

## **A MULTICENTER RETROSPECTIVE CASE SERIES OF 68 MORPHEA PATIENTS TREATED WITH MYCOPHENOLATE**

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**Background:** First line systemic therapy for morphea patients typically includes methotrexate (MTX) +/- systemic corticosteroids (SCS). In patients where this regimen is ineffective, not tolerated, or contraindicated a trial of mycophenolate mofetil (MMF) is recommended; however, evidence to support this remains weak.

**Objectives:** This study aimed to assess the efficacy and safety of MMF in patients with morphea.

**Methods:** A multicenter retrospective chart review including 68 morphea patients from 7 institutions was completed. Disease activity, severity, and response were collected at baseline, 3-6 months, and 6-9 months of treatment with MMF.

**Results:** 82.4% of patients were female and 17.6% of patients were male. Subtypes included circumscribed (N=5), generalized (N=35), linear face/scalp (N=5), linear trunk/extremity (N=9), mixed (N=6), and pansclerotic (N=8). 60.3% (N=41) patients had severe disease. Prior to MMF patients had been treated with phototherapy (20.6%), hydroxychloroquine (29.3%), MTX (74.1%) and/or SCS (62.1%). MMF was initiated after prior treatment was deemed ineffective (64.7%) or poorly tolerated (29.4%). 11 patients were treated with MMF as a first line therapy. After 3-6 months, 60/68 patients were stable (N=22) or improved (N=38). After 6-9 months, 41/62 patients were stable (N=13) or improved (N=28). 23/68 patients (33.8%) achieved disease remission. Treatments received in conjunction with MMF were frequent (hydroxychloroquine 10/68, MTX 17/68, and/or SCS 33/68). Overall, MMF was well tolerated. Gastrointestinal side effects were most common (32.4%). Less frequently, infections (N=2) and leukopenia (N=1) occurred.

**Conclusions:** This study suggests that MMF may be an effective and safe therapy for patients with recalcitrant, severe morphea.

Category: Sclerotic skin disease



## **GENERALIZED DISCOID LUPUS IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH MYELOPATHY**

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The co-existence of generalized discoid lupus erythematosus and myelopathy has not been reported. Among the subsets of cutaneous lupus erythematosus, discoid lupus is the least likely to progress to systemic lupus erythematosus and therefore implies a more benign prognosis. We report a 19-year-old woman who presented with non-pruritic red circumscribed plaques on the face, ears, and arms, with some showing scarring, telangiectasia, and pigmentation. Three months later, she developed paraplegia, an inability to urinate and defecate, and a sensory loss up to the level of T10. Oral ulcers, findings on skin biopsy, a positive antinuclear antibody test, and transverse myelitis on MRI all confirm the presence of SLE. Discoid lupus has 2 subtypes, localized and generalized, which affect the areas above and below the neck. Generalized discoid lupus poses a higher risk for developing SLE (15-28%) compared to the localized type (5-10%). Myelopathy is a rare presentation in SLE, occurring in only 1-2% of cases. The presence of generalized discoid lupus is associated with poor clinical outcome.

Category: Lichenoid inflammatory skin disease (lupus)

## RESPONSE OF CUTANEOUS ULCERATIONS IN ANTI-MDA5 DERMATOMYOSITIS TO VASODILATORS AND BOTULINUM TOXIN

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A 48-year-old male with anti-MDA5 dermatomyositis presented to our connective tissue disease clinic for management of disease-related hand ulcerations that resulted in severe pain and limited mobility. The patient was initially diagnosed with anti-MDA5 dermatomyositis 6 months prior to presentation following onset of dyspnea and skin changes. A chest computed tomography scan demonstrated interstitial lung disease. Four months prior to presentation, he developed hand ulcerations and worsening dyspnea, leading to a diagnosis of anti-MDA5 dermatomyositis, confirmed with antibody testing. He was initiated on prednisone 60 mg daily, azathioprine, hydroxychloroquine, and intravenous immunoglobulin prior to presentation and noted significant improvement in his dyspnea. Unfortunately, despite this regimen, he noted continued progression of his hand ulcerations. On presentation to our clinic, the patient had large, deep, well circumscribed ulcerations on multiple metacarpophalangeal joints as well as several smaller ulcerations on the proximal interphalangeal joints, fingertips, and left elbow. He also had violaceous erythema on the upper eyelids, oral ulcerations, non-scarring hair loss, and joint pain. The patient was initiated on sildenafil, aspirin, and pentoxifylline, and transitioned to mycophenolate mofetil in lieu of azathioprine. In addition, botulinum toxin was injected into the lateral and medial aspects of the patient's MCP joints. He noted rapid, impressive pain reduction and a halt in progression of his ulcerations within two weeks. The patient had complete closure of hand ulcerations within 10 weeks. While botulinum toxin has demonstrated benefit in the treatment of Raynaud's phenomenon<sup>1</sup> and nonoperative digital ischemia in systemic sclerosis<sup>2</sup>, this is the first documented case of its benefit in the treatment of anti-MDA5 dermatomyositis related hand ulcerations.

**Category:** Clinical Case/Dermatomyositis

**Teaching Point:** The patient's clinical presentation will review classic findings of anti-MDA5 dermatomyositis and highlight treatment options for cutaneous disease in this setting including the use of vasodilators and botulinum toxin in conjunction with immunosuppressive and immunomodulatory therapies for cutaneous ulcerations.

