AB001. Understanding transcriptional connections of chronic cutaneous lupus erythematosus between humans and animal models

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Abstract: Chronic cutaneous lupus erythematosus (CCLE) exhibits severe inflammatory processes that lead to decreased quality of life (QoL) and potential skin scarring with disfiguration; treatment of CCLE has a high unmet need for effective and safe therapeutics. To determine biological pathways and transcriptional networks unique to CCLE, we performed meta-analysis of published humans CCLE transcriptome studies and comparative correlation with spontaneous canine and murine MRL/lpr model CCLE skin lesions. Utilizing published microarray data of three human CCLE studies, we determined a comprehensive consensus CCLE shared gene list of 245 genes differentially expressed genes (DEGs) (>2-fold enhanced, P<0.05). The Th1 and interferon-related genes (STAT1, OASL, MX1, IFNγ, GZMB, ISG15) as well as T-cell trafficking chemokines, CXCL9, CXCL10 and CCL11, were among the strongest upregulated genes. Top enriched process networks by MetaCore overlap analysis of human CCLE studies revealed upregulation of interferon and IFNy signaling, innate immune response to RNA viral infection, NK-cell cytotoxicity and JAK-STAT pathway. Comparative analysis between canine and mouse CCLE DEGs with the human CCLE meta-analysis derived DEG list found that canine and murine CCLE lesions contained 57% (139/245) and 24% (59/245) shared genes, receptively. Spearman correlation coefficients of canine CCLE DEGs with three human CCLE studies showed significant moderate to strong positive correlation (r=0.52–0.67). The shared canine CCLE DEGs within the human CCLE lesional pathology signature reflected strongly activated pathway maps of IFNα/β signaling via JAK-STAT, antiviral actions of IFN and IFNγ signaling. In conclusion, canine spontaneous CCLE model appears the best to replicate human CCLE immune signatures.

Keywords: Cutaneous lupus; human; mouse; canine

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AB002. Quality of life is inversely related to income in patients with cutaneous lupus

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Abstract: Recent studies demonstrated cutaneous lupus erythematosus (CLE)'s profound impact on quality of life (QoL), but few have examined the association between income and QoL in CLE patients. To address this knowledge gap, we performed a cross-sectional analysis of 238 patients with CLE from outpatient dermatology clinics at University of Texas Southwestern Medical Center and Parkland Health and Hospital System, a safety-net hospital in Dallas, TX, from November 2008 to December 2018. First, we investigated differences in overall QoL, as measured by the four SKINDEX 29+3 subdomain scores (emotions, function, symptoms and lupus-specific), amongst CLE patients of different income groups (<$10,000/year, $10,000–$50,000/year, >$50,000/year). Next, we identified which aspects of QoL, as specified by individual SKINDEX 29+3 questions, were most frequently impaired in CLE patients of various incomes. Chi-squared tests were used to assess how responses to each question varied across income groups. Of the 238 patients, the majority of patients earned between $10,000–$50,000/year (n=88) or <$10,000/year (n=85). The four SKINDEX 29+3 subdomain scores decreased as annual income increased. In all cases, the lowest income group had higher scores (or worse QoL) than the other two groups ($P<0.05$ for lupus-specific, $P<0.01$ for function and symptoms, $P<0.001$ for emotions). Chi-square results of all SKINDEX 29+3 questions with annual income revealed 9 significant questions. Compared with patients with $10,000–$50,000/year, and >$50,000/year, those with <$10,000/year more often reported impairment in aspects regarding emotion, such as anger and embarrassment, as well as general function, particularly pertaining to isolation and desire to be with others ($P\leq0.001$ for all questions). In conclusion, we have shown that annual income has an inverse relationship to QoL in patients with CLE. Poor QoL, particularly in the context of social detachment, may hinder patients of low socioeconomic status to seek out necessary care, follow physician recommendations and communicate freely about changes in their disease state. We recommend clinicians remain cognizant of the socioeconomic status of patients with CLE, given its effects on their QoL.

Keywords: Quality of life (QoL); cutaneous lupus erythematosus (CLE); income

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AB003. Increased CD69+ tissue-resident memory T cells and STAT3 expression in cutaneous lupus erythematosus patients recalcitrant to antimalarials

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Background: Cutaneous lupus erythematosus (CLE) is an autoimmune disease involving T lymphocytes, plasmacytoid dendritic cells (pDCs), and myeloid dendritic cells (mDCs). While oral antimalarials, including hydroxychloroquine (HCQ) and quinacrine (QC) are first-line systemic therapy for all CLE subtypes, some patients remain refractory to both HCQ and HCQ + QC. To better understand reasons for refractoriness in CLE, we investigated the immunologic characteristics of patients who responded to antimalarials versus those who did not.

Methods: Biopsies from 65 CLE patients with well characterized treatment response to HCQ (n=22) and HCQ + QC (n=24), as well as treatment failure to HCQ + QC (n=19) were studied via immunohistochemistry and polymerase chain reaction. Lesional skin was biopsied prior to antimalarial treatment. The patient's CLASI score—a measure of disease activity—at the time of the biopsy was also determined.

Results: Immunohistochemistry showed CD69+ tissue-resident memory T (T_{RM}) cells were significantly higher in HCQ + QC-nonresponders compared to HCQ- and HCQ + QC-responders. mDCs were significantly higher in HCQ +QC-responders compared to HCQ-responders and HCQ + QC-nonresponders. There were significantly higher pDCs in the HCQ-responders compared to the nonresponders. CLASI scores of HCQ + QC-nonresponders correlated positively with the number of T_{RM} cells (r=0.6254, P=0.017) and macrophages (r=0.5726, P=0.041). mRNA expression demonstrated high STAT3 expression in HCQ + QC-nonresponders.

Conclusions: An increased number of CD69+ T_{RM} cells and correlation between CD69+ T_{RM} cells and macrophages with CLASI scores in the HCQ + QC-nonresponders, a finding not seen in either HCQ or HCQ + QC-responders, may suggest CD69+ T_{RM} cells and macrophages are involved in antimalarial-refractory skin disease.

