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BOOK OF ABSTRACTS

AMERICAS ASSOCIATION OF SARCOIDOSIS AND OTHER GRANULOMATOUS DISORDERS (AASOG) 2024 CONFERENCE:

THE ART OF WORKING TOGETHER FOR PROGRESS

AUGUST 15-16, 2024

SARCOIDOSIS

VASCULITIS AND DIFFUSE LUNG DISEASES

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Americas Association of Sarcoidosis and Other Granulomatous Disorders

(AASOG) 2024 Conference:

THE ART OF WORKING TOGETHER FOR PROGRESS

August 15-16, 2024

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Poster

A snapshot of American sarcoidosis patients and their perceived disease impact: The results of the Sarcoidosis Research Institute survey

Ogugua Obi[1], Paula Polite[2], Kenneth Fish[3], Robert Deluca[3], Paul Feustel[3], Alexandra Mandis[2], Annetta Coleman[2], Marc Judson[3]
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Background: Sarcoidosis patient priorities and concerns have not been well-described in the United States.

Methods: A survey was constructed by sarcoidosis doctors and patients that was administered to American sarcoidosis patients through social media and sarcoidosis clinician networks. The survey queried patients concerning their demographics, state of their disease, the impact of the disease on their health and well-being, their health care priorities and impressions of sarcoidosis care.

Results: 1093 American sarcoidosis patients completed this survey. 65% were woman, 63% were white, 34% were black, and 83% were > 45 years old. Organ involvement was as follows: lung 83%, heart 24%, eye 23%, skin 14%. 25% had a household income < $50K and 15% had a household income > $150K. There was a fairly even split between those living in urban (31%), suburban (41%), and rural (28%) environments.

Patient concerns are shown in Table 1. Sarcoidosis patients had significant concerns about the process of establishing their sarcoidosis diagnosis, medication side effects, and lack of sarcoidosis research. They had significant concerns about poor outcomes from sarcoidosis including worsening disease, additional sarcoidosis organ involvement, worse quality of life, and death from sarcoidosis. They were also concerned about the results of objective tests such as pulmonary function and chest imaging results. The patients were relatively less concerned with sarcoidosis effects on their personal relationships, compassion/understanding from others, or embarrassment from having the disease. They also had relatively less concerns with communication with their doctor and the doctor's level of knowledge about sarcoidosis.

Discussion: In this survey of over 1000 American sarcoidosis patients, they had major concerns about their sarcoidosis outcomes and medication side effects. The patients were relatively less concerned with their doctors' care and communication. They also were relatively less concerned about support from others. They were concerned about their diagnostic process. They had significant concerns about the sarcoidosis research effort. In summary, sarcoidosis patients seemed relatively satisfied with their sarcoidosis care and support. However, current sarcoidosis treatments and outcomes significantly concerned them.

Sarcoidosis Patient Concerns (N = 997 to 1003)	None (%)	A little(%)	Moderate(%)	A lot(%)	Great deal(%)	Average*
Difficulties in making the diagnosis	35	22	18	12	13	2.46
Lack of my doctor's knowledge	61	11	11	8	10	1.96
Ineffective communication with my doctor	63	15	9	6	8	1.82
Medication side effects	31	21	21	13	14	2.58
Inadequate health insurance/health coverage	39	20	15	10	15	2.41
Lack of research concerning sarcoidosis	22	19	22	16	22	2.97
Fear of worsening sarcoidosis	7	23	25	19	26	3.34
Fear of additional sarcoidosis organ involvement	8	24	24	17	27	3.31
Fear of sarcoidosis not improving	11	24	23	18	25	3.22
Fear of death from sarcoidosis	24	26	16	11	23	2.83
Pulmonary function test status	16	28	25	15	18	2.91
Chest imaging findings	21	28	24	13	14	2.71
Disability from sarcoidosis	20	25	18	14	23	2.95
Poor quality of life from sarcoidosis	16	25	21	16	22	3.03
Poor relationships from sarcoidosis	42	23	13	10	13	2.30
Lack of compassion/understanding of my sarcoidosis	35	23	17	10	15	2.47
Embarrassment from having sarcoidosis	61	17	8	7	7	1.82
Work performance affected by sarcoidosis	34	21	15	10	20	2.61

* Weighted average with None = 1, A little = 2, Moderate = 3, A lot = 4, Great deal = 5

Oral

Airway Epithelial Alarmin Responses to Cutibacterium acnes Identifies a Severe Cardiac Endotype of Sarcoidosis

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Background: Sarcoidosis is driven by an abnormal response to a particular antigen(s) in a genetically susceptible host. However, the patient-specific antigen or abnormal host response is rarely known. Sarcoidosis may be comprised of multiple "endotypes" such as Löfgren's syndrome which is associated with an *Aspergillus nidulans antigen*. Other possible "endotypes" include sarcoidosis driven by *Cutibacterium acnes* (*C. acnes* formerly Propionibacteria) or Mycobacteria. The antigens that may drive sarcoidosis first encounter airway epithelial cells upon inhalation; epithelial responses to these antigens may shape innate and adaptive immunity including granuloma formation. We implemented a non-invasive method to study host-specific epithelial responses to inhaled microorganisms. We hypothesized that epithelia from a subset of people with sarcoidosis will have an abnormal response to *C. acnes* exposure.

Methods: We obtained nasal epithelial basal stem cells from people with sarcoidosis (n=14) as well as sex/age matched healthy controls (n=8); we exposed epithelia grown at air-liquid-interface (ALI) to 275ug/ml freeze/thaw killed *C. acnes* extract, applied both apically and basolaterally for 18 hours. Epithelial derived cytokines and alarmins were measured from basolateral media using a multiplex protein assay and RNA sequencing was performed.

Results: Approximately one third (~30%) of epithelia from people with sarcoidosis have an excessive thymic stromal lymphopoietin (TSLP, an alarmin) response to *C. acnes*; this response was dose dependent. In contrast, none of the epithelia from healthy controls responded. Patients with hyper-responsive epithelia have similar rates of skin and lung disease but have significantly higher rates of cardiac involvement compared to non-responders.

Discussion: We identified a subset (30%) of excessive responders to *C. acnes* in epithelia from people with sarcoidosis. These patients have a more severe form of sarcoidosis involving higher rates of cardiac disease. TSLP responses may cause activation of innate and adaptive immune cells, eventually leading to granuloma formation. Our findings support that the syndrome of sarcoidosis may be composed of multiple endotypes, determined by excessive responses to distinct antigen triggers, including *C. acnes*. Identification of these triggers and the mechanisms involved will allow for the development of non-invasive diagnostic tools and therapeutic targets in sarcoidosis.

