEED TREATMENT?

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Dermatomyositis (DM) is a chronic inflammatory myopathy with variable clinical course, but little is known regarding disease remission. We conducted a retrospective cohort study of 246 patients to determine the rate of immunosuppressive discontinuation as a proxy for clinical remission. Inclusion criteria were diagnosis of DM after 18 years of age and having at least one clinic visit at the Stanford multidisciplinary rheumatology/dermatology clinic between 2013 to 2020. Included patients were exposed to at least one immunosuppressive medication for at least 3 months. Patients not returning to clinic were contacted via phone or email for follow-up. Survival analysis was performed using Kaplan-Meier curves and log rank analyses. Variables significantly associated with medication cessation or with p-value <0.15 on univariable analysis were used in multivariate analysis using Cox proportional-hazards models. 47 patients (19%) discontinued medications over a median follow-up time from disease onset of approximately 7 years. The median time to medication cessation from disease onset was approximately 3 years. Log rank analysis indicated that patients with at least one DM-specific autoantibody ceased all medications significantly earlier than those without (p= 0.018). In particular, those with anti-MDA5 autoantibodies had significantly shorter time to medication cessation compared to the negative autoantibody group (p=0.03). Multivariable modeling was performed including demographic features, specific organ involvement, and autoantibody status as covariates. Clinically amyopathic patients were 2.6-fold (CI 1.29-5.27) more likely to discontinue medications than those with muscle disease. Also, those with anti-MDA5, anti-NXP2, and anti-SAE1 antibodies had increased likelihood of medication cessation with hazard ratios of 11.4 (CI 2.42-53.7), 12.0 (CI 2.31-62.7), and 10.2 (CI 2.07-50.3) respectively compared to patients with no DM-specific autoantibodies. Medication cessation is a relatively uncommon event in our DM population, and those with clinically amyopathic disease, anti-MDA5, anti-NXP2, and anti-SAE1 autoantibodies appear to have a higher likelihood of getting off of their medication.

16. HIGH-DIMENSIONAL PROTEOMIC ASSAY TO IDENTIFY RESPONSE TO TREATMENT SKIN BIOMARKERS IN PATIENTS WITH DERMATOMYOSITIS

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Dermatomyositis (DM) is a rare inflammatory disease caused by a combination of genetic and environmental factors. DM typically leads to significant morbidity by causing disfiguring pruritic rash, photosensitivity, and muscle weakness, but the disease manifestations are highly heterogeneous. Therefore, identifying valid biomarkers is critical to predicting the prognosis, clinical manifestations, and response to treatment in an individual patient. Previous studies primarily focused on investigating the potential biomarkers in patients' serum. However, the clinical course of the skin and muscle disease are commonly discordant. We have leveraged the power of a high-dimensional proteomic assay capturing 92 inflammatory biomarkers coupled with a minimally invasive and non-scarring suction blistering technique to test the feasibility of investigating changes in the concentration of soluble proteins directly from interstitial skin fluid from DM patients in response to treatment. In this pilot study, we enrolled a single patient with active cutaneous DM. We performed high-throughput proteomics on the samples captured at baseline (before starting the treatment) and then four months following the treatment with hydroxychloroquine. We observed a 37% decrease in IL-17A, 29% decrease in IL-33, and 26% decrease in TRAIL. Interestingly, there was also a 27% increase in IL-13, 37% increase in NT-3, and 42% increase in GDNF. While we cannot make any conclusions based on findings from this proof-of-concept case study, we confirmed the feasibility of this approach as a safe, non-invasive method that we are planning to utilize in a large cohort of patients with DM in the future.

17. CROWDSOURCING AS A MEANS OF FUNDRAISING FOR JUVENILE DERMATOMYOSITIS

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Juvenile Dermatomyositis (JDM) is a rare idiopathic inflammatory myopathy with an annual incidence between 2-4 per million children. Previous research indicates significant financial and psychological hardship in patients and caregivers of orphan diseases. This study investigates how the crowdsourcing platform GoFundMe is being utilized by families caring for a child with JDM to offset the financial burden associated with this disease. Forty-eight campaigns for JDM were identified using the GoFundMe search engine containing entries from 2013-2021. In total, 83.3%, 6.3% and 10.4% of campaigns were fundraising for JDM-related care expenses, research, and unrelated expenses (i.e. college-funds), respectively. For campaigns fundraising for JDM-related care, the most cited expenses were treatment/medical bills (65.0%), travel for medical care (27.5%) and mobility/home renovations—i.e. ramp for home—(15.0%). While only 5.0% of campaigns were for uninsured patients, 40.0% cited inadequate insurance coverage of care. Loss of income was also common in caregivers (42.5%,) with 32.5% reporting a significant reduction in work-hours. In total, $237,219 was raised by 2,393 donors. For campaigns raising funds for JDM-related care, the median fundraising goal was $10,000 with an overall mean of 56.7% of funds raised. The mean percentage of funds raised increased to 62.5% for campaigns active for over one year. These results were consistent with prior studies demonstrating patient use of GoFundMe as a means of covering medical and other expenses surrounding their disease. Travel to academic hospitals was a significant expense, suggesting that alternative strategies for care such as incorporating telehealth and home-treatments may reduce burden on families. In addition, many medications for JDM are considered "off-label" which complicates insurance coverage. Overall, crowdsourcing appeared to be partially effective as a means of fundraising in JDM although this study highlights the gaps in coverage for out-of-pocket expenses associated with the care of children with this orphan disease.

18. TISSUES SPECIFIC EXOSOME AND DISEASE ACTIVITY IN DERMATOMYOSITIS

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Extracellular vesicles (EVs) are small lipid bilayer membrane structures that are released by normal, diseased, and transformed cells in vitro and in vivo. EVs carry nucleic acids (DNA, mRNAs, non-coding RNAs), lipids including peroxidized lipids, and proteins to mediate cell-cell communication. Many of the molecules carried by EVs act as damage-associated molecular patterns (DAMPs) that activate intrinsic immunity. EVs are elevated in plasma of dermatomyositis (DM) patients and have the ability to upregulate inflammation. We hypothesized that specific exosomes from affected organs in DM patients are associated with organ inflammation. We collected EVs from fresh plasma of 1 healthy control and 8 DM patients using ultracentrifugation and size-exclusion chromatography. The size and number of EVs were measured by Nanoparticle Tracking Analysis. Isolated EVs were adjusted to a concentration of 8.0×10^8 particle/ml and incubated with microarray chips coated with antibodies to CD9, CD63, CD81 (exosome surface markers), and CD41a (platelet marker). Exosomes were captured on the chips by antibodies, then stained with fluorescently labeled anti-K10, anti-SPC and anti-alpha-sarcoglycan. The number of stained exosome and anti-CD41a captured platelet derived EVs were counted by ExoView R100. The SPC (lung alveolar cell marker) positive exosome number was most upregulated in patient with lowest diffusing capacity of lungs for carbon monoxide (DLCO) % . K10 (skin keratinocyte cell marker) positive exosomes number was highest in the patient with the highest Cutaneous Dermatomyositis Disease Area and Severity Index (CLASI) score. On the other hand, alpha-sarcoglycan (skeletal muscle cells marker) positive exosome numbers decreased in those with elevated CPK. Lung and skin derived exosome numbers upregulated in the remarkable symptom case, but muscle derived exosome numbers were lower in those with elevated CPK. Plasma EVs have immunostimulatory properties and may play a role in some clinical aspects of DM.