Keywords: Cutaneous lupus erythematosus (CLE); antimalarials; tissue-resident memory T cell; myeloid dendritic cell (mDC)

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AB004. Evaluating differences in meaningful change in disease activity between different races and clinical subtypes affected by cutaneous lupus erythematosus

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Abstract: Cutaneous lupus erythematosus (CLE) has a profound impact on a patient's quality of life (QoL), despite epidemiologic differences disease presentation. Disease activity, rather than damage, has a greater impact on QoL, and improvement in disease activity, defined by the Cutaneous Lupus Disease Area and Severity Index score for activity (CLASI-A), is correlated to improvement in QoL. We aimed to evaluate the differences between meaningful improvement in disease activity, experienced by Caucasian and African-American patients and disease subtypes. This study included 144 patients seen at the Hospital of the University of Pennsylvania who participated in a longitudinal research database of lupus patients. Patients with an initial CLASI-A 4 were included, and classified by their self-identified racial background and clinical disease subtype. Linear regression models were used to calculate change in disease activity needed to predict meaningful improvement in QoL, defined as a respective 9.38-point in the Emotions subscale of Skindex-29. Due to the limited number of patients with acute CLE, we compared meaningful improvement between patients with discoid lupus erythematosus (DLE) and patients with subacute CLE (SCLE). An improvement of disease activity by 58.6% and 52.5% is associated with a meaningful impact on the Emotions subscale of Caucasian and African-American patients, respectively. Decreasing disease activity by 52.1% and 55.2% is meaningful for patients with DLE and SCLE, respectively. Regardless of individual differences in disease activity and presentation of CLE, patients experience improvement in QoL, particularly in the emotional component, with similar meaningful changes in their disease activity.

Keywords: Cutaneous lupus erythematosus (CLE); disparities; quality of life (QoL); patient-reported outcomes; efficacy measures

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AB005. Assessing meaningful changes in disease activity as clinical trial clinical efficacy measures for cutaneous lupus erythematosus

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Abstract: To date, there are no approved treatments for cutaneous lupus erythematosus (CLE), a disease known to significantly burden a patient's quality of life (QoL). Clinical trials are important for the advancement of treatments and outcome measures of these trials should reflect clinically meaningful improvement in disease activity and its effect on QoL. Currently, clinical trials use an efficacy measure of ≥50% improvement in disease activity, defined by the Cutaneous Lupus Disease Area and Severity Index activity (CLASI-A) score, in patients with an initial CLASI-A score of ≥10. However, the degree of improvement in disease activity needed to predict a meaningful impact on QoL has not been defined. This is a retrospective study of 126 patients enrolled in a longitudinal research database. Using a linear regression model, we calculated the percent change and difference needed in CLASI-A to have an important impact on QoL, defined as a 9.38-point and a 7.37-point improvement in the Emotions and Symptoms subscales of Skindex-29, respectively. In patients with an initial CLASI-A score ≥8, a decrease by 42.1% and a decrease by 31.0% in disease activity is associated with a meaningful impact in the Emotions and the Symptoms subscales, respectively. Using a CLASI-A score ≥8 for trial entry allows for inclusion of patients with milder disease for whom improvement of CLASI-A by ≥50% has a meaningful impact on QoL, as determined by the Emotions and Symptoms subscales. In patients with moderate to severe initial disease, a respective decrease in activity by seven and five-points is not only clinically significant, but also has a meaningful impact on the Emotions and Symptoms subscales. Our findings establish appropriate trial endpoints by determining clinically significant change in disease activity associated with meaningful changes in patients' QoL.

Keywords: Cutaneous lupus erythematosus (CLE); clinical trials, quality of life (QoL); patient-reported outcomes; efficacy measures

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AB006. A modular analysis approach to studying gene expression in cutaneous lupus erythematosus

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Abstract: Previous studies on blood transcription profiles of patients with cutaneous lupus (CLE) have primarily used a gene expression approach. The large amount of data involved in these studies can make data analysis and interpretation cumbersome. Consequently, a novel approach in gene expression analyses was devised that groups genes into transcriptional modules (i.e., apoptosis, protein synthesis, inflammation) to identify important themes and relevant genes. This approach was used to study gene expression in systemic lupus patients and subsequently identified a unique interferon signature. Thus, we aim to use the modular analysis approach to identify unique modules and genes of CLE patients in order to better understand their disease pathophysiology. We conducted RNA sequencing of whole transcriptomes of blood from 66 CLE patients and 10 human controls and subsequently performed modular analyses. Based on module scores, we performed an unsupervised cluster analysis to identify subgroups of CLE patients with distinct gene expression patterns. Statistical analyses comparing module scores of these clusters was performed using the Kruskal-Wallis tests with Bonferroni's correction. Modules were associated with patient subgroups distinguished by demographic, clinical, and laboratory features such as CLE subtypes, autoantibody profiles (BioPlex® 2200 ANA Screen with MDSS), and cytokine profiles (Thermo Scientific ProCarta xMAP cytokine assay kits). The unsupervised cluster analysis identified eight distinct clusters of CLE patients and controls. A neutrophilic predominant signature governed by azurophilic granule genes (i.e., BPI, LTF, MPO) and neutrophil chemotaxis genes (CEACAM6, CEACAM8) was seen in two groups of patients mostly with subacute lupus erythematosus (SCLE) [n=7 (77.8% of total SCLE)] or lupus erythematosus tumidus (LET) [n=6 (60% of total LET)] and European-American descent [n=28 (53.6% of total European-Americans)]. Four groups consisting of a majority of discoid lupus erythematosus (DLE) patients [n=29 (60% of total DLE)] had a predominant T cell signature driven by genes important for antigen presentation and T cell proliferation and differentiation (i.e., SKAP1, ITK). Our data suggests that unique cell populations may help differentiate CLE subgroups, which can potentially affect their disease course and treatment selection. Further studies examining individual gene and protein levels are necessary to confirm our hypotheses.