Poster

Alteration of the Mouse Fecal Metabolome is Associated with the Severity of Bleomycin Induced Lung Fibrosis

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Background: We had previously reported that mice housed in Animal Biosafety Level 2 (ABSL-2) conditions exhibit more severe lung fibrosis, than germ free (GF) or mice housed in ABSL-1 conditions due to differences in gut microbiota. We also reported increased pulmonary Th17 cells among mice housed in ABSL-2 conditions. Other studies have suggested that Th17 differentiation is influenced by the gut metabolome and we hypothesize that metabolome alterations associated with gut dysbiosis affects lung fibrosis through Th17 cells.

Methods: To identify relevant mechanisms by which gut microbiota induce pulmonary Th17 cell expression, we assessed the fecal metabolome. We performed liquid chromatography-mass spectrometry (LC–MS) analysis to quantify metabolites in the stool of mice housed in ABSL-2 and GF conditions, as well as GF mice gavaged with ABSL-2 stool.

Results: Significant distinctions in the fecal metabolome were observed in GF, WT ABSL-2 mice and GF mice gavaged with ABSL-2 stool, particularly in tryptophan metabolism which was previously shown to be important for Th17 cell development. The stool from ABSL-2 mice, as well as GF mice gavaged with ABSL-2 stool, showed decreased levels of tryptophan compared to GF mice. The tryptophan metabolites 5-HIAA and picolinic acid, were significantly higher in ABSL-2 stool, compared to GF stool, suggesting that the kynurenine pathway and the serotonin/melatonin pathway are associated with gut dysbiosis.

Discussion: The findings suggest that tryptophan levels are altered in gut dysbiosis, which in turn drives pulmonary T cell differentiation into more of a Th17 cell phenotype, resulting in increased lung fibrosis severity.

Poster

An advanced radiomics and ensemble deep learning approach for diagnosis of pulmonary sarcoidosis from CT

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Background: Pulmonary sarcoidosis is a granulomatous interstitial lung disease of unknown etiology with variable presentation, prognosis, and progression[1,2]. Untreated pulmonary sarcoidosis may cause progressive pulmonary fibrosis resulting in respiratory failure and death.

There is no gold-standard diagnostic test for sarcoidosis; clinically and radiologically pulmonary sarcoidosis may be often confused with infections or malignancies (LCa). Therefore, there is an unmet need to establish an accurate diagnosis of pulmonary sarcoidosis with the help of AI algorithms, as it would avoid biopsies and shorten the time for establishing the diagnosis, which might prevent disease complications. As part of our development of an AI algorithm to identify pulmonary sarcoidosis on chest CT scan, we examined the capability of this algorithm to distinguish pulmonary sarcoidosis from LCa.

Methods: A cohort of sarcoidosis (n=126) and chest CT volumes were collected from Albany Medical College and CT volumes with LCa (n=93) were used from publicly available LIDC-IDRI[3] database to develop the AI algorithm to diagnose sarcoidosis. An ensemble deep learning network of 3D Vision Transformers (ViT)[4] and 3D Convolutional Neural Networks (CNN) was developed with multichannel inputs as CT and radiomics texture[5] i.e., Haralick correlation derived from CT. (Fig. 1(a)). Radiomic textures are handcrafted mathematical features from images to distinguish between diseases in a machine learning framework. While deep learning-based CNN-ViT learn local and global features respectively to discriminate between diseases in the training phase. Visually explainable maps to show where the AI focuses during prediction were also generated using HiResCam[6] and filtered ViT Attention rollout[7] methods. The AI model was trained and validated using 5-fold cross-validation.

Results: The AI model showed accuracy, sensitivity, specificity and combined AUC of 0.93±0.04, 0.94±0.04, 0.93±0.08 and 0.97 for PS (n=126) and LCa (n=93) cases. Visually explainable maps for sarcoidosis in Fig. 1(c) show features such as granulomas prominently captured by CNNs, and other global features captured by ViT.

Discussion: This study shows the potential of an AI tool to accurately diagnose pulmonary sarcoidosis based on radiographic findings which would lessen the need for invasive lung biopsies and would allow such patients to receive appropriate treatment more rapidly.

Poster

Baseline Clinical Characteristics Associated with a Progressive Phenotype of Sarcoidosis: A Preliminary Analysis

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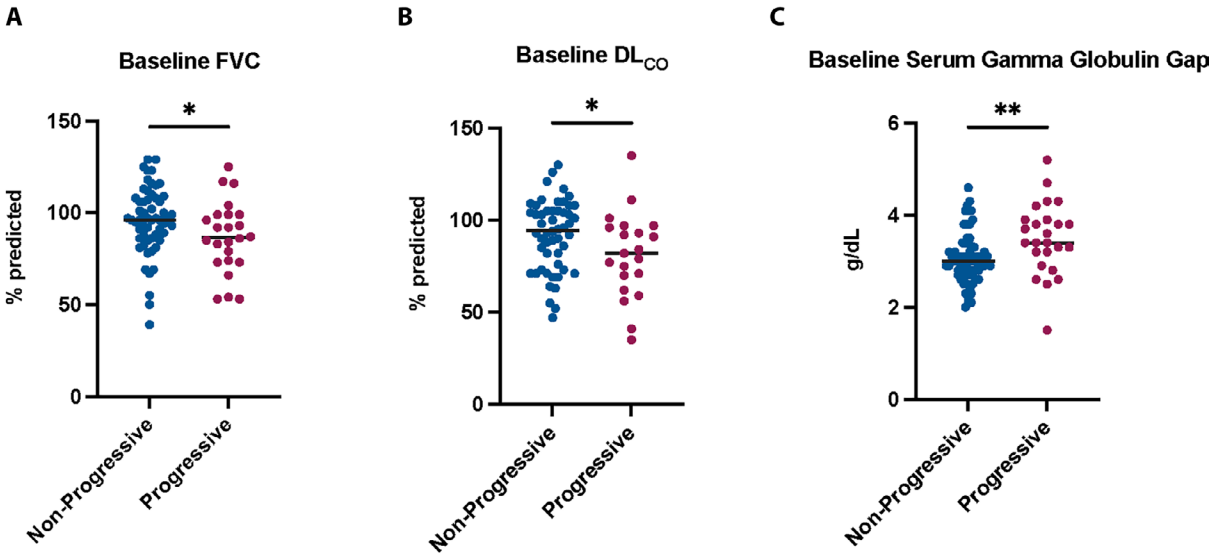
Background: A progressive fibrotic phenotype of interstitial lung disease other than idiopathic pulmonary fibrosis has been recently recognized and is informing trial design and clinical management.[1,2] Sarcoidosis is a heterogenous disease with significant variability in presentation and prognosis, sometimes resulting in fibrotic disease. Up to one third of patients develop chronic disease resulting in loss of organ function and impaired quality of life.[3,4] We therefore sought to determine the baseline clinical characteristics of patients with a "progressive phenotype" of sarcoidosis in a cohort of patients at our center.