1. Jenkins SN, Neyman KM, Veledar E, Chen SC A pilot study evaluating the efficacy of botulinum toxin A in the treatment of Raynaud phenomenon. *J Am Acad Dermatol*. 2013 Nov;69(5):834-5.
2. Wall LB, Stern PJ et al. Nonoperative treatment of digital ischemia in systemic sclerosis *J Hand Surg Am*. 2012 Sep;37(9):1907-9.

## **AN ATYPICAL, INDURATED PLAQUE WITH RAPIDLY PROGRESSING ULCERATION: DIAGNOSTIC AND THERAPEUTIC CHALLENGE**

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A 33-year-old healthy woman presented for management of biopsy-proven morphea on her right thigh. She had a long-standing, indurated, atrophic plaque with a central area of depressed scarring and poikilodermatous changes. Her outside hospital biopsy site failed to heal and resulted in ulceration. Upon presentation to our clinic, exam was not typical for morphea. An edematous, red plaque surrounded the inferior border of the long-standing indurated plaque, which had extensive white stellate changes suggestive of a vasculitic or vasculopathic process. Two additional biopsies were obtained. One showed vasculitis involving medium-sized vessels in the dermis and subcutis; the other demonstrated features suggestive of an urticarial reaction with vasculopathic changes. Given the previous diagnosis of morphea, her outside pathology was reviewed, which was consistent with thrombotic vasculopathic injury and deep dermal scar-like fibrosis. An extensive autoimmune and hypercoagulable workup was performed, which was unrevealing. The patient has had no evidence of systemic vasculitis and no additional lesions. She denies a history of trauma to the area. She was subsequently started on systemic corticosteroids and mycophenolate mofetil but continued to flare upon tapering of corticosteroids. Methotrexate was added to her regimen, and she was maintained on aspirin and pentoxifylline as well. Plaque size remained stable without frank ulcerations for over one year. Pain improved but was still present, and the addition of dapsone and colchicine did not provide additional improvement. Recently, the patient presented with increasing pain and a 2cm ulceration at a previously healed biopsy site. Within three weeks, the ulceration tripled in size despite the addition of high-dose systemic corticosteroids and sildenafil. An excisional wedge biopsy was performed, which demonstrated vasculitis of medium-sized vessels with secondary thrombotic vasculopathic injury and deep dermal tissue and subcutaneous fat necrosis.

**Category:** Clinical Case

**Teaching point:** The patient's clinical presentation is atypical for any well-characterized vasculitis. Additionally, her progression on robust immunosuppression has created a management challenge. With this case, we hope to incite discussion to guide further therapy.

## **ASSESSMENT AND COMPARISON OF DIAGNOSTIC CRITERIA FOR CLASSIC PYODERMA GANGRENOSUM**

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### **ABSTRACT**

Pyoderma gangrenosum (PG), is an inflammatory neutrophilic dermatosis, characterized by the presence of chronic and painful cutaneous ulcerations. PG diagnostic criteria exist; however, they are not widely accepted in clinical practice. A total of 85 institutional cases of PG identified by ICD-9/10 codes were reviewed independently by two different investigators. A subset of 47 patients, where two investigators, A and B, agreed in their blinded diagnoses of PG were used as an “expert agreement diagnosis” to assess the sensitivity of the Su, PARACELSUS, and Delphi criteria. A different cohort of 65 patients from our institution with “PG-like” diagnoses was used to assess the specificity of each of the diagnostic criteria. Using ICD-9/10 codes we found the sensitivities of each of the criteria to correctly identify patients with PG as follows: Su – 52%, PARACELSUS – 69%, Delphi – 55%. When using “expert agreement diagnosis” instead of ICD codes, the sensitivities increase to the following: Su – 77%, PARACELSUS – 92%, Delphi – 80%, thus emphasizing the importance of diligently working up patients carrying a pre-existing diagnosis of PG. The specificity of the criteria in accurately identifying patients without disease are: Su – 100%, PARACELSUS - 97%, Delphi – 92%. We measured the agreement between the two investigators, Su and PARACELSUS, and estimated a multi-rater kappa coefficient of 0.49 (95% CI 0.36 to 0.60), indicating moderate agreement. Overall, PARACELSUS had better sensitivity and specificity was comparable among criteria. Diagnostic consensus among criteria was moderate, supporting PG as a diagnostic challenge regardless of the use of new diagnostic criteria.

Category: Miscellaneous features and types of rheumatic–dermatologic skin disease

## **FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND OTHER AUTOIMMUNE SKIN DISEASES**

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Fatigue is a well-established symptom in systemic lupus erythematosus (SLE), but has not been well-characterized in other skin-limited autoimmune diseases such as cutaneous lupus erythematosus (CLE), amyopathic dermatomyositis (ADM), or autoimmune blistering diseases (AIBD). In this retrospective study, we compared fatigue in controls (n=84) to patients enrolled in prospective longitudinal databases with SLE (n=165), CLE (n=226), ADM (n=136), and AIBD (n=79). We used the Short-Form 36 (SF-36) vitality scale to analyze median scores and percentage of patients with clinically significant fatigue (defined as a score  $\leq 35$ ) between experimental groups and controls. Median vitality scores demonstrated greater fatigue in experimental groups (SLE=35, IQR=20-55; CLE=50, IQR=30-70; ADM=50, IQR=30-65; AIBD=55, IQR=35-70) than controls (73, IQR=65-85) ( $p < 0.05$  between each experimental group vs. control). The SLE group had worse fatigue than all other groups ( $p < 0.05$  SLE vs. each group), but there was no difference between CLE ( $p > 0.05$ ), ADM ( $p > 0.05$ ), or AIBD ( $p > 0.05$ ). In addition, experimental groups had more clinically significant fatigue (score  $\leq 35$ ) (SLE, 44.2%; CLE, 25.2%; ADM, 31.6%; AIBD, 24.1%) than controls (2%) ( $p < 0.01$  between each experimental group vs. control). The SLE group had more clinically significant fatigue compared to CLE ( $p < 0.01$ ), however, there was no difference in clinically significant fatigue between SLE versus ADM ( $p = 0.17$ ) or AIBD ( $p = 0.06$ ). These findings demonstrate that patients with skin-limited autoimmune disease experience more fatigue than controls. Fatigue is an important symptom that negatively affects quality of life for patients and should be addressed by clinicians and measured in future clinical trials.