Keywords: Cutaneous lupus erythematosus (CLE); modular analysis; RNA sequencing

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AB007. Worse skin disease severity may distinguish patients who progress from cutaneous lupus erythematous to systemic lupus erythematous

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Abstract: Up to 20% of patients with cutaneous lupus erythematosus (CLE) will develop systemic lupus erythematosus (SLE). Prior studies identified baseline clinical characteristics associated with progression to SLE, including generalized discoid lupus (DLE) and arthritis. Factors that change over time including skin disease severity have not been well studied. The objective of this retrospective cohort study was to identify fixed and variable risk factors that predispose patients with CLE to develop SLE. Sixty-five patients with CLE followed for a minimum of six months from December 2008 and August 2019 were included. 11 progressed from CLE to SLE (16.9%), while 54 (83.1%) remained CLE only. Demographic and clinical data from both groups were compared using Fisher's exact test or Wilcoxon Rank Sum test. At baseline, CLE to SLE patients had greater American College of Rheumatology SLE diagnostic criteria than CLE only [median 3 (IQR: 3–3) *vs.* 2 (1–3); P=0.003] and lower (worse) physician global assessment (PGA) overall skin scores [7 (5–7) *vs.* 8 (7–9); P=0.02]. Generalized DLE (n=6) was more associated with progression to SLE *vs.* localized DLE (n=22) (P=0.048). There were no significant differences in Cutaneous Lupus Erythematosus Activity and Severity Index (CLASI) scores and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores. Longitudinally, CLE to SLE patients had greater CLASI scores at year 1 [10 (4–17) *vs.* 2 (0–4.5); P=0.02] and year 3 [19 (12–16) *vs.* 0 (0–2); P=0.03]. PGA overall skin scores were worse in CLE to SLE patients at year 1 [5 (3–6) *vs.* 8 (7-9); P=0.003] and year 3 [5 (5–5) *vs.* 9 (8–10); P=0.04]. CLE to SLE patients had greater SLEDAI scores at year 3 [4 (4–4) *vs.* 0 (0–2); P=0.03]. Limitations include small sample size and missing follow-up visits. Our data suggests persistently worse skin disease activity may separate patients who progress from CLE to SLE from those who remain CLE. Further longitudinal data is being collected to verify these results. If validated, CLE patients with persistently high skin disease activity need close monitoring for SLE progression.

Keywords: Cutaneous lupus erythematosus (CLE); cutaneous lupus disease area and severity index; longitudinal; systemic lupus erythematosus (SLE); disease activity; disease damage

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AB008. Utility of repeat latent tuberculosis testing in patients with immune-mediated diseases taking biologics

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Background: Guidelines for repeat latent tuberculosis infection (LTBI) testing while on biologics are not clearly defined. The CDC and U.S. Preventive Services Task Force recommend routine serial LTBI screening in high-risk patients, such as those on immunosuppressive medications. Furthermore, recommendations for annual LTBI screening in patients on biologics have been incorporated into the Medicare Merit-Based Incentive Payment Systems and will impact physician reimbursement. However, little evidence supports that this practice is clinically valuable and/or cost-effective in patients on biologics. To evaluate the utility of serial LTBI screening in patients taking biologics and to identify risk factors in patients who convert from negative to positive QuantiFERON TB test (QFT) results while on biologics.

Methods: We retrospectively reviewed QFT results in patients treated with biologics for chronic immune-mediated inflammatory/autoimmune conditions (IMIDs) at a single, tertiary care center from 2007–2019. For each patient included in our study, detailed clinical information from their medical records was collected.

Results: We identified 5,212 patients who had IMIDs and >1 repeat QFT result after starting biologic therapy. The most common IMID diagnoses were inflammatory bowel disease (30%), rheumatoid arthritis (28%) and psoriatic disease (24%). The majority of patients had all negative QFTs (87.5%), whereas 172 patients (3.3%) had >1 positive QFT. Amongst patients with positive QFTs, 61/172 patients (35%) converted from a negative to a positive QFT after biologic therapy initiation. Of these 61 patients, only 28 patients were eventually treated for LTBI. Fourteen of the 28 patients treated for LTBI had documented risk factors for TB exposure, such as travel to endemic TB areas and/or exposure to individuals with TB. Only one case of active TB was diagnosed.

Conclusions: This represents the largest single-institution study evaluating rates of QFT test positivity conversion in patients taking biologics. Repeat LTBI testing in patients taking biologics revealed a low rate of conversion (1.17%). Our results suggest clinical utility and cost-effectiveness of repeat LTBI screening in patients on biologics may be more valuable if not performed routinely, but driven by a focused review of TB exposure risk factors in each patient.

Keywords: Biologics; immune mediated diseases; latent tuberculosis; interferon gamma release assay; QuantiFERON TB test (QFT)

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AB009. Successful treatment of severe systemic lupus erythematosus and psoriasis with IL-17A inhibition

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Abstract: The coexistence of psoriasis and systemic lupus erythematosus (SLE) is uncommon, with prevalence estimated at 0.5–5%. In this case, a 20-year-old woman with a history of severe SLE complicated by lupus nephritis and mesenteric vasculitis presented with a new rash on the face, scalp, and forearms. Skin biopsy revealed features of psoriasis within the epidermis, in addition to the palisaded neutrophilic granulomatous dermatitis within the dermis explained by her underlying SLE. Treatment options were considered in view of her possible cytokine profile and predominant inflammatory pathway. The Th17 pathway has been implicated as a common immune pathway in both diseases, leading to cytokine production including the proinflammatory cytokine interleukin-17A (IL-17A). Studies have shown increased level of IL-17A in the serum and involved tissues of patients with SLE as well as the biopsied plaques of psoriasis. Randomized control trials have shown efficacy of IL-17A inhibition in decreasing the severity and extent of psoriasis, and case reports have noted improvement in SLE activity scores in patients who had been refractory to other management strategies. This patient was treated with IL-17A inhibition, which dramatically improved her rash and allowed complete tapering of her baseline immunosuppressive regimen while maintaining SLE quiescence. This case demonstrates that there may be a subset of SLE patients who respond to IL-17A inhibition, particularly in the setting of overlap with diseases in which IL-17A inhibition has previously shown efficacy. Teaching point: IL-17A inhibition may be effective treatment for SLE overlapping with inflammatory diseases in which IL17A is known to play a role including psoriasis, seronegative spondyloarthropathies, and rheumatoid arthritis.