Results: 122 patients (median age 55 years [IQR 47-63], 59% male, 61% white) with available baseline data and sufficient longitudinal follow-up met established diagnostic criteria for sarcoidosis.[6] Of these, 36 (30%) met the above criteria for "progressive disease." Associations between this phenotype and longer duration of symptoms prior to diagnosis ($p<0.001$) and black or African American race ($p<0.001$) were observed. In addition, lower baseline FVC (Figure 1A, $p=0.04$) and DL_{CO} (Figure 1B, $p=0.04$) were associated with the progressive phenotype. While there was no significant difference between bronchoalveolar lavage cell count differentials, baseline chest imaging, or other baseline laboratory values, a significantly higher observed baseline gamma globulin gap was associated with progressive disease (Figure 1C, $p=0.001$).

Discussion: Our findings support the existence of a progressive sarcoidosis phenotype that is associated with baseline restrictive lung disease and hypergammaglobulinemia. The association with race and prolonged symptoms prior to diagnosis may also highlight the effects of care inequities.[7] Future studies should seek to elucidate underlying pathobiological and social mechanisms for this phenotype.


A
Baseline FVC
*
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Non-Progressive
Progressive
B
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% predicted
Non-Progressive
Progressive
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Baseline Serum Gamma Globulin Gap
**
6
4
2
0
g/dL
Non-Progressive
Progressive

Poster

Bronchoalveolar lavage neutrophils and matrix metalloproteinase-9 in sarcoidosis clinical phenotypes: Implications for tissue remodeling leading to pulmonary fibrosis

Rafael Perez[1], Jeffrey Ritzenthaler[1], Edilson Torres-Gonzalez[1], Prarthna Chandar[1], Daniel Kramer[1], Jesse Roman[1]
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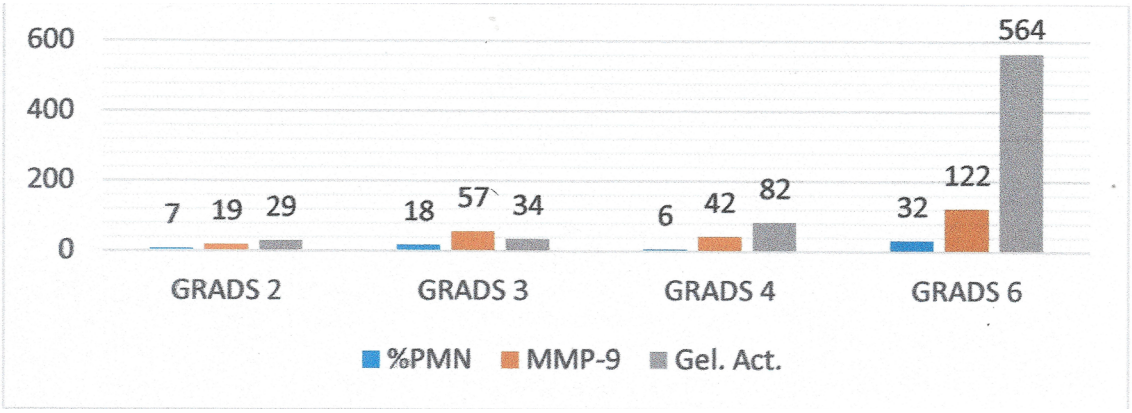
Background: Pulmonary sarcoidosis may resolve or progress to advanced stages. Increased lung neutrophils obtained by bronchoalveolar lavage are found in advanced pulmonary sarcoidosis. Persistence of a neutrophilic alveolitis has been postulated to result in tissue injury and remodeling that leads to fibrosis and clinical features of advanced disease. Since neutrophils are a source of matrix-degrading proteins like matrix metalloproteinases (MMPs), we hypothesized that PMNs promote disease progression through the release of MMPs. This work explores the relationship between lung neutrophils and MMP levels and activity and how they are associated with sarcoidosis clinical phenotypes.

Methods: Patients undergoing bronchoscopy for the diagnosis of sarcoidosis or assessment of disease activity were classified by the 9 Genomic Research in Alpha-1 Antitrypsin and Sarcoidosis (GRADS) clinical phenotypes. Bronchoalveolar lavage fluid (BALF) percent neutrophils (%PMN), matrix metalloprotein-9 (MMP-9), ng/ml, and gelatinolytic activity, O.D./mcg total protein, were analyzed against the GRADS phenotypes.

Results: Thirty-seven subjects were studied and compared by One-way Analysis of Variance. Subjects with untreated stage I pulmonary sarcoidosis (GRADS 2) or untreated stage II – III sarcoidosis (GRADS 4) had significantly fewer BALF %PMN and MMP-9 levels than subjects with untreated stage IV sarcoidosis (GRADS 6). Notably, individuals with stage II – III sarcoidosis on treatment (GRADS 3) tended to have higher %PMN, though not significantly higher, than those with untreated stage I – III (GRADS 2 and 3). There was no significant difference in %PMN between GRADS 3 and GRADS 6 subjects. MMP-9 levels were significantly higher in GRADS 6 versus all the other GRADS phenotypes. There was great variability in gelatinolytic activity and no significant differences by analysis of variance.

Discussion: Our study indicates that a low burden of lung PMN and lung matrix remodeling to normal define GRADS 2. A high burden of lung PMN and matrix remodeling to fibrosis may be expected in subjects with an advanced GRAD 6 presentation. Subjects with treated stage II – III disease, GRADS 3, have a higher lung PMN burden than untreated stage II - II, GRADS 4. Clinical phenotypes of sarcoidosis may reflect specific tissue remodeling paradigms that drive irreversible tissue fibrosis or repair to normal.