19. PHOTO VALIDATION STUDY USING THE CUTANEOUS DERMATOMYOSITIS DISEASE AREA AND SEVERITY INDEX (CDASI) IN DERMATOMYOSITIS PATIENTS

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The Coronavirus disease 2019 (COVID-19) pandemic revealed our need for reliable tools to evaluate patients with skin disease virtually. Thus far, there has not been a study that has attempted to score the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), a validated outcome measure, from photographs. In this study approved by the University of Pennsylvania's Institutional Review Board, patients were prospectively recruited during routine clinic visits and skin areas used in scoring the CDASI were photographed by research staff using two iPhone cameras (an iPhone 8 and iPhone 11). Of the 34 patients participating in the study, 82.3% were female, 85.3% were Caucasian with an average age of 54. Two dermatologists served as the raters. The in-person CDASI assessment was scored by rater 1 at the clinic visit and the photographs were scored at a later date by both rater 1 and rater 2. For the total activity score, the correlation coefficient between rater 1 and the in-person evaluation was 0.806 (95% CI 0.649-0.898 $p=2x10^{-9}$) and was 0.822 (95% CI 0.675-0.907 $p=4x10^{-10}$) between rater 2 and the in-person assessment. For the total damage score, the correlation coefficient between rater 1 and the in-person assessment was 0.54 (95% CI 0.254-0.739 p=0.004) and was 0.601 (95% CI 0.338-0.778 $p=6x10^{-5}$) between rater 2 and the in-person assessment. The inter-rater reliability was interpreted as "excellent" for skin activity, an important measure in clinical trials for dermatomyositis. More research is needed but photographs may be a useful tool for evaluating clinical trial patients in the future.

20. ANALYSIS OF DERMATOMYOSITIS SKIN SAMPLES USING SINGLE-CELL RNA SEQUENCING, SPECTRAL FLOWCYTOMETRY, AND PROTEIN BIOMARKER DISCOVERY WITH PROXIMITY EXTENSION REVEALED POSSIBLE NEW BIOMARKERS FOR THE DISEASE

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The autoimmune disease Dermatomyositis (DM) causes severe morbidity through chronic disfiguring rash, intense pruritus, and muscular weakness. The disease incidence is estimated to be ten per million people, and it disproportionately affects women and individuals with skin of color. The course of skin and muscle disease in DM is often discordant; approximately 20% of patients with DM lack any evidence of muscle involvement. The disease pathogenesis and the factors that lead to the initiation and progression of DM are not completely understood, and there is a necessity for the discovery of novel treatment targets. Using the minimally invasive suction blistering biopsies, we studied DM skin involvement by comparing lesional, non-lesional DM, and healthy skin. Samples were analyzed using single-cell RNA sequencing (scRNA-seq), spectral flowcytometry, and protein biomarker discovery with proximity extension assay. We were able to identify different subtypes of keratinocyte and increased presence of different immune cells. Both transcriptomic and proteomic assays revealed higher presence of type II interferon gamma in DM skin cells. scRNA-seq revealed significant increase of CXCL10 and 11 in DM keratinocytes, whereas flow cytometry and scRNA-seq showed that their shared receptor CXCR3 was highly upregulated in skin infiltrating T cells. Protein biomarker discovery revealed CXCL6, CXCL10, CXCL11, IL17, L18, IL18-R1 and IL-20RA as potential novel protein biomarkers for DM. Additionally, proteomics study of non-lesional DM skin identified CXCL6, CXCL11 and IL18 as differentially expressed proteins compared to healthy skin. We hypothesize these proteins may serve as biomarkers of preclinical disease or predictors of expanding skin involvement.

Sclerotic Skin Disease

21. LOCAL STRUCTURAL COMPLICATIONS AND SYSTEMIC COMORBIDITIES IN HEAD AND NECK VARIANTS OF LINEAR MORPHEA

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Parry Romberg Syndrome (PRS) and *en coup de sabre* (ECDS) are head and neck variants of linear morphea associated with atrophy of underlying structures and ophthalmological, oral, and neurologic complications. Due to the low prevalence, there is a paucity of clinical data that fully characterizes the structural complications and systemic comorbidities of PRS/ECDS. We retrospectively reviewed the medical records of 34 adult patients with PRS and/or ECDS seen within the University of California San Francisco Department of Dermatology between 2015-2021. Twenty-six patients (76.5%) had ophthalmological, oral, and/or neurological clinical symptoms related to PRS/ECDS. Ipsilateral ophthalmological symptoms were observed in 14 patients (41.2%), including enophthalmos, retinal hemorrhage, and/or vision loss. Ipsilateral oral findings were noted in 16 patients (47.1%), most prevalently tongue hemiatrophy and/or gingival recession. Nineteen patients (76.5%) reported neurologic symptoms, such as headaches/migraines, numbness/paresthesias, and/or dysphagia. Computed tomography, Magnetic Resonance Imaging (MRI), and plain film of 25 patients (73.5%) were evaluated for clinical utility. Eighteen of 24 (75.0 %) MRIs demonstrated potential disease-related damage, including deep involvement of the bone, muscle, and/or brain. In two patients, MRI detected disease progression and changed management decisions. Eight patients (23.5%) were identified as having concomitant autoimmune/inflammatory diseases, including Sjogren's syndrome, juvenile idiopathic arthritis, systemic lupus erythematosus, Grave's disease, alopecia areata, ulcerative colitis, and/or celiac disease. Overlapping autoimmune/inflammatory phenomena are described; of note, no patients developed systemic sclerosis. The association of PRS/ECDS with structural complications and autoimmune/inflammatory comorbidities suggests a spectrum of manifestations ranging from skin-only involvement to more complex presentations with functional and/or systemic associations. Screening for deep tissue and structural complications in patients with PRS/ECDS is strongly advised, with follow-up imaging as needed to assist with activity monitoring and management decisions. Presence of other concurrent inflammatory diseases should be assessed to optimize treatment decisions.