Keywords: Interleukin-17A inhibition (IL-17A inhibition); systemic lupus erythematosus (SLE); psoriasis

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AB010. Keloidal scleroderma with isolated intertriginous involvement

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Abstract: A 33-year-old African-American female with scleroderma, Raynaud phenomenon, and possible systemic lupus erythematosus (SLE) presented to dermatology clinic for evaluation of a 1-year history of slowly growing plaques in her bilateral axillae and inguinal region. The patient was initially diagnosed with scleroderma approximately five years prior to presentation following the onset of sclerodactyly, arthralgias, myalgias, and severe obstructive lung disease. Two years prior to presentation, she was started on monthly intravenous immunoglobulin infusions. Her other medications included hydroxychloroquine, mycophenolic acid, cilostazol, and amlodipine. One year ago, she began developing leathery, firm, dark plaques underneath both armpits. The plaques slowly enlarged and new plaques began forming in her inguinal region. They were nonpruritic but mildly tender. On exam, the patient had well-demarcated, linear, hyperpigmented, indurated plaques that coalesced in her bilateral axillae, bilateral inguinal folds, and bilateral peri-inguinal region with no evident secondary scale or crust. She also had sclerodactyly of the digits of her bilateral hands and blue-white discoloration of her 4th digit of the right hand. A 4 mm punch biopsy was performed from her left axilla and was consistent with keloidal morphea/scleroderma. Keloidal scleroderma, also known as nodular scleroderma, is a rare manifestation of systemic sclerosis that is usually characterized by innumerable nodules or keloidal plaques on the trunk. We present a case of isolated intertriginous keloidal scleroderma, an exceedingly uncommon distribution for this condition. A recent literature review of nodular scleroderma by Kassira et al. revealed only one reported case with lesions in intertriginous areas. Given the rarity of the diagnosis, our knowledge of efficacious treatment options remains limited. Possible options for treatment include methotrexate, ultraviolet A light therapy, and narrow-band ultraviolet B light therapy. Teaching point: the patient's biopsy-proven isolated intertriginous keloidal scleroderma represents an uncommon clinical presentation for an already rare variant of systemic sclerosis.

Keywords: Keloidal scleroderma; keloidal morphea; nodular scleroderma

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AB0011. A Gottron's papule mimicker: an unusual presentation of porokeratosis plantaris palmaris et disseminata

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Abstract: A 52-year-old woman with a past medical history of breast cancer presented for evaluation of a scaly eruption on bilateral dorsal and palmar hands for the preceding seven months. The patient also noted scaling of her right foot, hallux, and Achilles tendon. Her physical exam was notable for nail cuticle dystrophy with normal nail fold capillaries, scattered hyperkeratotic erythematous coalescing papules and plaques overlying her metacarpophalangeal and distal interphalangeal joints. The right palm was notable for tender, firm, subcutaneous nodules. The patient reported neither joint pain, muscle pain, nor weakness. The clinical appearance of Gottron's papules and presence of palmar papules, raises suspicion for dermatomyositis; therefore, a biopsy of a papule present on her right Achilles and a punch biopsy of a papule on her right fourth proximal interphalangeal joint were performed. The histopathology of both biopsies demonstrated interface alteration with columns of parakeratosis. There were also areas of epidermal invagination and dells with plugs of broad parakeratosis resembling cornoid lamellae and underlying interface alteration, suggesting a rare diagnosis of porokeratosis plantaris palmaris et disseminata (PPPD). In follow-up, the patient returned with new distinctly annular palmar lesions with peripheral scale, resembling porokeratosis. Of note, poikilodermatous skin in dermatomyositis may histologically display an interface dermatitis, seen in our patient, with epidermal atrophy and necrotic, dyskeratotic keratinocytes with basal layer vacuolization, increased dermal mucin deposition, and vascular damage. The histology of Gottron's papules is similar, and often shows a lymphocytic infiltrate, epidermal hyperkeratosis, papillomatosis, acanthosis and less epidermal atrophy. However, with the patient's developing clinical picture of palmar annular lesions and her pathology results showing cornoid lamellae (a hallmark of porokeratosis), dermatomyositis was considered less likely and PPPD more likely. Age appropriate malignancy screening was performed and normal. The patient is being followed closely and doing well. Teaching Point: biopsy can help confirm or refute a diagnosis of Gottron's papules which is often considered a pathognomonic sign of dermatomyositis. In this patient the hand lesions were a mimicker, and dermatomyositis was not diagnosed.

Keywords: Porokeratosis plantaris palmaris et disseminate (PPPD); Gottron's papules; XXX

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AB012. Clinical and demographic features of morphea patients with mucocutaneous involvement: a cross sectional study from the morphea of adults and children (MAC cohort)

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Abstract: While many clinical findings of morphea have been described by our group and others, mucocutaneous findings, including genital or oral lesions, have not been well characterized. To date, we don't know the frequency, demographic and clinical features associated with mucocutaneus lesions. To address this knowledge gap, we performed a cross-sectional analysis of patients enrolled in the Morphea in Adults and Children Registry from 2007 to 2018. Of the 737 patients analyzed, 48% (n=353) had linear morphea, 31% (n=232) had generalized morphea, 12% (n=87) had plaque morphea and 6% (n=45) had mixed. Oral lesions were present in 23 patients (3%), out of which 20 (87%) had linear morphea, nine had En Coup de Sabre (39%) and 12 had Parry Romberg syndrome (PRS) (52%). Genital lesions were present in 28 patients, the majority of which (24/28, 86%) had generalized morphea. Patients with oral involvement had a younger age of onset when compared to patients with genital involvement (12 years old and 58 years old, respectively; P<0.001). Seventy-nine percent (n=22) of morphea patients with genital involvement had lichen sclerosus et atrophicus (LsA) overlap, compared to 17% (n=4) with oral involvement (P<0.001). Eighty-three percent(n=19) patients with oral involvement were classified as having morphea profunda, or deep involvement, compared to 14% (n=4) of patients with genital involvement (P<0.001). Median mLoSSI ad PGA-A scores for patients with oral involvement (0, IQR 0–4 and 0, IQR 0–24, respectively)) was lower than patients with genital involvement (10, IQR 6–27 and 23, IQR 15–40, respectively) (P<0.001 and P=0.002, respectively). PGA-D scores were higher in patients with oral involvement (50, IQR 30–60) than in patients with genital involvement (20, IQR 10–25) (P<0.001). In conclusion, have demonstrated that mucocutaneous involvement of morphea lesions occurs most frequently in patients with linear and generalized morphea. Providers may not be aware of the prevalence of these findings and thus they may go undiagnosed for many months or years, leading to the development of potentially permanent and devastating sequalae.