600
400
200
0
7
19
29
18
57
34
6
42
82
32
122
564
GRADS 2
GRADS 3
GRADS 4
GRADS 6
%PMN
MMP-9
Gel. Act.

Poster

CD4+ T cell Immunophenotypes of Severe Pulmonary Sarcoidosis in PBMCs

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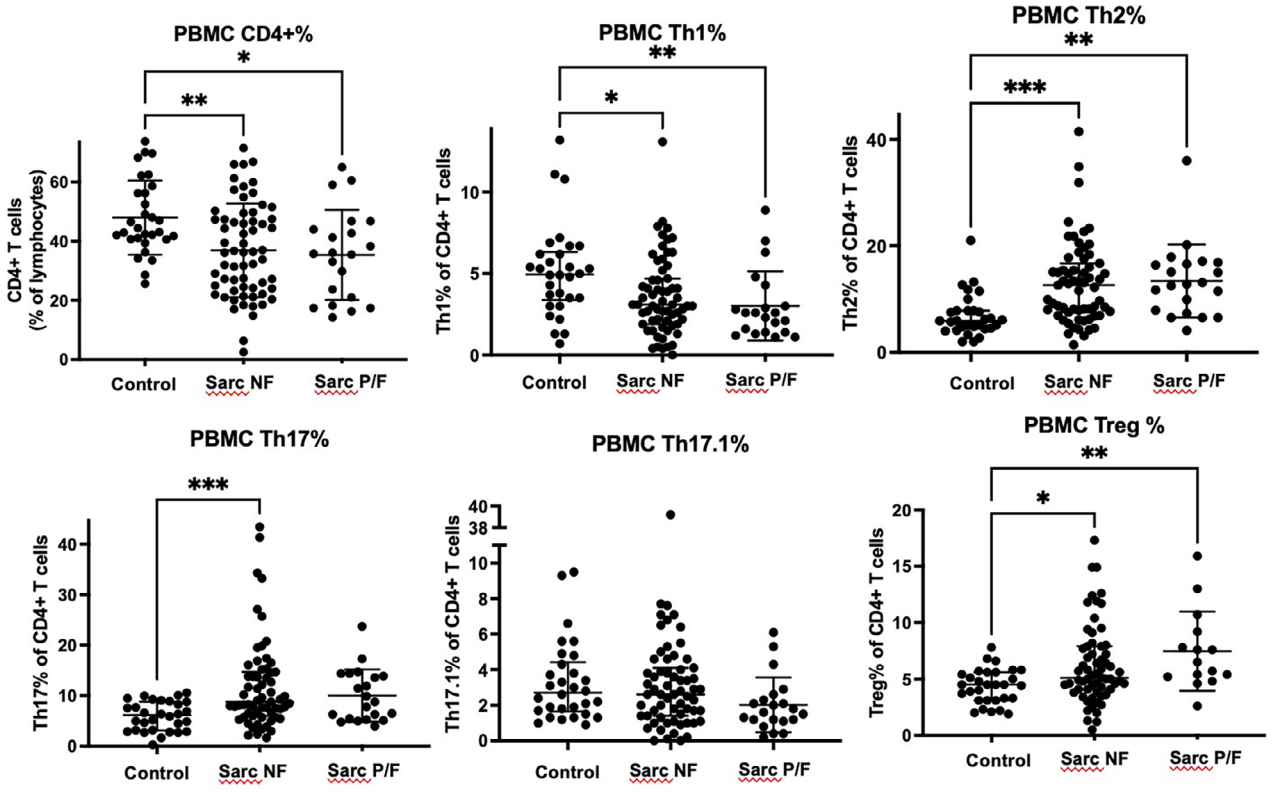
Background: Sarcoidosis is a rare disease of unknown cause that results in significant morbidity and mortality. The reason why some develop this disease and others do not and why some develop more severe forms of this disease, especially fibrotic sarcoidosis, is not well understood.

Methods: All sarcoidosis cases were categorized as non-fibrotic sarcoidosis (NF, including non-progressive and progressive/non-fibrotic) or progressive/fibrotic (P/F) phenotypes. We enrolled a total of 21 P/F and 63 NF sarcoidosis cases and 30 controls. PBMCs were isolated by Ficoll-Paque PLUS Cytiva following manufacturer's instructions. PBMCs were stained and analyzed using multiparameter flow cytometry to acquire cell counts, their relative frequencies and numbers of T helper cells (Th1, Th17, Th17.1 and Th2) and Treg cell. Th1 cells were CD4+CCR6-CCR4-CXCR3+, Th2 CD4+CCR6-CCR4+CXCR3-, Th17 CD4+CCR6+CCR4+CXCR3-, Th17.1 CD4+CCR6+CCR4CXCR3+, and Tregs were CD4+CD25+CD127low. Cells were evaluated using LSRFortessa flow cytometer equipped with FACSDiva (BD Biosciences) and analyzed with FlowJo software.

Results: We observed fewer CD4+ T cells in NF and P/F sarcoidosis compared to controls in PBMCs, consistent with the notion that CD4+ T cells are compartmentalized in the lungs, with recruitment from the blood to the lung. No difference was found between groups in Th17.1 PBMCs. Interestingly, more Th17 cells were present in NF sarcoidosis PBMCs vs. control with a trend of higher Th17 in P/F. We found more Treg cells in PBMCs in NF and P/F sarcoidosis compared to controls.

Discussion: NF and P/F sarcoidosis have significant difference CD4+ T cell Immunophenotypes compared to controls. This observation of potential differences in Th17/Th17.1 cells could relate to plasticity of Th17-cell subsets *in vivo* as they are transitioning from blood to the inflamed lung or homing to the lung. Recently,Th17.1 cells have been implicated as important in the disease process. However, there was no significant difference between NF and P/F sarcoidosis.