22. HEALTH-RELATED QUALITY OF LIFE IN ADULTS WITH MORPHEA: A QUALITATIVE STUDY USING FOCUS GROUPS

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Morphea is known to impact health-related quality of life (HRQoL) in children due to unique clinical features, including skin sclerosis, musculoskeletal effects, and cosmetic disfigurement. However, detailed qualitative studies of adults with morphea are lacking. Therefore, we performed a qualitative exploration of the experience of morphea in adults using focus groups in order to identify domains of HRQoL impact. Eleven adult patients representing all major clinical subtypes of morphea, were recruited from the Morphea in Adults and Children (MAC) cohort at the University of Texas Southwestern Medical Center in Dallas. Purposive sampling was used to ensure a range of ages, genders, and clinical subtypes. Facilitators used discussion guides with prompts for topics based on literature review and brainstorming with clinical experts, including symptoms, functional and relational effects, and emotions related to morphea. Two sessions that included 5-6 participants were performed, each led by a trained facilitator, and audio-recorded with IRB-approved equipment. Content analysis was performed of de-identified transcripts to identify conceptual themes and representative patient quotations. Analysis revealed that patients experienced physical symptoms (itch, burning, stiffness), and impact on physical functioning (limited mobility, impact on family planning, restricted clothing choices); treatment burden (malaise, lifestyle restrictions, financial burden); social and relational impact (impaired body image, social stigma or negative assumptions, impact on intimate relationships); and emotional/psychological effects (worry about disease prognosis, traumatic diagnostic experiences, and enhanced self-advocacy). Adults with morphea experience HRQoL impact in many domains, some of which are unique to adults when compared to the pediatric population. An improved understanding of the patient experience of morphea based on this qualitative methodology can inform improved educational content, more appropriate patient reported outcomes (PROs) for research, and comprehensive patient-centered care in the clinical setting. This qualitative methodology can serve as a model to be used in other cutaneous conditions.

23. RECONSTRUCTIVE PROCEDURES IN MORPHEA: PROVIDER ATTITUDES AND BELIEFS

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Morphea is an autoimmune disease that causes scarring and atrophy of the skin. Linear morphea of the head and neck (localized scleroderma, Parry Romberg syndrome, progressive hemifacial atrophy, en coup de sabre, and craniofacial scleroderma) can cause limited ROM, pain, and disfigurement. Surgical reconstructive options for these patients include flap procedures, fat transfers, filler, and cartilage/bone grafting. These reconstructive procedures remain controversial amongst providers. Our study aimed to gather current attitudes and beliefs regarding these reconstructive procedures across different specialties of providers who care for these patients. We accomplished this via a cross-sectional survey of providers registered with the Pediatric Dermatology Research Alliance (PeDRA), Rheumatologic Dermatology Society (RDS), and Childhood Arthritis and Rheumatology Research Alliance (CARRA) groups. The survey was distributed electronically from May to September 2021. 69 complete responses were recorded for a response rate of 49.6%. 94.1% of respondents reported that they would refer patients for any of the corrective procedures listed, most commonly for cosmetic purposes (98.4%). Of the procedures listed, providers were most comfortable with referring patients for either fat transfer/grafting (45.3%) or filler (35.9%). Only 4.7% of respondents were comfortable referring for cartilage/bone grafting or surgical flap procedures. 10.9% of providers were not comfortable with referring for any of the procedures listed. The majority of respondents did not believe that any of the above procedures slow or stop disease activity, however a small subset of respondents believe that fat transfer (3.1%), filler (1.6%) or cartilage/bone transfer (1.6%) can slow or even stop disease activity. We present the first report of provider attitudes toward reconstructive procedures in patients with morphea. Our survey suggests that the majority of providers are most comfortable with less invasive reconstructive procedures like fat transfer or filler, primarily for cosmetic purposes.

24. LICHEN SCLEROSUS IS ASSOCIATED WITH AN INCREASED RISK OF METABOLIC SYNDROME AND CARDIOVASCULAR COMORBIDITIES

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Lichen sclerosus (LS) is a chronic inflammatory skin condition that often coexists with morphea and may lead to pruritus, ulceration, and genital scarring, as well as squamous cell carcinoma. LS may have a profound impact on patients' quality of life, and its symptomatology and associated chronic inflammation may lead to the development of systemic comorbidities. The objective of this study was to evaluate the association between LS and systemic cardiovascular comorbidities including metabolic syndrome (MS). A cohort of 2,364 dermatology and gynecology patients with LS seen between 2015-2019 was age-, sex-, and race/ethnicity-matched with dermatology and gynecology patients without LS. The prevalence of multiple cardiovascular comorbidities was assessed. LS patients had a 2.1-fold increased risk of MS compared to those without LS ($p<0.001$). LS patients were also more likely to have hypertension, type II diabetes mellitus, coronary artery disease, and peripheral vascular disease (RR=1.2, p=0.02; RR=1.4, p=0.01; RR=1.9, p=0.02; RR= 3.2, $p<0.001$, respectively). No differences were observed for rates of stroke, statin administration, or for recorded body mass indices (BMI) or lipid panel results; this was maintained when corrected for annualized rates of change in BMI and lipid panel results. The increased risk for cardiovascular comorbidities, including MS, observed in LS patients may be due to behavioral changes as well as sustained inflammation from chronic disease. Due to the increased risk of mortality associated with MS, patients with LS should receive appropriate counseling and screening. Limitations include the observational, retrospective nature of this study, which was performed at an urban tertiary referral center.

25. SUBCUTANEOUS BLEOMYCIN INDUCED MOUSE GENE EXPRESSION SIGNATURES PARALLEL INFLAMMATORY GENE EXPRESSION IN MORPHEA PATIENTS

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Morphea, or localized scleroderma, is an autoimmune disorder of the skin and underlying tissue that can result in functional limitation and disfigurement. The course of morphea is characterized by an inflammatory, active stage, which entails erythema and edema, and an inactive stage, marked by dyspigmentation, atrophy and sclerosis. Animal models for studying disease are immensely useful in studying pathophysiology and developing therapies for disease, and no model has yet been determined for morphea. We utilized whole transcriptome RNA sequencing of human morphea skin and subcutaneously injected bleomycin mouse (BM) skin to determine genetic signatures recapitulated in the mouse model. Skin from BM (n=18) was compared to skin from PBS control mice (n=6). Additionally, skin from patients with morphea (n=26) was compared to skin from age-matched healthy controls (n=10). Differential gene expression analysis using DESeq2 identified 317 differentially expressed genes (DEGs) in BM skin and 2216 DEGs in morphea skin. Gene set enrichment analysis with Broad Institute Hallmark gene lists was performed on identified DEGs for both mouse and human skin. Significant overrepresentation of interferon-gamma (normalized enrichment score (NES)=2.51, $p<0.001$), interferon-alpha (NES=2.19, $p<0.001$), and inflammatory response (NES=2.20, $p<0.001$) pathways was noted in BM skin. A concordant overrepresentation of interferon-gamma (NES=1.88, $p<0.001$) and interferon-alpha (NES=1.79, $p<0.001$) pathways was observed in human morphea skin. We demonstrate a concordant inflammatory gene signature primarily driven by interferon expression in both BM and morphea skin when compared to their respective controls, suggesting potential utility of BM as an animal model for the study of morphea.