Keywords: Morphea; mucocutaneous lesions; localized scleroderma

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AB013. CXCL4-DNA immune complexes drive inflammation in systemic sclerosis by amplifying TLR9-mediated interferon-α production

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Abstract: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by inflammation-driven tissue fibrosis and vasculopathy. CXCL4 is a chemokine overexpressed in SSc and represents an early serum biomarker of severe disease. CXCL4 likely contributes to inflammation via chemokine signaling pathways, but the exact role of CXCL4 in SSc pathogenesis is unclear. Here, we combine X-ray scattering, confocal microscopy, immune cell experiments, and analysis of SSc skin biopsies to elucidate an unanticipated mechanism for CXCL4-mediated immune amplification in SSc. We find that CXCL4 organizes "self" and microbial DNA into liquid crystalline immune complexes that drastically amplify Toll-like receptor 9 (TLR9)-mediated plasmacytoid dendritic cell (pDC) hyperactivation and interferon-α production. Surprisingly, this immunomodulatory activity is independent of CXCR3, the CXCL4 receptor. Importantly, we find that CXCL4-DNA complexes are present in vivo and correlate with type I interferon (IFN-I) levels in SSc blood, and that CXCL4-positive skin pDCs coexpress IFN-I-related genes. Taken together, we establish a direct link between CXCL4 overexpression and the IFN-I-gene signature in SSc and identify a potential therapeutic opportunity to disrupt inflammation in SSc by inhibiting the self-assembly of CXCL4-DNA complexes. Our findings are consistent with an emerging general paradigm in which nucleic acid-scaffolding proteins like antimicrobial peptides, bacterial amyloids, and chemokines can drive autoimmunity by modulating innate immune receptors without being direct agonists.

Keywords: Systemic sclerosis (SSc); scleroderma; CXCL4; Toll-like receptor 9 (TLR9); self-assembly; immune complexes; nanocrystals

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AB014. Developing classification criteria for skin-predominant dermatomyositis: assessing the methodology of the prospective validation study

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Abstract: The Dermatomyositis Delphi Criteria Project created 25 provisional clinical, laboratory and contextual classification criteria after an extensive literature search, three rounds of consensus exercises and nominal group discussions. These criteria will be subjected to a case-control validation study to create a combination of items that will define a more inclusive cohort of DM patients with skin-predominant disease for clinical research. Several measurement properties that need to be assessed prior to the conduct of a multicenter prospective validation study include the final purpose of the criteria set, population and disease characteristics of cases and controls for study entry, sources of samples, definition of criteria items, methods of item ranking and reduction, and consideration of criteria set validity against a comparator backdrop "gold standard" criteria. An expert committee Delphi and several online discussions among participants from the fields of dermatology, and adult and pediatric rheumatology have been conducted in order to address such issues. Constant evaluation of the methodologic process is vital to produce classification criteria which are valid and reliable to identify patients with DM and delineate these patients from those with mimicker diseases.

Keywords: Dermatomyositis; amyopathic; skin-predominant; classification; criteria

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AB015. Skin disease activity and autoantibody phenotype are major determinants of blood interferon signatures in dermatomyositis

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Abstract: Interferon signaling is upregulated in dermatomyositis and thought to play a role in pathogenesis. An interferon gene signature in peripheral blood of dermatomyositis patients correlates with skin disease. However, studies have not analyzed how interferon signaling differs across dermatomyositis subtypes or with multiple organ system involvement. We hypothesized that strength and clinical utility of the dermatomyositis blood interferon signature depends on autoantibody subtype and clinical factors. Utilizing RNA sequencing of 377 blood samples derived from a cohort of 205 clinically phenotyped dermatomyositis patients, we found that blood interferon score is significantly elevated in the anti-MDA5 subtype compared to other subtypes (average 16.12, P<0.001). Change in cutaneous disease area and severity index-activity correlates most strongly with change in interferon score in anti-MDA5 (R=0.85, P<0.001) patients, followed by anti-Tif-1g (R=0.59, P<0.001) and anti-SAE1 (R=0.64, P=0.048). The correlation is weak in anti-Mi2 and anti-NXP2 subtypes. These patterns persist after adjustment for lung disease, muscle disease, cancer, and medications. The correlation is stronger when baseline interferon score is greater than 1.5 (R=0.59, P<0.001). The correlation is weaker in patients with active muscle disease and stronger in patients with active lung disease but is unaffected by cancer status. Using a large prospective dataset of DM patients, we demonstrate that interferon-driven gene expression as an activity measure in dermatomyositis is related to specific autoantibody subtypes and is impacted by clinical factors. Careful attention to antibody status and clinical factors could help inform interpretation of interferon biomarker data in future clinical trials.

Keywords: Dermatomyositis; type 1 interferon; autoantibody subtypes; anti-MDA5, biomarker

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AB016. A double-blind, placebo-controlled, phase 2 trial of a novel toll-like receptor 7/8/9 antagonist (IMO-8400) in dermatomyositis

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Background: Dermatomyositis (DM) is an inflammatory disease of skin and muscle. Increased interferon (IFN) signaling is a prominent feature of DM, but the mechanisms leading to IFN production in DM are not understood. As toll-like receptor (TLR) 7/8/9 activation can lead to type I IFN production, TLR7/8/9 antagonism may provide therapeutic benefit in DM.

Methods: A double-blind, randomized, placebo-controlled, 24-week trial of IMO-8400 [a novel oligonucleotide TLR7/8/9 antagonist (Idera Pharmaceuticals, Inc.)] was conducted with 30 participants meeting definite or probable criteria of Bohan and Peter for DM. Participants were randomized to treatment with IMO-8400 0.6 mg/kg, IMO-8400 1.8 mg/kg, or placebo. The primary endpoint was the change in the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score. Exploratory analysis included type I IFN signaling and the 5-D Itch Scale. Blood and skin samples were obtained at baseline and end of treatment to measure changes in type I IFN signaling.