PBMC CD4+%
CD4+ T cells (% of lymphocytes)
Control
Sarc NF
Sarc P/F
PBMC Th1%
Th1% of CD4+ T cells
PBMC Th2%
Th2% of CD4+ T cells
PBMC Th17%
Th17% of CD4+ T cells
PBMC Th17.1%
Th17.1% of CD4+ T cells
PBMC Treg %
Treg% of CD4+ T cells

Oral

Chest computed tomography contributes information on the extent of physiologic impairment beyond chest X-ray alone in pulmonary sarcoidosis

William Lippitt[1], Bryan Benn[2], Isabel Cortopassi[3], Balasubramani Goundappa[4], Eduardo Barbosa[5], Wonder P. Drake[6], Erica Herzog[7], Kevin Gibson[4], Edward Chen[8], Laura Koth[9], David Lynch[10], Naftali Kaminski[7], Stephen Wisniewski[4], Nichole Carlson[1], Lisa Maier[10]

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Background: Sarcoidosis staging has primarily relied on the Scadding chest radiographic system, although chest CT is finding increased clinical use. Whether standardized CT assessment provides additional understanding of lung function beyond Scadding stage and demographics is unknown and the focus of this study.

Methods: We used the NHLBI study Genomics Research in Alpha-1 Anti-Trypsin Deficiency and Sarcoidosis (GRADS) sarcoidosis cases (N=351) with Scadding stage and Chest CT scans obtained in a standardized manner. One chest radiologist scored all CT scans with a visual scoring system, with a subset read again by another chest radiologist. We compared demographic features, Scadding stage and CT findings, and correlation between these measures. Associations between spirometry and DLCO and CT and Scadding stage were determined using regression analysis (N=318). Agreement between readers was evaluated using Cohen's Kappa.

Results: CT features were inconsistent with Scadding stage in about ~40% of cases. Most CT features assessed on visual scoring were negatively associated with lung function. Associations persisted for FEV1 and DLCO when adjusting for Scadding stage, although some CT feature associations with FVC became insignificant. Scadding stage was primarily associated with FEV1 and inclusion of CT features reduced significance in association between Scadding and lung function. Multivariable regression modeling to identify radiologic measures explaining lung function included Scadding stage for FEV1 and FEV1/FVC ($P<0.05$) and marginally for DLCO ($P<0.15$). Combinations of CT measures accounted for Scadding stage for FVC. Correlations among Scadding and CT features were noted. Agreement between readers was poor to moderate for presence/absence of CT features and poor for degree/location of abnormality.

Discussion: CT features explained additional variability in lung function beyond Scadding stage, with some CT features obviating the associations between lung function and Scadding. Whether CT features/phenotypes/endotypes could be useful for managing patients with sarcoidosis needs more study.

Poster

Clustering of Pulmonary Sarcoidosis Visual Assessment Scores

Jared Rieck[1], William Lippitt[1], Tasha Fingerlin[2], Shu-Yi Liao[2], Margaret Mroz[2], Briana Barkes[2], Ruchi Yadav[3], David Lynch[2], Lisa Maier[2], Nichole Carlson[1]
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Background: Patients with pulmonary sarcoidosis can exhibit markedly different disease trajectories, with prior research pointing to pulmonary hypertension, extensive fibrosis, and age as predictors of increased mortality risk. Increasingly, clinical evaluation of pulmonary sarcoidosis involves use of high-resolution computed tomography (HRCT) scans to allow detailed visualization of parenchymal abnormalities. Findings on HRCT in sarcoidosis are complex with many different abnormalities present on a single scan. Meanwhile, little is known about the associations of co-occurrence patterns of visually assessed abnormalities with disease severity. We used novel statistical clustering methods to establish the relationship between visually assessed pulmonary abnormalities and to identify patient subtypes of pulmonary sarcoidosis.

Methods: This study included individuals with sarcoidosis from two large medical centers who had an HRCT within one year of pulmonary function testing (PFT, N=638). Presence vs. absence of HRCT abnormalities were assessed by eight expert radiologists, and 13 features viewed as the most clinically relevant were included in analysis. To describe the level of association between visually assessed abnormalities, hierarchical clustering using a mutual information metric was used to produce network diagrams. To identify clusters of participants based on their HRCT abnormalities, we then applied model-based clustering (VarSelLCM). Linear regression was used to assess how disease severity differed among lung abnormality profiles based on PFT.

Results: The strongest associations were among visually assessed features of fibrosis, with strong associations also observed for lymphadenopathy. Six distinct clusters of patients were identified, with strong associations observed between cluster groups and PFT including the diffusion capacity of the lungs for carbon monoxide (DLCO, $p<0.001$), post-bronchodilator forced expiratory volume (FEV1, $p<0.001$), and pre- and post-bronchodilator forced vital capacity (FVC, $p<0.001$).

Discussion: The development of networks describing the relationship between visually assessed abnormalities shows how co-occurrence of abnormalities happen within an individual. The strong associations between sub-groups of pulmonary sarcoidosis patients and PFT indicate that standardized visual assessment scores of HRCT scans provide clinically important information that can be used to understand the severity of disease. Taken together, these results can be utilized to better understand how HRCT visual assessment can be utilized as an endpoint for clinical assessment of pulmonary sarcoidosis.

Poster

Collaboration and Development of Standard Operating Procedures for Prospective Evaluation and Collection of Biospecimens in Neurosarcoidosis

Susana Carolina Dominguez Penuela[1], Greer Waldrop[2], Paula Barreras[3], Evan Johnson[1], Arshdeep Kaur[2], Miranda Sullivan[2], Kathryn C. Fitzgerald[1], Samuel J. Pleasure[2], H. Benjamin Larman[4], Michael Wilson[2], Barney Stern[1], Jeffrey Gelfand[2], Carlos Pardo-Villamizar[1]
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Background: Sarcoidosis is a multisystem inflammatory disorder characterized by granulomatous inflammation of affected organs. Central or peripheral nervous system involvement is present in 5-26% of patients with sarcoidosis. There is a need to establish multicenter collaborations to prospectively define clinical profiles and neuroimaging findings and secure biological samples to advance our understanding of the pathogenesis of neurosarcoidosis (NS) and identify disease biomarkers. In a longitudinal observational cohort study, we aim to establish a comprehensive research protocol for clinical assessment of patients with NS to precisely characterize clinical phenotypes, pathogenic mechanisms, and biomarkers.

Methods: We designed a protocol to recruit newly diagnosed or established patients with sarcoidosis with evidence of active neurological disease (defined by clinical manifestations and imaging or cerebrospinal fluid findings). We used clinical tools to characterize neurological function longitudinally. We evaluated mobility, cognition, processing speed, and disability using the Timed 25-Foot Walk, Montreal Cognitive Assessment, Symbol Digit Modalities Test, and Expanded Disability Status Scale. To comprehensively assess patient reported outcomes, we evaluated health status, fatigue, pain, bladder and bowel control, mental health, perceived deficits, and walking scale. Abbreviated scale versions were selected when available. We established standard operating procedures for neuroimaging assessment, biospecimen collection, and biobanking.