Category: Lichenoid inflammatory skin disease (lupus/ dermatomyotitis)

## **RATES AND FACTORS ASSOCIATED WITH DISEASE ACTIVITY REMISSION AND RECURRENCE IN CUTANEOUS LUPUS ERYTHEMATOSUS**

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Little is known about the rates of disease remission and recurrence in patients with CLE. We conducted a retrospective cohort study of 97 participants with CLE to determine rates and clinical characteristics associated with disease remission and recurrence. Inclusion criteria included CLE patients with at least three study visits spanning a minimum of six months. Disease remission was defined as reaching Cutaneous Lupus Erythematosus Activity and Severity Index activity (CLASI-A) equal to 0. Disease recurrence was defined as having a CLASI-A $\geq$ 1 after remission. Participants had a mean follow-up period of 39 (IQR: 22-62) months. 47% (46/97) of participants reached disease remission. Median time to remission was 17 (IQR: 8-29) months from the initial visit. After remission, 63% (29/46) of participants experienced disease recurrence within a median of 13 (IQR: 7-19) months. Lower percentages of patients with discoid lupus (DLE) (63% vs. 88%,  $p=0.004$ ) and higher percentages of patients with oral ulcers (83% vs. 24%,  $p<0.0001$ ) were seen in patients achieving remission vs. those who did not. Patients who experienced recurrence were more likely to have DLE (72% vs. 29%,  $p=0.005$ ) and longer duration of disease prior to their initial visit (median: 3 years, IQR: 0-6) than those who did not have recurrence (median: 0 years, IQR: 0-0,  $p=0.002$ ). We found that most patients with CLE can achieve remission within months after starting therapy; however, the risk of experiencing recurrence is high. Furthermore, DLE and longer disease duration may be associated with a relapsing-remitting disease course.

CATEGORY: (1) Lichenoid inflammatory skin disease

ABSTRACT BODY WORD COUNT: 245



# **Hemophagocytic Lymphohistiocytosis Associated with Dermatomyositis: A Case and Study**

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## **Abstract:**

Dermatomyositis (DM) has been associated with hemophagocytic lymphohistiocytosis (HLH) and may precede HLH or occur concurrently. Cutaneous T cell lymphoma has been associated with both DM and HLH. We report a 62 year old woman with a history of dermatomyositis treated with a variety of systemic medications including prednisone, methotrexate, azathioprine, plasmapheresis, intravenous immunoglobulin (IVIG), rituximab and isotretinoin who developed a nodule on her right arm. Biopsy revealed an atypical lymphocytic infiltrate with panniculitis without evidence of systemic lymphoma. She presented to our institution for evaluation of fever of unknown origin of 2-3 months' duration. Her lymphadenopathy, neurologic symptoms, hepatomegaly, cytopenias (specifically anemia, thrombocytopenia, lymphopenia), markedly elevated serum ferritin, liver failure and recurrent fevers established a diagnosis of HLH. Biopsy of the skin revealed features of subcutaneous peripheral T cell lymphoma (SPTCL), but PCR analysis failed to identify a clonal T cell receptor gamma gene rearrangement. She expired shortly thereafter. The relationships of DM, HLH, and SPTCL will be reviewed and challenges associated with diagnosing lymphoproliferative disease in the setting of negative molecular studies will be explored. Identifying the most efficient path to diagnosis offers the best opportunity for successful treatment.

Additionally, we performed a study of 3,453 patients with DM identified from the MarketScan database with mean 5.66 (SD 2.8) years of continuous follow up. 6 confirmed cases of HLH were identified in these patients; 3 in children, and 2/3 adults with lymphoma. Most cases developed within 1 year of DM. No patient experienced both HLH and pulmonary fibrosis.

Category: 5. Clinical Case, 1. Lichenoid Inflammatory

## **Evaluation of the Reliability and Validity of the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) in Pediatric Cutaneous Lupus Among Pediatric Dermatologists and Rheumatologists**

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### **Background/Purpose:**

Cutaneous lupus erythematosus (CLE) refers to skin manifestations of the autoimmune disease lupus erythematosus (LE). While CLE has been extensively researched in the adult population, few studies exist in the pediatric population. The CLASI is a reliable outcome measure for CLE in the adult population, where it is commonly used in clinical trials for SLE. However, no study has validated this assessment tool in children, potentially limiting the conduct of clinical trials in pediatric SLE.

### **Methods:**

The study took place at the autoimmune disease clinic of the University of Pennsylvania, on March 3rd, 2018. Physician participants included 5 pediatric rheumatologists and 1 pediatric rheumatology fellow and 4 pediatric dermatologists and 2 dermatology fellows. 11 pediatric patients with active CLE participated in this study. All physicians were given a 45-minute training session on the assessment of cutaneous lupus using 2 measurement tools: the CLASI and

the Physician Global Assessment (PGA), which allow grading of skin activity and skin damage. Physicians then individually rated each patient using both tools. Following a 45-minute break, all physicians reassessed 2 patients using the same tools. Inter- and intra-rater reliability within each physician group was determined by intraclass correlation coefficient (ICC), type ICC and its confidence interval.