Results: CDASI activity scores decreased in all arms by the end of the trial, per repeated measures mixed model analysis: –9.3 in 0.6 mg/kg, –8.8 in 1.8 mg/kg, and –7.3 in placebo. We observed no change in skin and blood type I IFN signature scores or CDASI activity scores across treatment arms. We found an association between CDASI and skin IFN signature scores (β =12.9, P=0.0002), an association between 5-D Itch Scale and skin IFN signature scores (Rho =0.65, P<0.0001), a lack of association between 5-D Itch Scale and blood IFN signature scores (Rho =0.22, P=0.24), and a positive trend that did not reach significance between CDASI and 5-D Itch Scale scores. 5 patients experienced treatment-emergent adverse effects prompting discontinuation: 3 in low-dose (abdominal discomfort/flu, anxiety, urticaria), 1 in high-dose (thrombocytopenia), and 1 in placebo (muscle weakness).

Conclusions: IMO-8400 did not significantly reduce DM disease activity or type I IFN expression. Our study demonstrates that cutaneous DM disease activity may be better studied through skin biopsies, rather than peripheral blood draws, and that type I IFN signaling could be a potential target in improving pruritus in DM patients.

Keywords: Clinical research; dermatomyositis (DM); toll-like receptors (TLRs)

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AB017. Increased dendritic cells and IFN-beta and MxA protein expression in spongiotic dermatitis differentiates dermatomyositis from eczema

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Background: Dermatomyositis (DM) is conventionally characterized by interface dermatitis (ID) on skin histopathology. A subset of patients with clinically diagnosed DM have skin biopsies showing spongiotic dermatitis (SD), a histopathology more commonly seen in eczema. Diagnosis of DM is challenging, with significant delays following initial presentation. (I) To identify the percentage of clinically diagnosed DM patients with skin biopsies showing SD, (II) to identify cytokine and cell markers that can determine if a skin biopsy showing SD is consistent with DM in a patient with clinical DM.

Methods: Biopsies from 10 DM patients with SD histopathology were compared to biopsies from 10 healthy controls, 10 patients with eczema, and 12 patients with DM with ID histopathology. Skin biopsies were stained by H&E and by immunohistochemistry for MxA, IFN-beta, CD11c (mDC), and BDCA2 (pDC). Cytokines were quantified by area and intensity. Cells were quantified per HPF. Fisher's exact test was used to compare baseline patient characteristics. One-way ANOVA with Bonferroni's multiple comparison test was used to compare protein expression between groups.

Results: Eleven of 164 (6.7%) patients with a clinical diagnosis of DM at our tertiary care center were identified as having SD. MxA, IFN-beta, CD11c (mDC), and BDCA2 (pDC) protein expression is significantly higher in DM-SD compared to eczema and healthy controls. Expression of MxA, IFN-beta and BDCA2 were not significantly different between DM-SD and DM-ID.

Conclusions: Increased MxA, IFN-beta, CD11c, and BDCA2 protein expression can help distinguish between DM-SD and eczema.

Keywords: MxA; IFN-β; dendritic cells; spongiotic dermatitis (SD); interface dermatitis (ID); dermatomyositis (DM)

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AB018. Myeloid dendritic cells (mDCs) are major producers of interferon-beta in dermatomyositis and increased numbers of mDCs are found in hydroxychloroquine nonresponders

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Background: Dermatomyositis (DM) is an autoimmune disease affecting skin, skeletal muscle, and lungs. Pathogenesis is considered largely driven by interferon-beta (IFN-beta) and involves CD4+ cells and dendritic cells (DCs). (I) Quantify inflammatory cells and IFN-beta in skin; correlate with Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) scores. (II) Identify DC type contributing to refractoriness to hydroxychloroquine (HCQ). (III) Compare IFN-beta production by mDCs vs. pDCs in DM.

Methods: (I) DM skin biopsies evaluated for cells and cytokines using IHC from 12 patients with moderate-severe skin disease at baseline and after 12 weeks of therapy. (II) IHC performed on skin biopsies to compare myeloid DC (mDC) and pDC expression in HCQ-responders *vs.* -nonresponders. (III) Flow cytometry performed on PBMCs from 5 healthy controls and 5 DM patients.

Results: (I) CD4+ cells, macrophages, mDCs, and TRM cells were the most populous in DM skin, followed by CD8+ cells, mast cells, and pDCs. Change in CD4+ and CD8+ cells/HPF significantly correlated with change in CDASI scores ($r=0.82$, $P<0.05$; $r=0.81$, $P<0.05$). Changes in IFN-beta protein expression correlated with change in CDASI scores ($r=0.63$, $P<0.05$). (II) Significantly increased mDCs/HPF found in skin of HCQ nonresponders ($P<0.05$). (III) mDCs and pDCs both produced IFN-beta in DM patients; pDCs were dominant producers of IFN-beta in healthy controls.

Conclusions: mDCs are major producers of IFN-beta in DM patients and may play an important role in DM pathogenesis.

Keywords: Dermatomyositis (DM); interferon-beta (IFN-beta); dendritic cells (DCs)

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AB019. Response to tofacitinib in a case of refractory TIF-1 positive amyopathic dermatomyositis with arthritis