Results: To date, 48 patients with active NS have been recruited at both sites (JHU n=28; UCSF n=20). 54% of the participants are female, with a median (IQR) age of 55 years (49-64). We have reached 32% of our recruitment goal.

Discussion: In this multicenter, prospective, observational, federally funded study of NS, we establish an approach to obtaining clinical and biological research data along with the standard-of-care clinical management to facilitate a reliable characterization of clinical and biological profiles in NS patients. This standardized approach can be applied to future studies of NS patients.

Poster

Do socioeconomic health disparities impact Pulmonary Sarcoidosis disease severity at presentation?

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[1]Virginia Commonwealth University, [2]Virginia Commonwealth University School of Medicine

Background: There is an increasing awareness of the importance of socioeconomic disparities in the disease course of sarcoidosis. This study evaluates the relationship between socioeconomic factors and severity of sarcoidosis at initial presentation to a sarcoid center of excellence.

Methods: This retrospective cohort study consisted of 729 patients with sarcoidosis who presented to Virginia Commonwealth University between April 2015 and April 2023. 678 patients had complete medical records which included age, sex, race, insurance status, residential ZIP code, and chest imaging. Disease severity was assessed using the Scadding stages and evidence of fibrosis on computed tomography (CT). We obtained area-level median household income by ZIP code from the US Census Bureau's 2022 5-Year American Community Survey. We summarized patient characteristics overall and by household income quartile, insurance provider, and race. All numerical measurements were summarized with mean and standard deviation. Categorical measures were summarized with frequencies and percentages.

Results: The study population demographic and Scadding stages are detailed in Table 1. Of patients with chest CTs available, 22% had fibrosis at presentation. Older age was associated with increased risk of fibrosis [OR (95% CI): 1.03 (1.01, 1.05) per 1 year increase in age]. There was no difference in fibrosis based on sex or representative median income. Black patients had 2.8 times the risk of fibrotic lung disease compared to White patients [2.83 (1.80, 4.44)].

Discussion: This study aids in our risk stratification and identification for high risk sarcoidosis. A limitation of our study was how socioeconomic status was stratified; there was no statistically significant difference in disease severity at presentation with regard to median zip code income. There was a statistically significant difference when considering age, race, and insurance status. Currently, there is no well-defined system of disease severity classification for the sarcoidosis population. The well-known Scadding stages were initially based upon plain radiographs prior to the advent of CT scans. The progression to overt fibrotic lung disease portends the worst prognosis; however, how to care for these patients is still unclear.

RACE	Percentage (%)/Response
Black	51
White	46
Other	3
INSURANCE	
Medicaid	22
Medicare	20
Private	53
No documented insurance	5
SCADDING STAGE	
Stage 0	46
Stage I	19
Stage II	15
Stage III	12
Stage IV	8

Poster

Does corticosteroid treatment affect biopsy results in patients with suspected Sarcoidosis?

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Background: The diagnosis of Sarcoidosis is usually performed by conducting a biopsy of suspected organs involved. The firstline therapy of sarcoidosis is corticosteroids, which in some cases are being prescribed before biopsy due to clinical suspicion and need (fever, weight loss, risk to an organ, pain, etc.). Whether biopsy can be effectively done in patients with suspected sarcoidosis and who are being treated empirically with corticosteroids is unknown, and decisions are based on expert opinion rather than evidence-based data. Our assumption is that similar to other inflammatory conditions, sarcoidosis pathologic findings will not be affected from prior corticosteroid treatment and biopsy can be effectively done during or after treatment if necessary.

Methods: To examine our hypothesis, we retrospectively collected data from all cases when sarcoidosis was highly suspicious due to typical clinical and radiologic presentation but biopsy was performed only after initiation of corticosteroids treatment.

Results: Data from 22 patients were collected. Patients' average age at biopsy was 52±9 years and 60% were males. The median length of treatment prior to the biopsy was 118 days and median accumulated dosage of corticosteroid was equivalent to 1200 mg of Prednisone. All patients had non-necrotizing granulomas with pathologic features typical of diagnosis of sarcoidosis. The pathologic diagnosis of sarcoidosis was confirmed regardless of the site of biopsy (in our cases, lung, lymph nodes, liver, skin and kidney) or the method of biopsy used.

Discussion: The results of the study demonstrate that the non-necrotizing granuloma pathologic structures, which are the hallmark of sarcoidosis, remains visible in spite of corticosteroid treatment. Our results also show that this observation remains valid for various biopsy sites and methods and is not influenced by the accumulated corticosteroid dosage. In conclusion, corticosteroid treatment for Sarcoidosis should not necessarily be withheld prior to biopsy, as non-necrotizing granuloma will likely remain visible for diagnostic confirmation.

Poster

Effect of B Cells on the Formation of Granulomas in Sarcoidosis

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Background: Sarcoidosis is an inflammatory disorder characterized by non-caseating granulomas. Granulomas develop through the complex interplay of several immune cells. The role each cell type has in the formation and persistence of non-caseating granulomas remains poorly understood. In M*ycobacterial* infections, B-cells control infection and participate in caseating granuloma formation. B-cell depletion with rituximab can be beneficial in some select cases of sarcoidosis, however the role of B cells in non-caseating granuloma formation is unclear. We utilized an *in vitro* granuloma model to study the impact of B cell depletion on granuloma formation in sarcoidosis. We hypothesized that B cells are required for granuloma formation in sarcoidosis.

Methods: We obtained peripheral blood mononuclear cells (PBMCs) from people with sarcoidosis (n=22), not currently on therapy, and we either depleted their samples of CD19+ cells (B cells) with anti-CD19 antibodies (confirmed with flow cytometry) or left them un-depleted. Both populations of cells were exposed to either uncoated or purified protein (PPD)-coated, DAPI florescent beads. *In vitro* granuloma formation was evaluated by counting the number and measuring the size of granulomas formed on days 4 and 7 with an epifluorescence microscope. Secreted cytokines were measured with a multiplex assay on day 7.

Results: Approximately ~45% (n=10) of the donors with sarcoidosis produced *in vitro* granulomas in the presence of PPDcoated beads. The size of granulomas formed were similar in both un-depleted and CD19+ depleted groups on both days 4 and day 7. The number of granulomas formed on day 7 was similar between un-depleted and CD19+ depleted groups, however there were more granulomas formed in the CD19+ depleted group on day 4.