**Results:**

The CLASI activity scores demonstrated excellent inter- and intra-rater reliability ( $ICC > 0.90$ ) among both dermatologists and rheumatologists. The PGA activity score had a good inter-rater reliability (ICC between 0.77-0.73) for both specialties. It had excellent intra-rater reliability for dermatologists ( $ICC = 0.89$ ), and good intra-rater reliability for rheumatologists. The CLASI damage score had good inter-rater reliability among dermatologists ( $ICC = 0.76$ ) and poor inter-rater reliability among rheumatologists ( $ICC = 0.43$ ). It had excellent intra-rater reliability among dermatologists ( $ICC = 0.87$ ) and good intra-rater reliability among rheumatologists ( $ICC = 0.76$ ). The PGA damage scores ranged from good to moderate ICC inter- and intra-rater reliability among both specialties (ICC between 0.76-0.50).

**Conclusions:**

These results demonstrate that the CLASI is a reliable and valid instrument tool to measure skin disease, especially activity, in pediatric CLE patients. The CLASI can be used in future clinical trials as well as in clinical practice for pediatric CLE to help standardize the evaluation of treatment effects on this disease.

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## **Mastectomy and chemotherapy in patient with breast cancer and active generalized pyoderma gangrenosum**

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### **Abstract**

Forty-six year-old female with new diagnosis of breast cancer presented with rapid onset of erythema and swelling on her right upper arm after two weeks of placement of a port-a-cath and one week after first round of neoadjuvant chemotherapy. She was found to have fever, hypotension and elevated white cell counts requiring intensive care. CT of the right arm showed skin thickening and subcutaneous tissue stranding. She was diagnosed with possible necrotizing infection; port-a-cath was removed from right chest and underwent surgical debridement of affected areas on right arm and right chest; negative-pressure wound therapy and broad spectrum intravenous antibiotics were started. However, ulcers continued to increase in size and they were surgically debrided in three more occasions. Also, PICC line site on left arm placed upon admission developed an ulcer which was also surgically debrided. Histopathology revealed a diffuse neutrophilic infiltrate within the dermis and subcutaneous tissue with focal necrosis. Blood and tissue microbiological cultures were negative. Pyoderma gangrenosum was suggested as possible diagnosis and patient was started on systemic prednisone with rapid improvement within three days. However, her breast cancer treatment was paramount. It was recommended tapering off oral prednisone and start IVIG within 1-2 weeks prior to mastectomy and left sentinel node biopsy. She had a successful surgical treatment. Prednisone was further tapered down in the next 8 weeks and she was started on neoadjuvant therapy which included dexamethasone for 12 more weeks. After, 8 months PG ulcers have almost healed with no evidence of recurrence.

**Category:** clinical case

### **Teaching points:**

- Breast cancer and pyoderma gangrenosum
- Chemotherapy and drug-induced pyoderma gangrenosum
- Clinical clues in pyoderma gangrenosum vs necrotizing fasciitis
- Perioperative management of pyoderma gangrenosum: medical and wound care

## FACTOR ANALYSIS OF THE UT SOUTHWESTERN CUTANEOUS LUPUS ERYTHEMATOSUS (CLE) REGISTRY

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Factor analysis is a dimension reducing test that seeks to describe variability seen amongst observed, correlated variables through a set of latent, or unobserved, variables called factors. (1) This analysis can be applied to skin diseases like CLE to objectively determine clinical factors that tend to co-exist and thus define disease subtypes. We performed a cross-sectional analysis of 268 patients enrolled in the University of Texas Southwestern Cutaneous Lupus Registry between November 2008 and July 2018. Clinical variables include individual American College of Rheumatology lupus diagnostic criteria, Physician's Global Assessment and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) scores, autoantibodies, and demographics. The factor analysis was performed using IBM SPSS Statistics. Results showed that approximately 42% of the variance was explained in the first 6 factors (F1 through F6). F1 delineated patients with high CLASI activity scores and involvement in the neck, chest, arms and back, which likely describe those with subacute cutaneous lupus erythematosus. F2 described patients with high CLASI damage scores on the scalp, ears and face, which are indicative of those with discoid lupus erythematosus. F3 described patients with skin damage in the trunk and legs, while F4 characterized skin damage predominately on hands and feet. F5 delineated patients with clinical characteristics of SLE. The factor analysis helps characterize where lesions of CLE tend to occur together and confirm clinical subtypes. Further analyses will be done to identify new unrecognized clinical patterns in CLE to better inform providers.

CATEGORY: 1) Lichenoid inflammatory skin disease - lupus

(1) Gorsuch, R. L. (1983). *Factor Analysis, 2nd edition*. Hillsdale, NJ: Erlbaum.

## **A REVIEW OF DERMATOMYOSITIS INDUCED BY NON-HYDROXYUREA DRUGS**

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**Background:** Drug-induced amyopathic dermatomyositis (DM) is a well-known adverse reaction of hydroxyurea. However, reviews on association between non-hydroxyurea drugs and DM are limited.

**Objective:** To review case reports of drug-induced DM attributed to non-hydroxyurea therapies.

**Methods:** The English-language literature from the PubMed database was reviewed and reports of new DM onset attributed to non-hydroxyurea therapies were identified. The World Health Organization-Uppsala Monitoring Center system was used to assess causality and only cases that determined to be at least possibly due to the offending agents were included.