26. DIAGNOSING FASCIAL INVOLVEMENT IN A COHORT OF EOSINOPHILIC FASCIITIS PATIENTS

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Eosinophilic fasciitis (EF) is a rare sclerosing disorder characterized by fascial inflammation. The gold standard for diagnosis of this orphan disease has traditionally been full-thickness wedge biopsy with a depth of sampling that captures fascial tissue. This can be challenging to obtain and potentially difficult to heal in sclerotic skin disease. Although magnetic resonance imaging (MRI) has been reported as a potential tool in evaluating fascial inflammation, no study to date has evaluated whether this less invasive diagnostic procedure is noninferior to a wedge biopsy. We aimed to determine whether MRI could be done in lieu of a fascial wedge biopsy. Fifty-four patients (62% female and 38% male) with a diagnosis of EF from two academic centers were retrospectively reviewed to better assess how the diagnosis was established; most identified as White (90%), while a minority were Black (5%) or other (5%). All patients had classic clinical findings of EF. Fifty-nine percent of patients underwent a wedge biopsy with fascial evaluation, 23% had a superficial biopsy with no fascial evaluation (typically at a referring institution), 67% had an MRI performed, and 38.5% (n = 15) had both a wedge biopsy performed as well as an MRI. Twelve of these patients (80%), had evidence of fascial involvement by both. One case of EF (6.7%) was not detected by MRI but diagnosed with a wedge biopsy. Similarly, one case demonstrated MRI changes suggestive of EF that were not observed on wedge biopsy, and one EF case did not show suggestive changes on either modality. Overall, in this cohort, MRI had a sensitivity of 92.3% in detecting fascial changes suggestive of EF while a wedge biopsy had a sensitivity of 91.7%. Despite its low sample size, our data suggests that MRI may be noninferior to wedge biopsy for confirmation of an EF diagnosis. Not only is MRI less invasive than a wedge biopsy for the diagnosis of EF, it also affords the ability to monitor patient response to therapy over time.

Vasculitis

27. CUTANEOUS POLYARTERITIS NODOSA TREATMENT: A RETROSPECTIVE CASE SERIES

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Cutaneous polyarteritis nodosa (CPAN) is a small-to-medium vessel vasculitis limited to the skin. It is diagnosed via characteristic cutaneous manifestations, absence of systemic vasculitic features, and supporting histopathologic findings. Cardinal features include subcutaneous nodules, livedo reticularis, ulcers, purpura, and cutaneous necrosis. There is limited data to guide the management of CPAN. We reviewed therapeutic regimens used to treat CPAN and evaluated patient response at our center. We conducted a retrospective chart review at rheumatology and dermatology clinics at Vancouver General Hospital and St. Paul's Hospital to identify patients with both histologic and clinical features of CPAN. Patients with systemic involvement were excluded. We identified 16 patients with CPAN. Time between symptom onset and diagnosis ranged from 2-189 (median 32 months), demonstrating the difficulty in obtaining a timely confirmatory biopsy. Inconclusive biopsies were common with 6 out of 16 patients required more than 1 biopsy. The most commonly used medications were methotrexate (68.8%), prednisone (68.8%), and azathioprine (50%). 8/11 patients who received methotrexate had at least a partial response. Five of those patients responded to methotrexate after failing other therapies such as dapsone, azathioprine, and prednisone. Most patients had a chronic relapsing course with 1 patient going into remission without therapy, 4 patients achieving drug free remission, 1 patient in remission on treatment, and 10 patients having relapsing disease despite treatment. Our series demonstrates the difficulty confirming a diagnosis of CPAN with many patients requiring multiple biopsies. Expert opinion at our site is that biopsy of a nodule may carry the highest diagnostic yield. Most patients require trials of multiple medications and methotrexate may be a reasonable option if first line agents fail. Our study is limited by its single center nature as well as lack of data regarding treatment doses and duration. Cutaneous polyarteritis nodosa can be a challenging condition to diagnose, often requiring multiple biopsies. Patients often have a chronic relapsing course and methotrexate may be a reasonable treatment option.

Miscellaneous Rheumatic Skin Disease

28. MORTALITY RISK ANALYSIS OF INFLAMMATORY SKIN DISEASES

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Skin and subcutaneous diseases were the 18th leading cause of global disability and mortality, contributing to 1.79% of the global morbidity and mortality worldwide according to the Global Burden of Disease. In this study we aim to determine which specific dermatological conditions have the greatest mortality and worst prognosis. We compared the age and gender-controlled death rate and hazard ratios of 8 skin conditions: systemic lupus erythematosus, cutaneous lupus erythematosus, dermatomyositis, localized scleroderma, pyoderma gangrenosum, melanoma, Merkel cell carcinoma, and Basal cell carcinoma. All data was obtained from the TriNetX database. Our results show that patients with inflammatory skin disease have an increased hazard ratio compared to the general population for all of the dermatological diseases included in this study (Table 1). The diseases with the highest hazard ratios among men include dermatomyositis (4.82), pyoderma gangrenosum (4.45), and systemic lupus erythematosus (3.66). The diseases with the highest hazard ratios among women are pyoderma gangrenosum (6.89), systemic lupus erythematosus (4.87), and dermatomyositis (4.31). Our results show that these rheumatic skin diseases have a markedly higher hazard ratio than even most skin cancers—including Merkel cell carcinoma, melanoma, and Basal cell carcinoma. Among men, the hazard ratios for Merkel cell carcinoma, melanoma, and Basal cell carcinoma are only 2.40, 2.25, and 1.46, respectively. A similar trend is observed among women. The hazard ratio is only 3.87 for both Merkel cell carcinoma and melanoma, and only 1.42 for Basal cell carcinoma. This data demonstrates that rheumatic skin disease is not only a significant cause of morbidity but also leads to increased mortality. Therefore, more attention, resources, and research funds should be dedicated to these diseases.