Discussion: Our preliminary data suggests that B cells are not critical for *in vitro* granuloma formation in sarcoidosis. However early (day 4) granuloma formation was increased in the absence of B cells but normalized by day 7. This suggests a time-dependent role for B cells in non-caseating granuloma formation similar to that observed in *Mycobacterial* granulomas. Identification of the essential cells in granuloma formation will allow for the development of more specific therapies in sarcoidosis and improved outcomes.

Poster

Efzofitimod: Immunomodulation of Myeloid Cells and Therapeutic Potential in Pulmonary Sarcoidosis and Interstitial Lung Diseases

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Background: Pulmonary sarcoidosis is a complex interstitial lung disease (ILD) characterized by inflammation and fibrosis that lacks effective treatments. Emerging research highlights myeloid cells as key drivers of inflammation and fibrosis in ILDs. Efzofitimod, a myeloid cell immunomodulator currently in Phase 3 trials for pulmonary sarcoidosis, targets neuropilin-2 (NRP2), a receptor upregulated on myeloid cells in inflammation sites. In murine ILD models, efzofitimod reduces inflammation and fibrosis, A Phase 1b/2a trial in pulmonary sarcoidosis patients showed promising dose-dependent improvements in lung function and reduction of pro-inflammatory serum biomarkers.

Methods: To investigate efzofitimod's mechanism of action we have previously looked at the elicited responses in primary human monocyte-derived macrophages via live cell imaging, cell surface marker expression by flow cytometry, RNA sequencing and analysis of secreted proteins, highlighting efzofitimod's anti-inflammatory effects in cells from both normal healthy donors and sarcoidosis patents. We have expanded this work to include analysis of activated signaling pathways by Western Blot and ELISA.

Results: To build on these findings, new data will be presented that delves deeper into the downstream signaling pathways relevant to efzofitimod's mechanism of action.

Discussion: These insights underscore efzofitimod's potential therapeutic impact by targeting myeloid cells in sarcoidosis and suggest broader applicability across chronic inflammatory and fibrotic diseases.

Poster

Evaluating the Toronto Consensus Criteria as a Diagnostic Tool for Sarcoidosis Associated Small Fiber Neuropathy

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Background: Small fiber neuropathy (SFN) is an understudied but important complication of sarcoidosis as it can significantly impact quality of life. There is currently no gold standard to diagnose sarcoidosis-associated SFN, making the diagnosis difficult. Various screening tools such as Toronto Consensus Criteria (TCC) for SFN, the Utah Early Neuropathy scale (UENS) and skin biopsy (for intraepidermal nerve fiber density/small fiber involvement) may be used for diagnosis. This study aims to determine if the TCC for SFN is a valid screening instrument for SFN as compared to physician impression of neuropathy (PIN).

Methods: This is a cross-sectional study comparing 20 patients with biopsy-proven sarcoidosis with positive and negative TCC scores. Patients who scored "possible, probable, and definite" for TCC were grouped together as "positive" given the low number of participants, and those who did not meet the criteria were considered negative. The patients were also evaluated with UENS, EMG, and skin biopsy.

Results: Twenty patients, 70% female, aged 30 to 70 years, participated in the study. 10/13 PIN patients had positive TCC scores, and 3/13 had negative TCC scores. Of non-PIN patients, only 1/7 had a positive TCC score (p=0.0198). In addition, patients with a positive TCC score had a higher mean UENS score (7.8) compared to those with a negative score (5.74, p=0.193). 40% of patients with a positive TCC score had an abnormal EMG compared to 22.2% of patients with a negative score (p=0.628). Only 4/8 skin biopsies were abnormal; 2 had a positive TCC score and 2 had a negative score.

Discussion: The correlation between PIN and TCC was the only correlation that was statistically significant. Patients who scored positive on the TCC were also more likely to have more symptoms on the UENS and an abnormal EMG although these correlations were not statistically significant. An abnormal skin biopsy did not correlate well with the TCC score because most patients had a normal skin biopsy. This study is limited due to a small sample size. In the future, we recommend larger studies to help determine if TCC is a valid scoring tool.

Poster

Evidence for Casual Relationships Between Sarcoidosis and Metabolic Phenotypes

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Background: Sarcoidosis is a multisystem disease of unknown etiology characterized by the formation of non-necrotizing granulomas. The most affected organ is the lungs, but it can affect many different organs. Multiple factors, including environmental and genetics, can affect the development and outcome of the disease. Co-morbidities include metabolic conditions, cardiovascular disease, and many more. Metabolic phenotypes, such as blood pressure, obesity, cholesterol, and glycemic traits (Fig. 1), have increased with sarcoidosis, though no genetic relationship between them has been established.

This study investigated the causal relationship between metabolic phenotypes and sarcoidosis, focusing on two clinical phenotypes: Löfgren's syndrome (LS) and non-Löfgren's syndrome (nonLS).

Methods: To ensure the robustness of our findings, we employed a well-phenotyped sarcoidosis cohort from Sweden, consisting of 7000 individuals (2000 cases and 5000 controls). Summary statistics of metabolic phenotypes were obtained from public databases. Our approach was based on Mendelian Randomization methods (Fig. 2) for assessing causality. Selection of independent variables was based on genome-wide significance (p-value <5e-8, minor allele frequency > 0.01, and no linkage disequilibrium (LD r^2 = 0.001 and 10 Mbp window). Heterogeneity and horizontal pleiotropy assessments were evaluated using Cochrane's Q value and MR-Egger intercept. Detection of outliers was performed using MR-PRESSO. Sensitivity analysis was performed using leave-one-out analysis.

Results: MR Analysis showed that there is no direct causal link between obesity and sarcoidosis but rather a complex relationship where obesity-related traits adjusted by smoking or by physical activity were linked to sarcoidosis LS and nonLS ($p < 0.05$), suggesting a gene-environment and gene-physical activity interaction between obesity and sarcoidosis. Glycemic traits, i.e., Fasting glucose and 2h-glucose were found to have a causal association with non-LS sarcoidosis ($p < 0.05$). No causal link between blood pressure or lipid traits and sarcoidosis was found.