**Results:** In 40 reported cases of non-hydroxyurea induced DM, 65% were female and the median age was 52 years (range 10-81 years). A total of twenty three unique drugs were identified that were prescribed for a wide range of conditions including autoimmune disorders (32.5%), cardiovascular diseases (30%), and cancers (17.5%). The latency period between initiation of the drug and DM onset ranged from 3 days to 10 years (median 2 months). While seven patients (17.5%) had an underlying malignancy prior to initiation of the offending agent, the screening did not reveal any occult malignancy in the remainder. Seventy seven percent of the patients presented with proximal muscle weakness. Myositis was confirmed by elevation of muscle-derived enzymes alone (48.4%) or in combination with classic muscle biopsy findings (41.9%).

**Conclusions:** It is difficult to implicate a drug as the certain cause of DM. However, an increasing number of case reports suggest DM may be induced or unveiled by different classes of medications. Unlike hydroxyurea, the majority of such cases are associated with muscle involvement.

# UNILATERAL VOCAL CORD PARESIS IN CLASSIC DERMATOMYOSITIS

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Proximal symmetric muscle weakness is a common manifestation of dermatomyositis, though small muscles may also be involved. Despite being well-documented in systemic lupus, vocal cord dysfunction has only been reported in severe systemic dermatomyositis. A 23-year-old female professional vocalist with a two-year history of moderately well-controlled classic dermatomyositis on hydroxychloroquine, methotrexate, and prednisone developed worsening myalgias, arthritis, and typical rash while tapering prednisone. She noted new-onset hoarseness that was initially attributed to gastroesophageal reflux. Endoscopy demonstrated mild gastritis and a 24-hour esophageal pH probe demonstrated reflux episodes, but symptoms did not noticeably respond to ranitidine and esomeprazole therapy. Esophageal manometry did not demonstrate muscular abnormalities. Stroboscoped laryngoscopy demonstrated left vocal cord paresis, Reinke edema attributed to laryngopharyngeal reflux, and a left vocal cord cyst. Further workup by CT scan, edrophonium stimulation, laryngeal electromyography, and nerve conduction studies were unremarkable, and the patient started speech therapy. Due to worsening muscle symptoms, prednisone was increased during workup, leading to improvement in hoarseness. Subsequent prednisone tapers and dose escalations inversely correlated with hoarseness symptoms. Dose adjustment of methotrexate, in combination with continued speech therapy, led to gradual improvement of hoarseness and stability in cutaneous and systemic symptoms. Vocal cord paresis has been described in asymptomatic professional vocalists, but this patient's striking correlation between dermatomyositis flares with hoarseness and immunosuppressive titration is suggestive of treatment effect. While not typical, the patient's professional training may have provided exquisite sensitivity to her unilateral vocal cord paresis.

## Teaching Point:

Dermatomyositis may affect laryngeal muscles and cause vocal cord paresis with resultant hoarseness. Treatment of underlying dermatomyositis, in combination with speech therapy, may lead to clinical improvement.

Category: Lichenoid inflammatory skin disease, Clinical case

# **CLINICALLY AMYOPATHIC DERMATOMYOSITIS GEOSPATIALLY CORRELATES WITH FIXED SOURCES OF AIRBORNE POLLUTION**

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Dermatomyositis (DM) may result from exogenous triggers in genetically susceptible individuals. The EPA's 2011 National Air Toxics Assessment (NATA) models health risks associated with airborne emissions, available by ZIP code tabulation area (ZCTA). Important contributors include point (fixed), on-road, and secondary sources. The objective was to investigate the geospatial distributions of DM and subtypes, classic DM (CDM) and clinically amyopathic DM (CADM), and their associations with airborne pollutants. This retrospective cohort study identified 642 adult DM patients from 336 unique ZCTAs. GeoDa v.1.10 was used to calculate global and local Moran's indices and generate local indicator of spatial autocorrelation (LISA) maps. All Moran's indices and LISA maps were permuted 999 times. Univariate global Moran's indices for DM, CDM, and CADM prevalence were not significant, but LISA maps demonstrated differential local spatial clustering and outliers. CADM prevalence correlated with point sources, with a bivariate global Moran's index of 0.071 (pseudo p=0.018), in contrast to CDM (-0.0053, pseudo p=0.46). Bivariate global Moran's indices for DM, CDM, and CADM prevalence did not correlate with other airborne toxics, but bivariate LISA maps revealed differential local spatial clustering and outliers. Thus prevalence of CADM, but not CDM, is geospatially correlated with fixed sources of airborne emissions. This effect is small but significant and may support the hypothesis that triggering exposures influence disease phenotype. Important limitations are NATA data and ZCTA population estimates were collected from 2011 datasets and ZCTA of residence may not have been where patients had greatest airborne pollutant exposure.

Category: (1) Lichenoid inflammatory skin disease (lupus/dermatomyositis)



# INCREASED MYELOID DENDRITIC CELLS AND TNF- $\alpha$ EXPRESSION PREDICTS POOR RESPONSE TO HYDROXYCOLOQUINE IN CUTANEOUS LUPUS ERYTHEMATOSUS

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**Objective:** Although antimalarials are the primary treatment for cutaneous lupus erythematosus (CLE), not all patients are equally responsive. We investigated whether different inflammatory cell population and cytokine profiles in lesional CLE skin could affect the antimalarial responsiveness, and if hydroxychloroquine (HCQ) and quinacrine (QC) differentially suppress inflammatory cytokines.