29. ASSOCIATION BETWEEN SARCOIDOSIS AND ENVIRONMENTAL TOXINS IN MASSACHUSETTS: A GEOSPATIAL ANALYSIS

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Sarcoidosis is an inflammatory granulomatous disease of unclear etiology with a propensity to affect multiple organ systems. To date, there has been no data on mapping the geographic distribution of sarcoidosis cases in the context of environmental triggers. This study analyzes sarcoidosis period prevalence in geospatial relation to sources of environmental toxin exposure to elucidate the potential impact of exposures on disease clusters. Evaluation of data from 1989-2020 yielded 1,742 patients with sarcoidosis meeting inclusion criteria. ArcGIS Pro 2.7 was used for sarcoid geographic distribution maps and overlaid with maps of environmental toxins. Statistical analysis was performed using Spearman rank correlation coefficients. The period prevalence of sarcoidosis demonstrated a significant positive correlation with increased quantities of oil release sites ($r=.30$, $p<.01$), hazardous waste ($r=.24$, $p<.01$), chemicals covered by the Clean Air Act ($r=.12$, $p<.01$), and carcinogens ($r=.23$, $p<.01$) within the same zip code. Furthermore, Black patients with sarcoidosis are more likely to live in areas with increased quantities of environmental toxins. Specifically, zip codes where a greater proportion of patients were Black had a significant positive correlation with increased quantities of oil release sites ($r=.38$, $p<.01$), hazardous waste ($r=.26$, $p<.01$), chemicals covered by the Clean Air Act ($r=.20$, $p<.01$), carcinogens ($r=.26$, $p<.01$), and toxic metals ($r=.11$, $p=.01$). Analysis utilizing census data maintained the trends yielded by our patient data set. Our study provides insight into the potential role of environmental toxins on the development of sarcoidosis and further supports prior studies which demonstrate that Black communities experience disproportionate burdens of toxic environmental exposures. This study contributes new data to help elucidate potential etiologic exposures contributing to sarcoidosis and allows us to gain a better understanding of why sarcoidosis is more prevalent in Black populations. Future studies should include wider geographies and explore the immunologic mechanism of environmental antigens in sarcoidosis.

30. THE RISK OF SKIN CANCER DEVELOPMENT IN PATIENTS WITH AUTOIMMUNE CONNECTIVE TISSUE DISEASES WHO ARE SYSTEMICALLY IMMUNOSUPPRESSED: A RETROSPECTIVE COHORT STUDY

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The increased risk of skin cancer in immunosuppressed solid organ transplant recipients is well-known, but despite comparable pharmacotherapy, there is limited data assessing this risk in autoimmune connective tissue disorder (AICTD) patients. This retrospective cohort study at an urban tertiary referral center evaluated whether immunosuppressed AICTD (IS) patients had a greater risk of developing skin cancer versus their non-immunosuppressed (NIS) counterparts. In our interim analysis of 2,984 AICTD patients seen in dermatology or rheumatology outpatients clinics from 2008-2018, 817 met inclusion criteria with 77.1% female (n=630) and mean age 41.5 years (SD=17.9 years). AICTD diagnoses included: dermatomyositis (8.0%, n=65), lupus erythematosus (36.2%, n=295), mixed connective tissue disease (2.5%, n=20), morphea (13.1%, n=107), sarcoidosis (1.8%, n=15) Sjogren syndrome (12.5%, n=102), systemic sclerosis (7.7%, n=63), vasculitis (17.2%, n=140), and other (1.0%, n=8). 77.1% (n=630) were treated with systemic immunosuppressives. 8.4% (n=53) of IS patients had skin cancer ever, compared to 3.7% (n=7) of NIS patients (RR=2.2, p=0.037). The mean number of skin cancers per patient was 2.5 (SD=3.3) in the IS cohort compared to 1.1 (SD=0.4) in the NIS cohort (p=0.340). Proportional hazards modeling demonstrated the hazard ratio for skin cancer development in IS patients was 1.44 (95% CI 0.65-3.22, p=0.371) versus NIS patients. Our results indicate that IS patients have an increased risk of skin cancer versus NIS patients, but there is need for prospective studies to validate these findings and guide skin cancer screening recommendations. Relatively few incident skin cancers and the retrospective nature of this study are important limitations.

Clinical Cases

31. HIGHER DOSE OF GUSELKUMAB FOR TREATMENT OF PYODERMA GANGRENOSUM

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Pyoderma gangrenosum (PG) is a rare, ulcerative neutrophilic dermatosis. PG pathophysiology is incompletely understood, making targeted therapeutic approaches challenging. IL-23, a cytokine implicated in neutrophilic disease processes, has shown promise as a PG treatment target. We report a case of recalcitrant PG treated with guselkumab (IL-23 inhibitor) at a higher dose than approved for other inflammatory conditions. A 49-year-old woman with diabetes mellitus presented with a non-healing ulcer on her left lower extremity (LLE) from a previously sutured laceration; systemic antibiotics yielded little improvement. Subsequently, she had several emergency department and primary care visits for pain and swelling and was diagnosed with a vascular ulcer complicated by cellulitis and diabetes. Sharp debridement led to further ulcer expansion, prompting dermatology referral and consideration of a diagnosis of PG. The patient suffered an additional accidental laceration to the right lower extremity (RLE), which progressed to another full-thickness PG ulcer. Over the next 11 months, multiple treatment approaches were trialed, including systemic prednisone, dapsone, cyclosporine, and adalimumab, with minimal improvement. She was also hospitalized three times during this period for cellulitis and sepsis secondary to PG. Throughout her disease course, this patient had several gram-negative wound infections and 3 LLE distal venous thromboses. Due to continued ulcer progression, the decision was made to trial high-dose Guselkumab (200mg). Two weeks after initiation, the patient's ulcers had decreased in size and drainage. She received a second dose (100mg) 4 weeks later, then two more doses (100mg each) at 6-week intervals. After 4 doses of Guselkumab, the patient achieved complete healing of both ulcers. She will continue to receive Guselkumab (100mg) every 6 weeks for 1 year of therapy. Treatment of recalcitrant PG is multifaceted and presents significant challenges. This case report suggests high-dose Guselkumab may be another safe and effective alternative for treatment of PG.

Teaching point: High-dose guselkumab may be an alternative therapeutic option for patients with recalcitrant PG who have failed several other modes of systemic therapy.