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Abstract: A 47-year-old woman with a previous diagnosis of undifferentiated connective tissue disease presented to our clinic for evaluation of rash and joint pains. She had a significant history of severe fatigue, musculoskeletal and joint pains. She described her joint pain as constant, stating it severely impacted her activities of daily living, but denied muscle weakness. She was previously diagnosed with systemic lupus erythematosus (SLE), and treated unsuccessfully with low dose systemic steroids and antimalarial therapy. Upon examination, she was found to have heliotrope eruption, Gottron's sign and Gottron's papules, fulfilling EULAR/ACR classification criteria for dermatomyositis. On the myositis panel she tested positive for antibodies to TIF1 and NXP2, confirming the diagnosis. She was also found to have RF positive but CCP negative arthropathy, without evidence of radiographic erosions. She was responsive to prednisone but either skin or joint symptoms remained refractory to several steroid-sparing agents including hydroxychloroquine, mycophenolate mofetil, methotrexate, intravenous immunoglobulin and eventually infliximab. With subsequent visits, she reported worsening of joint pain, despite improvement of cutaneous burden of disease on mycophenolate mofetil. In the setting of debilitating joint pain, she was started on tofacitinib 11mg PO daily in addition to hydroxychloroquine 200mg PO BID with discontinuation of mycophenolate mofetil. After two months of treatment she reported 90% improvement in symptoms, with resolution of joint pains and no recurrences of her rash, and was able to return to baseline functional status. Teaching points: (I) overlap syndrome with dermatomyositis has been previously reported in a case report showing 19% overlap with other connective tissue diseases, including rheumatoid arthritis. (II) The overlap of the two conditions can be extremely debilitating to patients, with few options for complete symptom resolution. (III) Tofacitinib is an inhibitor of Janus kinase 1 (JAK1) and Janus kinase 3 (JAK3) and works by inhibiting JAK signaling for many pro-inflammatory cytokines. Maximizing this mechanism can be a novel approach to treating recalcitrant immune-mediated inflammatory diseases.

Keywords: Amyopathic dermatomyositis; refractory; TIF-1; JAK inhibitors

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AB020. A case report on cutaneous necrotizing vasculitis treated with colchicine in a Filipino adult male

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Abstract: Cutaneous necrotizing vasculitis is a condition characterized by vessel wall necrosis secondary to neutrophil infiltration classically presenting as palpable purpura on the lower extremities. Several etiologic agents have been identified but, literature showed that majority of cases have an unidentifiable cause. First-line pharmacologic management consists of systemic glucocorticoids with colchicine being used merely as second-line therapy. We report a case of a 59-year-old male with cutaneous necrotizing vasculitis treated with colchicine as monotherapy. This is the case of a 59-year-old male with a ten-day history of multiple discrete to confluent well-defined vesicles and bullae, some eroded with hemorrhagic exudates on the bilateral lower extremities, with accompanying round palpable purpura seen on the abdomen extending to the bilateral upper extremities. Skin biopsy was consistent with leukocystoclastic vasculitis. The patient completed 3-month treatment with colchicine 500 mcg twice daily with adjunct therapy of prednisone 20 mg once a day for 2 weeks tapered down by 5 mg. By 4th week of treatment, 50% improvement over the lesions were observed. By 3rd month of treatment, complete clearance was noted. This case highlights the effectiveness of colchicine as monotherapy for cases of cutaneous necrotizing vasculitis due to its action in suppressing granulocytic inflammatory reaction. Moreover, relative safety of colchicine is more favorable compared to the possible long-term side effects of systemic glucocorticoids. Especially for patients at risk for developing adverse effects to glucocorticoids, colchicine is a feasible yet often overlooked alternative treatment option compared to the conventional treatment with systemic glucocorticoids.

Keywords: Cutaneous necrotizing vasculitis; leukocytoclastic vasculitis; small vessel cutaneous vasculitis; colchicine

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AB021. Comparing the performance of two interferon-gamma release assays in autoimmune skin disease patients: a prospective study

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Abstract: Autoimmune skin disease patients are standardly screened for tuberculosis (TB) via interferon-gamma release assays (IGRAs) prior to starting immunosuppressive drugs or enrolling in clinical trials. Two commercial IGRAs, T-SPOT.TB (T-SPOT) and QuantiFERON-Tb Gold (QFT-G), are reported as either determinate (positive or negative) or indeterminate. Both tests utilize similar immunoenzymatic reactions for interferon-gamma detection, but differ in quantification. Though QFT-G is more widely used, studies have demonstrated that T-SPOT has lower rates of indeterminate results in immunosuppressed patients. The newest generation of QFT-G, QuantiFERON-TB Gold Plus (QFT-Plus), has not been compared to T-SPOT in this patient population. We aim to investigate the performance of T-SPOT and QFT-Plus in autoimmune skin disease patients. This prospective study included 48 patients. Venous blood samples were collected and underwent TB screening with QFT-Plus and T-SPOT IGRAs. The proportions of indeterminate and determinate results among the two tests were compared. There were 2 indeterminate results with QFT-Plus and no indeterminate results with T-SPOT. There was one positive result for QFT-Plus and T-SPOT. Using a one-tailed Fischer test, there was no statistical significance when comparing QFT-Plus and T-SPOT in autoimmune skin disease patients (P=0.25). Although not statistically significant, it is clinically important as indeterminate results preclude these patients from receiving necessary treatment. Compared to previous studies on QFT-G, QFT-Plus showed improvement in reducing the amount of indeterminate results. We suggest using T-SPOT in TB screening for autoimmune skin disease patients who have an indeterminate QFT-G or QFT-Plus, as this test did not display any indeterminate results.

Keywords: Autoimmune skin disease; interferon-gamma release assay; T-SPOT.TB (T-SPOT); QuantiFERON-Tb Gold (QFT-G)

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AB022. Biologics and vaccination: relationship of influenza, pneumonia and zoster

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Abstract: The use of biologics for inflammatory skin disease is increasing. Although manufacturers recommend pneumococcal, influenza and varicella zoster vaccines in patients treated with tumor necrosis factor inhibitors to mitigate the risk of infection, data regarding adherence in this group of patients is limited. The European League Against Rheumatism and American College of Rheumatology also issued the recommendations to advocating for influenza, pneumococcal pneumonia and Zoster for this high-risk patient group. We queried the MarketScan data base (which includes about 47 million people) to determine rates of vaccination and infection. In 2014, we identified 41,607 patients, aged 18–60 on adalimumab, etanercept or infliximab (TNFi) for 6 months or more. Of these patients, only 157 received a pneumococcal vaccine. We will present similar data describing utilization of influenza and zoster vaccination in psoriatic utilizing TNFi, from 2014–2016. Rates of in relevant infection (influenza, pneumonia and varicella) will be compared between vaccinated and unvaccinated biologic users. We hypothesize that immunosuppression due to biologic therapy (specifically TNF-inhibitors) incurs a higher risk of infection. Our preliminary data likely highlight an important practice gap in the use of TNFi within dermatology. Teaching points: biologics are associated with a higher risk of influenza, pneumococcal pneumonia, and varicella zoster. Although infection can lead to significant morbidity and mortality, vaccination prior to the initiation of biologic therapy can mitigate risk. Vaccination is probably underutilized in these patients.