**Methods:** CLE patients were grouped according to their response to antimalarials (HCQ vs HCQ+QC). Inflammatory cell composition of plasmacytoid dendritic cells (pDCs), myeloid dendritic cells (mDCs), neutrophils, and macrophages, and gene expression of type I interferon (IFN) signatures and tumor necrosis factor (TNF)  $\alpha$  were evaluated in CLE lesions. The suppressive effects of antimalarials on toll like receptor (TLR)-mediated production of inflammatory cytokines (IFN- $\alpha$ , TNF- $\alpha$ , and IL-6) and NF- $\kappa$ B phosphorylation were evaluated on peripheral blood mononuclear cells (PBMCs) isolated from CLE patients.

**Results:** Among inflammatory cells, only mDCs were significantly increased in the HCQ+QC group compared to HCQ group. Gene expression of type I IFN signatures, including LYE, OAS1, OASL, ISG15, and MX1, was significantly upregulated in HCQ group, whereas TNF- $\alpha$  level was higher in the HCQ+QC group. HCQ and QC had differential suppressive effects on cytokine production and NF- $\kappa$ B phosphorylation. QC inhibited TNF- $\alpha$  and IL-6 more profoundly than HCQ did, while both QC and HCQ inhibited IFN- $\alpha$  from TLR-stimulated PBMCs. QC also suppressed phospho-NF- $\kappa$ B p65 more than HCQ.

**Conclusion:** Increased numbers of mDCs with higher TNF- $\alpha$  expression might contribute to HCQ-refractoriness and a better response to QC. Differential suppressive effects of HCQ and QC could also affect antimalarial responses in CLE patients.

Category: Lichenoid inflammatory skin disease (Cutaneous Lupus Erythematosus)

# CHARACTERISTICS OF MALIGNANCY-ASSOCIATED DERMATOMYOSITIS IN HOSPITALIZED PATIENTS: A NATIONALLY REPRESENTATIVE RETROSPECTIVE COHORT STUDY

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**Background:** Dermatomyositis (DM) is well-known to be associated with underlying malignancy. Although numerous studies have explored malignancy in DM population-based studies, little is known about malignancy-associated DM (MADM) in hospitalized inpatients.

**Methods:** We analyzed data from the 2009-2015 National Inpatient Sample, which includes a 20% nationally representative sample of U.S. hospitalizations, to characterize MADM in hospitalized inpatients.

**Results:** 255,260,410 hospitalizations were included. Of 39,253 DM hospitalizations, 4,278(10.9%) occurred in MADM patients and 34,975(89.1%) were related to other DM subtypes. DM inpatients were significantly more likely to have malignancies of the breast(1.7-fold), bronchus(1.4-fold), ovary(5.5-fold), head/neck(1.7-fold), esophagus(1.9-fold), and non-Hodgkin lymphoma(1.8-fold) compared to non-DM inpatients. DM inpatients were less likely to have malignancies of the prostate(3.2-fold), rectum/anus(1.8-fold) and multiple myeloma( $p=0.0015$ ) than non-DM inpatients. Older DM patients (particularly  $\geq 60$  years) and Caucasian DM inpatients were more likely to have a malignancy ( $p<0.0001$ ) than other DM patients. There were no significant differences in sex or whether patients died during hospitalization between MADM patients and patients with other DM subtypes. **Conclusions:** When compared to similar non-DM patients, DM inpatients may have increased risk of different malignancies than DM outpatients. This implies optimal malignancy screening protocols may differ for DM patients encountered in clinic as opposed to during hospitalization. Other relevant characteristics to consider for developing optimal malignancy screening protocols for DM inpatients include patient age, gender and ethnicity. Although percentage of DM inpatients with malignancy is shifting over time, there has been no significant change in prevalence of malignancy in the DM inpatient population since 2009.

**Words: 250**

(1) Lichenoid inflammatory skin disease (lupus/ dermatomyositis)

# **“HYDROXYCHLOROQUINE IS AN EFFECTIVE TREATMENT OF MORPHEA: A RETROSPECTIVE REVIEW OF 105 PATIENTS FROM MAYO CLINIC, 1996-2013”**

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## **ABSTRACT:**

**Background:** Few studies exist to support the treatment of morphea (localized scleroderma) with hydroxychloroquine.

**Objective:** To assess the efficacy of hydroxychloroquine treatment of morphea.

**Methods:** Retrospective study of 105 patients who were diagnosed with morphea and treated with hydroxychloroquine at our institution between 1996 and 2013. To assess the median time to initial and maximal responses, a time- to- event analysis was conducted using Kaplan-Meier analysis.

**Results:** Of 105 patients (median age at diagnosis, 34 years), 82 (78.1%) were female. Forty-three patients (41.0%) had a complete response; 41 (39.0%) had a partial response >50%; 13 (12.4%) had a partial response <50%; and 8 patients (7.6%) had no response to hydroxychloroquine. The median time to initial response was 5 months; while the median time to maximum response was 14 months. Sixty-nine of 84 patients (82.1%) who had either a complete response or partial response >50% received hydroxychloroquine as monotherapy. Eleven patients (10.5%) experienced side effects of hydroxychloroquine; the most common was nausea (7 patients).

**Limitations:** Retrospective study.

**Conclusion:** Hydroxychloroquine is a valuable treatment option of morphea due to its high response rate and low rate of adverse effects; however, prospective studies are needed to demonstrate its true efficacy in morphea.