32. SCLEROTIC SKIN DISEASE PROGRESSION FOLLOWING COVID-19 VACCINATION: A CASE SERIES

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Vaccination is an essential preventative measure against infectious disease. However, there may be an association between vaccination and subsequent autoimmune reactions. We present two cases of patients with prior autoimmune skin disease progressing to new-onset sclerotic skin disease following COVID-19 vaccination. Case 1: A 60-year-old female patient with a history of discoid lupus presented with severe widespread muscle pain and a new rash that began two weeks after the first dose of the Moderna COVID-19 vaccine. Physical exam showed hidebound skin with shiny surfaces on the face, chest (Figure 1), lower legs (Figure 2, 3), back, abdomen, and forearms (Figure 4). Pathology collected two weeks after the second vaccine dose demonstrated dermal mucin deposition and perivascular and perifollicular lymphoplasmacytic inflammation. Laboratory testing showed creatine kinase of 2757 U/L (ref. 32 - 182 U/L), aldolase of 40.8 U/L (ref. 3.3-10.3 U/L), and positive Ku, U1 SNRNP, and U2 SNRNP antibodies. A second biopsy demonstrated dermal sclerosis. Altogether these findings were consistent with new-onset scleroderma-myositis overlap. Treatment with prednisone and mycophenolate mofetil led to normalization of creatine kinase while skin thickening continued to progress. Case 2: A 72-year-old female patient with a history of morphea presented with a new rash that began within 4 weeks of receiving the second dose of the Pfizer-BioNTech COVID-19 vaccine. Physical exam showed skin thickening on the arms and legs as well as puckering of skin on the arms. Laboratory testing showed eosinophil count of 1280/mm^3 (ref. 0-700/mm^3) or 13.9% eosinophils (ref. 0-6%). MRI of the calf demonstrated moderate diffuse skin thickening with perifascial and intramuscular edema (Figure 5). These findings were consistent with new-onset eosinophilic fasciitis. Treatment with mycophenolate mofetil and prednisone led to normalization of the eosinophil count and skin softening. These cases demonstrate the temporal association of sclerotic skin disease development following COVID-19 vaccination.

Teaching Point: Patients with underlying rheumatic dermatologic diseases may develop new-onset sclerotic skin diseases following COVID-19 vaccination.

33. FATAL HEPATIC FAILURE IN A PATIENT WITH ANTI-MDA-5 ANTIBODIES

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Individuals with dermatomyositis (DM) and anti-melanoma differentiation-associated gene 5 (anti-MDA-5) antibodies frequently develop cutaneous ulcerations, joint disease, and interstitial lung disease (ILD). This subtype of DM is recognized for its severe and aggressive clinical course – especially for the subset with rapidly-progressive ILD. We present the case of a 35-year-old female with DM and anti-MDA-5 antibodies who died of liver failure within six months of her DM diagnosis. This case offers insight into a possible connection between anti-MDA-5 DM and liver dysfunction. Our patient initially sought medical care for shortness of breath and abdominal pain and was found to have persistently elevated transaminases (ALT 145-153 IU/L, normal 0-60 IU/L; AST 112-149 IU/L, normal 5-40 IU/L). She then presented to the rheumatology-dermatology clinic with severe weakness, continued gastrointestinal symptoms and classic cutaneous DM features, and was admitted to the hospital for expedited treatment initiation. Her serum antibody testing and skin biopsies confirmed a diagnosis of anti-MDA-5 DM. Over the next six months her skin and lungs improved on an aggressive and evolving treatment regimen that included intravenous immunoglobulins (IVIG), rituximab, mycophenolate mofetil, tacrolimus and oral steroids. However, her liver dysfunction persisted, and three subsequent liver biopsies showed rapid progression from steatosis (November 2020) to steatohepatitis (December 2020) and ultimately steatohepatitis with cirrhosis (April 2021). Her transaminases peaked with AST 1009 IU/L and ALT 630 IU/L – only declining as her total bilirubin rose to 25.5mg/dL (normal < 1.4mg/dL). Her INR peaked at 2.0 (normal 0.9 – 1.1), her albumin nadired at 1.7g/dL (normal 3.5-5.2g/dL) and she suffered fatal liver failure. Despite positive anti-smooth muscle antibodies, her liver biopsies were inconsistent with autoimmune liver disease and her elevated transaminases preceded IVIG and high-dose corticosteroids. This case suggests that anti-MDA-5 autoimmunity may be associated with hepatic dysfunction that can have profound clinical consequences.

Teaching Point: Anti-MDA-5 dermatomyositis associated with liver failure.

34. BULLOUS HERPES ZOSTER IN A LUPUS NEPHRITIS PATIENT TREATED WITH RITUXIMAB: A CASE REPORT AND LITERATURE REVIEW

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Herpes zoster is a clinical syndrome associated with reactivation of varicella zoster virus (VZV), often occurring years after VZV infection, and characterized typically by painful grouped vesicles in a dermatomal distribution. Bullous herpes zoster, an atypical presentation of herpes zoster, is a relatively rare phenomenon; to the authors' knowledge, there have only been eight reports in the worldwide literature. We present a case of a 59-year-old female with lupus nephritis who presented with multiple grouped vesicles evolving into large tender bullae filled with serosanguinous fluid on the lateral aspect of the right leg, and dorsal and medial aspects of the right foot, 4 days after the first dose of 1g of rituximab therapy. The diagnosis of bullous herpes zoster along L4-L5 dermatomes was made based on the clinical presentation and the presence of multinucleated giant cells on Tzanck smear. The giant bullae were drained and dressed, and the patient was treated with valacyclovir at the renally adjusted dose of 1g once a day for 7 days and pregabalin 150 mg once daily. After 7 days of antiviral treatment, there were no new bullae or vesicles, and the pain improved. However, at this point, there was noted onset of superimposed bacterial infection, which was managed with vancomycin and Plastic Surgery referral for wound care. Recognizing this atypical presentation of a common disease, especially in patients with an immunocompromised state, highlights the importance of prompt recognition and treatment.

Teaching Point: Recognizing bullous herpes zoster, an atypical presentation of a common disease, especially in patients with an immunocompromised state, highlights the importance of prompt recognition and treatment.

35. RECALCITRANT ERYTHROMELALGIA SUCCESSFULLY TREATED WITH MISOPROSTOL

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A previously healthy 19-year-old male presented with a two-month history of a painful eruption on the feet. He noted that this worsened with heat or physical activity, and was profoundly affecting his quality of life, as running and rock climbing had become nearly unbearable. He also endorsed frequent exacerbations at night, with severe sleep disturbance. Exam revealed edematous, mottled erythematous and violaceous plaques diffusely involving both feet and all toes. Punch biopsy of the right fifth toe showed no features of pernio or vasculitis, and a diagnosis of erythromelalgia was made. Complete blood count was unremarkable. After initiating lifestyle modifications, topical betamethasone, and oral meloxicam without effect, oral misoprostol was prescribed. At two month follow up, he endorsed dramatic improvement, and had been able to return to his usual activities without event. Erythromelalgia is a condition characterized by transient episodes of erythema accompanied by a burning sensation. It typically occurs on extremities, and classically is exacerbated by heat and improved with cooling. It can be associated with underlying thrombocythemia or other myeloproliferative disorder. Further, there is a familial subtype related to mutation in the *SCN9A* gene, which encodes a voltage-gated sodium channel. While the pathogenesis is poorly understood, it is thought to involve dysregulation of vascular dynamics. Theories include inappropriate shunting leading to cutaneous hypoxia, versus a prolonged hyperemic state with associated release of pain mediators. After ruling out any underlying primary causes, treatment centers on conservative management with cooling, elevation of affected area, and oral analgesia. While a variety of topical and oral agents have been utilized with inconsistent success, several studies have demonstrated the utility of the prostaglandin E1 analog misoprostol in refractory cases, owing to its effect as a vasodilator and platelet activation inhibitor.