Keywords: Vaccination; tumor necrosis factor inhibitors; influenza; varicella zoster; pneumococcal pneumonia

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Cite this abstract as: Patel D, Maczuga S, Helm M, Foulke G. Biologics and vaccination: relationship of influenza, pneumonia and zoster. Ann Transl Med 2020;8:AB022.

AB023. An atypical clinical presentation of alopecia in two patients with systemic lupus erythematosus

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Abstract: Alopecia in varying patterns is a common feature of lupus erythematosus (LE). Several forms of alopecia that are not specific to LE can occur in the setting of lupus, such as alopecia areata, telogen effluvium, and anagen effluvium. LE-specific alopecias are defined as those with histology consistent with LE, and include forms of acute, subacute, and chronic cutaneous lupus erythematosus (CCLE). Common patterns of LE-specific alopecia include the non-scarring diffuse hair thinning and fragility of acute LE and the scarring, erythematous scaly plaques with follicular keratotic plugs, peripheral hyperpigmentation, and central hypopigmentation of discoid lupus erythematosus (DLE). Lupus erythematosus tumidus (LET) may also present on the scalp as well-defined, non-scarring alopecia without overlying scale, atrophy, and dyspigmentation. We report two male patients with large circular non-scarring alopecic plaques on the scalp without overlying scale or erythema, but with central hyperpigmentation and scarring – findings reminiscent of but also distinct from both DLE and LET. Punch biopsy from the hyperpigmented area of alopecia revealed peri-follicular lymphocytic infiltrate, follicular dropout, and increased dermal mucin consistent with LE; further workup and serologic testing revealed systemic lupus in both patients. These two cases demonstrate a unique clinical presentation of central scarring alopecia within a larger non-scarring alopecic plaque in the setting of SLE that deviates from typical lupus-related alopecia. Teaching point: these two cases underscore the morphologic heterogeneity of CCLE and need for thorough evaluation of systemic disease in patients presenting with both scarring and non-scarring alopecia.

Keywords: Alopecia; chronic cutaneous lupus erythematosus (CCLE); discoid lupus erythematosus (DLE); lupus erythematosus tumidus (LET); systemic lupus erythematosus (SLE)

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AB024. A case of bullous systemic lupus erythematosus confined to the oral mucosa

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Abstract: Bullous systemic lupus erythematosus (BSLE) is a rare antibody-mediated blistering disease that presents in association with systemic lupus erythematosus (SLE). Features of BSLE can present as a diagnostic challenge as they often mimic other bullous skin diseases. We present a case of a 45-year-old female with history of celiac disease, Raynaud's syndrome, chilblains, and Sicca symptoms who presented with 10 months of recurrent vesicles and erosions of the gingiva. Review of symptoms was positive for arthralgias and recurrent photosensitive rashes. Physical examination was notable for multiple 4 mm vesicles with mild surrounding erythema confined to anterior upper gingiva without further mucosal or cutaneous involvement. Two biopsies obtained prior to presentation revealed a mixed inflammatory infiltrate with focal eosinophils, negative for viral cytopathic changes. A biopsy of the maxillary frenum for direct immunofluorescence (DIF) demonstrated a weak, fine linear deposition of IgG and IgA along the basement membrane zone initially suspicious for mucous membrane pemphigoid. Serum ELISA for antibodies against BP180, BP230, and collagen VII were negative. Further lab workup was notable for an ANA of 1:160, anti-Ro60 774 (normal 0–19), anti-Sm 20.7 (normal 0–19), and C4 15.1 (normal 16.3–47.8). The patient was found to meet SLICC criteria (joint disease, chronic cutaneous lupus (chilblains), positive ANA, positive Anti-Sm, and low C4) for SLE diagnosis. The patient was started on dapsone 100 mg by mouth daily with improvement in symptoms. BSLE can affect the oral mucosa and has been described in the absence of anti-collagen VII positivity, but has not been described in the absence of cutaneous bullae. Although atypical, the DIF staining pattern in the context of SLE raises support for a diagnosis of oral BSLE. Teaching point: BSLE can manifest as an oral vesicular eruption and can be differentiated from other oral bullous diseases based on histologic and immunopathologic features

Keywords: Bullous systemic lupus erythematosus (BSLE); lupus; bullous disease

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AB025. Acute arthritis with dermatitis: a case of multicentric reticulohistiocytosis

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Abstract: A 56-year-old woman presented with a 5-day history of arthralgias and an erythematous papular eruption affecting the face, arms, chest, and upper back, for which she was started on high potency topical corticosteroids. She was noted to have associated synovitis of the hands and wrists bilaterally and was started on celecoxib. One week later, the patient returned with worsening pain and swelling in her hands in addition to new confluent, somewhat firm, erythematous papulonodules on the face, trunk, forearms, and dorsal hands. Two biopsies were performed with evidence of dermal histiocytic proliferation consistent with multicentric reticulohistiocytosis (MRH). Mycobacterial and malignancy screening were completed, and the patient was started on hydroxychloroquine, methotrexate, and systemic corticosteroids. MRH is a rare histiocytic disorder predominantly affecting Caucasian women in the fourth decade of life. Associations include arthritis, which can be mutilating in nature, and malignancy. Given the frequently destructive nature of the associated arthritis, timely diagnosis and treatment is crucial and may prevent long-term disability. Teaching points: (I) highlight the clinical manifestations of MRH, including the differential diagnosis of arthritis-dermatitis syndromes. (II) Underscore that MRH can mimic dermatomyositis. (III) Describe the differential diagnosis of arthritis mutilans (e.g., RA, PsA, gout, MRH). (IV) Examine the evidence for therapeutic options in MRH.

Keywords: Multicentric reticulohistiocytosis (MRH); coral bead sign; arthritis mutilans

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