Category: Sclerotic skin disease

## **CUTANEOUS LUPUS ERYTHEMATOSUS PATIENTS WITH A NEGATIVE ANA MEETING ACR AND/OR SLICC CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS**

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Systemic lupus erythematosus (SLE) is a disorder that is heterogeneous and can be difficult to diagnose. One hallmark of the disease is the presence of anti-nuclear antibodies (ANA), a feature that has been incorporated into multiple classification criteria over the years. In this study, we use a database of 454 cutaneous lupus erythematosus (CLE) patients to determine how many have a negative ANA and meet criteria for SLE using ACR and/or SLICC criteria. Of the 406 patients with a known ANA, 147 had a negative ANA (36.2%) and 39 of all patients who had multiple ANAs checked (n = 114) had an ANA that fluctuated (34.2%). 30 ANA negative patients met SLE criteria (20.4%) and 19 patients with fluctuating ANA met SLE criteria (48.7%). Of all patients who had either a negative or a fluctuating ANA and met criteria for SLE (n = 49), 40 patients had involvement of at least 1 organ system other than skin (81.6%), and 22 patients had involvement of at least 2 organ systems other than skin (44.9%). Of the 40 patients with non-mucocutaneous organ involvement, 35 patients had arthritis, 14 patients had leukopenia, 9 patients had renal involvement, 4 patients had serositis, 3 patients had neurologic involvement, and 1 patient had thrombocytopenia. Our results demonstrate that a positive ANA is not always present in patients with SLE involving non-mucocutaneous organ systems. This should be taken into consideration when devising SLE classification criteria to be used for clinical trials.

Category: Lichenoid inflammatory skin disease (lupus/ dermatomyotitis)

# ASSESSING A CONCEPTUAL FRAMEWORK OF QUALITY OF LIFE IN A CUTANEOUS LUPUS ERYTHEMATOSUS POPULATION

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This purpose of this study was to describe the quality of life (QoL) in persons with CLE and examine factors that may affect QoL, using the Revised Wilson and Cleary's Model for QoL. Biological factors (CLE subtype, disease activity, disease damage, disease duration), symptoms (pain, pruritus, fatigue), functioning (body image, depression, comorbidity), general health perception (side effects from CLE medications, skin health perception, pill burden), characteristics of the individual (age, gender, education, race/ ethnicity, smoking status), and characteristics of the environment (marital status, income, and social support) were examined to determine their potential impact on overall QoL.

A cross-sectional, correlational study was conducted in 101 CLE patients recruited from an outpatient university-based dermatology clinic in Dallas, Texas. Demographic and clinical characteristics were collected from patients. Data were analyzed using SPSS v24.

The majority of the participants were female (87%), African American (59%), married (42%), and averaged 10±11 years since diagnosis. Patients ranged between 19-48 years old (mean±SD, 48±13) and most had chronic CLE (83.2%). The final model explained 85% of the variability in overall QoL, with disease activity, pain, fatigue, body image, and side effects being significant predictors. These studies underscore several of the issues affecting QoL in CLE patients. Using a theoretical framework, patient-centered and clinical outcomes were integrated to facilitate a fuller understanding of the several factors impacting QoL in CLE patients. As such, future studies aimed at understanding QoL in CLE patients should consider using a theoretical framework, as healthcare becomes more patient-centered.

**Category:** (1) Lichenoid inflammatory skin disease (lupus/dermatomyositis)

## **CHARACTERIZATION OF HELPER T CELL SUBPOPULATIONS IN EARLY, MID-, AND LATE-STAGE DISCOID LUPUS ERYTHEMATOSUS (DLE)**

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DLE is characterized by early erythematous papules and plaques that progress to hyperpigmented and hypopigmented plaques with central scarring. The immunopathology of early and late stage DLE is not well characterized. In a previous study comparing multiple immune cell populations in different DLE stages, we found higher CD8<sup>+</sup> T cells and lower CD20<sup>+</sup> B cells in early DLE skin versus later DLE skin.<sup>1</sup> To follow up on these findings, we compared helper T (Th) cell subpopulations in early (inflammatory), mid (inflammatory with scarring) and late-stage (scarring) DLE skin. We hypothesized a shift from Th1 response (pro-inflammatory) in early DLE skin to Th2 (pro-fibrotic) response in late DLE skin. We performed double immunohistochemistry to compare Th1 (CD4<sup>+</sup>T-bet<sup>+</sup>) and Th2 (CD4<sup>+</sup>GATA3<sup>+</sup>) cells in formalin-fixed, paraffin-embedded skin biopsies of early (N=4), mid (N=4), and late stage DLE (N=3). Single positive and double-positive cells were manually counted in representative high-powered field areas of the epidermal-dermal junction (interface), perifollicular and perivascular areas. There were non-significantly higher percentages of Th2 cells within the perivascular (p=0.11) and interface (p=0.14) areas in late DLE skin compared with early and mid DLE skin. Early DLE skin also showed higher percentages of Th1 cells than Th2 cells in the perifollicular (p=0.13) and perivascular areas (p=0.13) but did not reach statistical significance. Larger samples are being collected to verify our findings. Elucidating immunologic differences in various stages of DLE will be important to finding therapies that reduce the chronic skin sequelae of scarring and dyspigmentation in DLE.

CATEGORY: (1) Lichenoid inflammatory skin disease

ABSTRACT BODY WORD COUNT: 247 (Maximum 250)

### References

1. O'Brien JC, Hosler GA, Chong BF. Changes in T cell and B cell composition in discoid lupus erythematosus skin at different stages. *J Dermatol Sci.* 2017 Mar;85(3):247-9.