Teaching Point: Oral misoprostol can have a profound effect on recalcitrant erythromelalgia.

36. PATIENT WITH POSITIVE DESMOGLEIN 1 AND 3 PRESENTING WITH CLINICAL AND HISTOPATHOLOGICAL FINDINGS OF PEMPHIGUS ERYTHEMATOSUS

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Pemphigus erythematosus (PE) is a variant of pemphigus foliaceus with lesions localized to the malar region of the face and other seborrheic distributions. We report the case of a 35-year-old male referred to our connective tissue disease clinic for presumed refractory discoid lupus erythematosus (DLE). The patient presented with pruritic scaly lesions of the scalp, malar face, central chest, and upper back of one-year duration. Although his eruption was responsive to high potency topical and systemic corticosteroids, he reported no prior improvement with hydroxychloroquine and developed thrombocytopenia on methotrexate. Physical examination was notable for pink to violaceous eroded plaques, some with fine overlying scale, on the malar distribution of the face and scalp, as well as hyperpigmented to violaceous patches and plaques on the central chest and upper back. Appreciable follicular plugging and atrophic scarring were absent, and conchal bowls and mucosal sites were notably spared. Laboratory findings included a negative ANA. Punch biopsy of the scalp demonstrated a subcorneal split with epidermal acantholysis as well as perivascular lymphocytic infiltrate with occasional eosinophils. Direct immunofluorescence revealed deposition of IgG and C3, both intercellularly within the epidermis and along the basement membrane zone in a granular pattern. These results, along with the clinical findings, were compatible with a diagnosis of PE. Indirect immunofluorescence was ultimately positive for desmoglein (Dsg) 1 and 3 antibodies on ELISA. While the presence of Dsg-3 antibodies is typically suggestive of mucosal involvement in pemphigus vulgaris, there have been reports of this finding in a small number of pemphigus foliaceus and PE patients as well. The patient was recently started on Rituximab with a prednisone taper with improvement of his disease.

Teaching Point: Dsg-3 can be present in a minority of pemphigus foliaceus and pemphigus erythematosus patients, highlighting the importance of correlating serology with clinical and pathological findings.

37. A PATIENT WITH DISCOID LUPUS, SUBACUTE LUPUS, AND DERMATOMYOSITIS: A CLINICAL AND IMMUNE CHARACTERIZATION

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A 59-year-old female patient presented to our clinic with a history of lupus, Sjögren's syndrome, and myositis. Her history included weight loss, arthralgias, and fatigue. She reported having cutaneous lupus erythematosus (CLE) for four years (SCLE confirmed by photos). Her serologies included a positive ANA 1:1280, SS-A, SS-B, and PL-12. She had a creatinine of 1.02 and 1+ proteinuria. She had been treated with hydroxychloroquine, chloroquine, quinacrine, belimumab, mycophenolate mofetil, methotrexate, and azathioprine. On exam she had erythema on her V of neck, forehead, eyelids, conjunctiva, scarred erythematous macules over her extensor arms, telangiectatic violaceous patches on her back, erythema and scale on her elbows, mild mechanic's hands, and erythema over the joints on her hands. In summary, this patient has SCLE, SLE, DLE, secondary Sjögren's and antisynthetase dermatomyositis (DM). Notably, the patient's clinical presentation with SCLE preceded and was separate from her recent presentation to clinic with more typical dermatomyositis features. Biopsies of lesional SCLE, DLE, and DM were obtained for imaging mass cytometry. For comparison, we also utilized 44 CLE and 17 DM biopsies as controls. DM skin demonstrated increased B cells (median 40% DM, 11% CLE, $p<0.01$), IFNγ (median MPI 1.31 DM, 1.07 CLE, $p<0.05$), phospho (p) STAT6 (median MPI 1.61 DM, 0.96 CLE, $p<0.001$), pJAK1 (median MPI 0.70 DM, 0.42 CLE, $p<0.001$) compared to CLE. CLE displayed increased pJAK2 (median MPI 1.80 DM, 2.44 CLE, $p<0.05$). Similarly for our overlap patient, B cells were 72.8% (515 cells) of the infiltrating leukocytes in the DM lesion compared to 0.68% in SCLE (1 cell) and 15.2% in DLE (411 cells). We also saw increased IFNγ in her DM biopsy (1.682 MPI) compared to DLE (1.13 MPI) and SCLE (0.85 MPI). This case highlights the potential immune drivers of distinct clinical phenotypes, with potential actionable targets identified for DM in particular.

38. NEUTROPHILIC DERMATOSIS OF CONNECTIVE TISSUE DISEASE IN A PATIENT WITH MIXED CONNECTIVE TISSUE DISEASE

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Neutrophilic dermatosis of connective tissue disease is a rare entity that has been previously described, most often in the setting of systemic lupus erythematosus (SLE). We present a case of a 20-year-old female who was referred for evaluation of refractory pernio and ultimately diagnosed with neutrophilic dermatosis of connective tissue disease. Her history included autoimmune hepatitis and mixed connective tissue disease (MCTD), initially characterized by fatigue, Raynaud's phenomenon, polyarthralgia, high titer ANA (1:2560), high titer RNP, and leukopenia. She subsequently developed myositis. Six months prior to referral, she developed extremely painful pink-red, juicy plaques, some targetoid in nature, on the bilateral hands. The patient denied recent viral or other illnesses. At the time of presentation, the patient's lesions were worsening despite a regimen for her MCTD that included pulse intravenous as well as oral corticosteroids, leflunomide, adalimumab, and hydroxychloroquine. Biopsy of a right palmar lesion demonstrated papillary dermal edema with a superficial-to-deep predominantly neutrophilic infiltrate and no evidence of vasculitis, consistent with neutrophilic dermatosis of connective tissue disease. The patient was initiated on dapsone 50 mg daily and noted improvement within one week of starting treatment. Previously, nonbullous and nonvasculitic neutrophilic dermatosis in association with SLE was considered to potentially be a dampened manifestation of bullous SLE given its occurrence in the setting of immunosuppression. However, more recent reports have favored that this is a distinct cutaneous manifestation, particularly associated with progression to systemic involvement of SLE. Interestingly, our patient was admitted to the hospital within two months of presentation for flaring autoimmune disease, with decreasing complements and other features most compatible with an SLE phenotype. Hence, in our patient, this cutaneous presentation is consistent with the evolving literature on neutrophilic dermatosis of connective tissue disease, likely heralding differentiation of her MCTD towards an SLE phenotype.

Teaching Point: Neutrophilic dermatosis of connective tissue disease, which often responds to dapsone, is most often seen in patients with SLE and may herald SLE onset.

39. NEW DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS AFTER COVID-19 VACCINATION

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An 18-year-old female with autism was brought in with a rash of one-month duration. A few days before the rash developed, she had received the coronavirus disease 2019 (COVID-19) mRNA vaccine, after which the patient developed facial swelling and a red, painful, persistent rash involving the face, and extremities. There was no history of photosensitivity, oral ulcers, or Raynaud's phenomenon. Examination showed ill-defined, erythematous, tender plaques on the frontal scalp, face, arms, legs, and chest (figure 1). Laboratory workup revealed leukopenia, positive anti-nuclear (1:2560) and anti- smith antibodies, low complement levels, and elevated urine protein to creatinine ratio. A biopsy from a plaque on the thigh was consistent with a connective tissue disease. A diagnosis of systemic lupus erythematosus (SLE) was established. The patient was treated with oral hydroxychloroquine and tapering doses of systemic steroids. The rash resolved with brown macules and atrophic plaques (figure 2).
SLE can be triggered by several external factors, including drugs and vaccines. An interferon-γ driven pathogenesis has been implicated in the exacerbation and new onset of lupus following the administration of the combined influenza and diphtheria, pertussis, and tetanus vaccine. The COVID-19 infection and vaccines activate proinflammatory cytokine pathways and orchestrate an immune response involving type I interferon similar to those involved in SLE itself. In the light of this clinical and scientific data, we believe that in our patient the administration of the mRNA vaccine disrupted the immune balance to cause the asymptomatic disease to flare. Vaccines against COVID-19 have led to flares of immune-mediated diseases like pericarditis, neuropathy, sarcoidosis, and myasthenia gravis. However, despite the potential of these vaccines to elicit flares of autoimmune diseases, this risk must be weighed carefully against the importance of protecting these patients against COVID-19 infection, which has the potential to cause severe disease in immunosuppressed individuals.

Teaching Point: With the ongoing COVID-19 pandemic, there is an increased use of mRNA vaccines and it is important for physicians to be aware of the potential for these vaccines to induce exacerbations of existing autoimmune disorders or potentially unmask de novo autoimmune diseases in predisposed individuals.

40. CUTANEOUS MANIFESTATIONS OF RHEUMATOID ARTHRITIS AND ANTIPHOSPHOLIPID SYNDROME: LESSONS FROM A PATIENT CASE

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Rheumatoid arthritis (RA) presents with a variety of extra-articular cutaneous manifestations, most commonly rheumatoid nodules and neutrophilic dermatoses such as pyoderma gangrenosum (PG) and rheumatoid neutrophilic dermatosis. Antiphospholipid antibodies are autoantibodies that recognize phospholipids or phospholipid-binding proteins. They may occur in the absence of underlying disease or in combination with other diseases. Cutaneous manifestations include livedo reticularis and livedoid vasculopathy. We present a 36-year-old female with a history of RA and anti-phospholipid antibodies who presented with bilateral hip, leg, and foot pain, and a purpuric rash on the upper and lower extremities. Examination revealed pinpoint areas of trauma that enlarged to full-thickness ulcers with granulation tissue and violaceous, undermined edges, consistent with pyoderma gangrenosum (Figure 1). Retiform purpura was present on the bilateral upper and lower extremities (Figures 2 & 3). Punch biopsies of the edge of the purpuric rash were subtle and positive for dermatitis, attributed to hypercoagulability due to antiphospholipid antibodies. Laboratory results were positive for rheumatoid factor and beta-2-glycoprotein IgM antibodies. She received 60 mg prednisone, with improvement of her leg ulcers but no improvement in her rash. She was subsequently started on methotrexate until insurance approval of adalimumab.

PG can occur as an independent disease, but is associated with multiple systemic and autoimmune diseases. Approximately 12% of PG cases occur in the setting of RA. It is diagnosed clinically and characteristically appears as a full-thickness ulcer with purple undermined borders and exhibits pathergy. Livedoid vasculopathy is frequently the only manifestation of antiphospholipid syndrome (APS) and presents as retiform purpura with painful ulcerations. It results from intraluminal thrombosis of dermal micro vessels, leading to hypoxia and ulcerations that present as pruritic, stellate, retiform papules and plaques. Treatment for both disorders differs, and differentiating the etiology of multiple cutaneous manifestations is important for proper treatment.

Teaching Point: There is overlap between the cutaneous manifestations of RA and APLA, however, multiple unique cutaneous findings may indicate different pathogenesis with differing treatments. It is important to determine the underlying cause of cutaneous disease when treatments differ.

Figure 1. Right lower leg with full-thickness ulcers with granulation tissue and violaceous, undermined edges, consistent with pyoderma gangrenosum.

41. A Novel *NFkB1* Mutation Linking Pyoderma Gangrenosum and Common Variable Immunodeficiency

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The etiology of pyoderma gangrenosum (PG) remains unclear. Frequently associated with autoimmune diseases and hematologic malignancy, PG rarely co-occurs with immunodeficiency. We present a young woman with recurrent PG and common variable immunodeficiency (CVID), found to have a novel mutation in *NFkB1*. The patient initially presented after laparoscopic cholecystectomy with fever, leukocytosis, and five well-demarcated, deep ulcers with undermined borders. Clinical impression and histopathology were consistent with PG. Given her severe PG at a young age with coexisting immunodeficiency, exome sequencing was completed, revealing a likely pathogenic variant in *NFkB1* (C.A2415G, p.Q805Q). The variant lay two base-pairs 5' to the end of exon 21, and *in silico* analysis predicted complete obliteration of normal splicing. Years later, the patient presented with a left scaphoid fracture after a car accident and developed a 30cm undermined ulcer on the lower abdomen with purulent drainage. Biopsy was again consistent with PG. Prednisone 0.5 mg/kg, infliximab 5 mg/kg and topical 0.05% clobetasol improved abdominal lesions, but infliximab caused debilitating arthralgias. The third episode of PG occurred after scaphoid repair surgery. She developed fever, pain and a purulent ulcer at the surgical wound consistent with PG. Biopsy was deferred due to pathergy risk, and she was managed with cyclosporine 5mg/kg and prednisone 0.2mg/kg daily, which resulted in full healing of the surgical site. *NFkB1* mutations have been associated with three cases of CVID and PG, but our case is unique because unlike prior reports, this is the first patient with a novel *NFkB1* mutation who developed severe, recurrent PG episodes with co-existing immunodeficiency at a young age. This case expands the phenotypic landscape of *NFkB1* mutations and further supports the association between NF-kB pathway dysregulation and CVID and PG pathogenesis.

Teaching point: A novel, likely pathogenic *NFkB1* variant may link both PG and CVID