## **ANNULAR AND POLYCYCLIC CUTANEOUS ERUPTIONS WITH HYPER-FERRITINEMIA AND FEVER RESPONDING TO TOCILIZUMAB – ATYPICAL ADULT ONSET STILL’S DISEASE?**

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We report on the clinical course of 72 year old male presenting with a 1 year history of a recurrent annular polycyclic eruption of the trunk, face and limbs with intermittent fevers, fatigue and arthralgias. Skin biopsies showed variably perivascular lymphocytic infiltration without dermal mucin and neutrophils. He had associated hyper-ferritinemia and elevations of CRP. His symptom constellation responded to prednisone at doses above 10 mg. He failed therapeutic trials of antimalarials, methotrexate, mycophenolate mofetil and dapson. He had a partial response to anakinra. He was started on tocilizumab at 3 years post presentation with control of symptoms for the following 4 years of follow up and recurrence upon therapy interruption. Clinical images, clinical course, pathology and laboratory investigations will be presented for discussion.

Category: Clinical Case

Teaching points:

1. Differential diagnosis of polycyclic and urticarial eruptions in patients with rheumatic disease.
2. Use of tocilizumab in patients with primarily dermatologic manifestations of rheumatic disease.

Word count: 124





# **LANGERHANS CELLS LIMIT PHOTSENSITIVITY IN LUPUS ERYTHEMATOSUS VIA EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) SIGNALING**

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Photosensitivity, or skin sensitivity to ultraviolet radiation (UVR), is a feature of lupus erythematosus (LE) and other autoimmune and dermatologic conditions. Photosensitive lesions can be aesthetically disfiguring and can exacerbate systemic manifestations of LE. The pathogenesis of photosensitivity remains poorly understood, however, UVR-induced keratinocyte apoptosis is thought to play a key role. Langerhans cells (LCs), mononuclear phagocytes positioned primarily in the epidermis, can play regulatory roles in various types of skin injury and inflammation. As LCs are closely associated with keratinocytes, we hypothesized that LCs can limit UVR-induced keratinocyte injury and overall skin inflammation. Here, we identify a Langerhans cell (LC)-keratinocyte axis that limits UVR-induced keratinocyte apoptosis and skin injury via keratinocyte epidermal growth factor receptor (EGFR) stimulation. We show that absence of LCs in Langerin-DTA mice leads to photosensitivity and that, in vitro, mouse and human LCs can directly protect keratinocytes from UVR-induced apoptosis. LCs express EGFR ligands and ADAM17, the metalloprotease that activates EGFR ligands. Deletion of ADAM17 from LCs leads to photosensitivity and UVR induces LC ADAM17 activation and generation of soluble active EGFR ligands, suggesting that LCs protect by providing activated EGFR ligands to keratinocytes. Photosensitive systemic LE (SLE) models and human SLE skin show reduced epidermal EGFR phosphorylation and LC defects, and topical EGFR ligand reduces photosensitivity. Together, our data establish a direct tissue-protective function for LCs, reveal a mechanistic basis for photosensitivity, and suggest EGFR stimulation as a novel treatment for photosensitivity in LE and potentially other rheumatologic and dermatologic conditions.

Category: Lichenoid inflammatory skin disease (lupus/dermatomyositis)

SHI, K

## DEVELOPMENT AND ONSET OF AUTOIMMUNE DISEASES IN CUTANEOUS LUPUS ERYTHEMATOSUS PATIENTS

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Patients with systemic lupus erythematosus (SLE) harbor an increased risk for developing additional autoimmune diseases.<sup>1</sup> A recent cross-sectional study reported that cutaneous lupus erythematosus (CLE) patients without SLE had significantly elevated rates of co-existing autoimmune disease(s).<sup>2</sup> In a case-control study, we characterized the timing and prevalence of autoimmune diseases in a group of 122 CLE patients in relation to their CLE diagnosis. We also identified demographic and clinical factors associated with the presence of additional autoimmune diagnosis. 117 patients with SLE were used as controls. At the time of lupus diagnosis, 12.3% of CLE and 16.2% of SLE patients had a prior-onset autoimmune disease ( $p=0.38$ ). After lupus diagnosis, 19.7% of CLE and 18.0% of SLE patients had a new-onset autoimmune disease ( $p=0.69$ ). For CLE patients, the most common prior-onset and new-onset diagnoses were autoimmune thyroid disease and SLE, respectively. Univariate analysis showed that patients with prior-onset disease were older ( $p=0.02$ ) and more likely to be antinuclear antibody (ANA) positive ( $p<0.001$ ) at CLE diagnosis. Patients with new-onset autoimmune disease were more likely to be ANA positive at any point during follow-up ( $p=0.001$ ). Multivariate analyses showed that positive ANA was significantly associated with prior-onset (odds ratio (OR) 6.95,  $p=0.001$ ) and new-onset autoimmune diagnosis (OR 5.65,  $p=0.003$ ). Thus, CLE patients have an elevated risk for acquiring autoimmune diseases before and after their diagnosis at rates similar to those of SLE patients. CLE patients with positive ANA histories have a greater risk for additional autoimmune conditions, which may help providers focus their screenings.

Abstract Category: 1) Lichenoid inflammatory skin disease (lupus/ dermatomyositis)

### References:

1. Chambers SA, Charman SC, Rahman A, Isenberg DA. *Annals of the rheumatic diseases*. 2007;66(9):1173-1177.
2. Kunzler E, Hynan LS, Chong BF. *JAMA dermatology*. 2018;154(6):712-716.