Discussion: Our study sheds light on the complex relationship between sarcoidosis and obesity, emphasizing the need to consider mediators such as physical activity and smoking when investigating obesity in sarcoidosis. Our findings also suggest that glucose is implicated in sarcoidosis. However, further analysis is required to examine these relationships in more depth, underlining the urgency and importance of future research in this area.

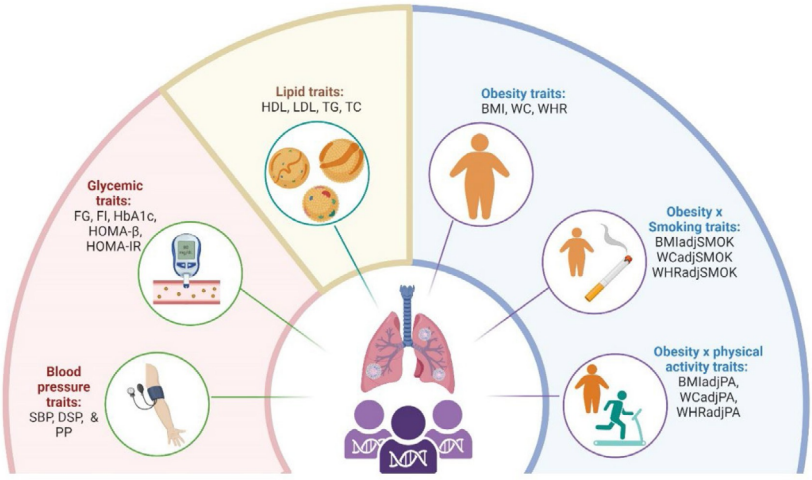
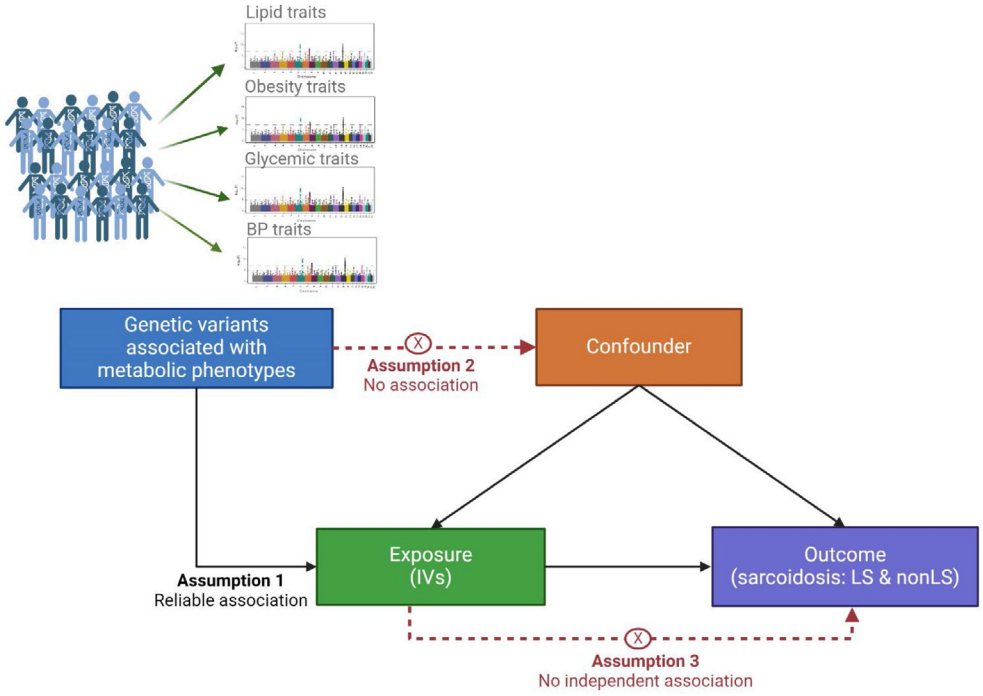


Fig. 1. Conceptualization of metabolic phenotypes on sarcoidosis risk (created with BioRender.com)



Poster

Factors affecting corticosteroid adherence in sarcoidosis patients

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Background: Medication nonadherence is a major issue in sarcoidosis. In one university sarcoidosis clinic, 66 percent of the patients reported nonadherent behavior. We measured corticosteroid medication adherence and its potential causes using patient reported outcome measures (PROs) in patients attending a university sarcoidosis clinic.

Methods: Sarcoidosis patients who were currently receiving corticosteroid medication were eligible for this study. Information concerning demographics, socioeconomic status, and corticosteroid side effects was elicited from the patients. Pulmonary function and chest radiographic data were also obtained. The patients completed several PROs, including the Medication Adherence Response Scale-10 (MARS-10), a validated measure for patient medication adherence. The patients also completed several other validated PROs concerning their attitudes toward medications, strength of the patient-doctor relationship, anxiety, depression, level of function, and quality of life.

Results: 132 sarcoidosis patients completed this study: mean age 55+12 years; 59% male; 73% white and 26% black. The lung was the target organ for therapy in 54%. Laboratory results included FVC 80+20%pred, FEV1 73+22%pred; 61% had a Scadding 2-4 chest radiograph. The average daily dose of prednisone was 7.5+10mg and the total dose of prednisone over the previous year was 2700+3397mg. Using a MARS-10 cutoff of >6 as adherent, 101/132 (77%) were adherent and 31/132 (23%) were not adherent. The following variables were associated with better adherence (Table 1): the patient-doctor relationship, patient satisfaction with life, the patients' sense of need for medication, number of organs involved with sarcoidosis, and length of time receiving prednisone. The following variables were inversely associated with adherence: Scadding stage, anxiety, depression, corticosteroid side-effects, concerns about the harmful effects of taking medicines, and specific concerns of corticosteroids. Race, age, gender, spirometry, number of organs involved with sarcoidosis, and Scadding stage were not associated with corticosteroid adherence. In a multi-logistic regression, only concerns about the harmful effects of taking medicines was negatively associated with adherence.

Discussion: Patient concern about the negative effects of medications is a major driver of corticosteroid nonadherence in sarcoidosis patients. These data suggest that interventions to improve patient understanding about the use of medications may significantly improve corticosteroid adherence.

***Table 1**: Association of Mars 10 (+ is better medication adherence) with other variables using Pearson (n=132)*

variable	Pearson Corr	P value
PDRQ (Doctor-patient relationship)	0.47	0.00 ***
SAT Satisfaction	0.20	0.01***
SAT Daily activities	0.07	0.37
FVC	0.14	0.12
FEV1	0.07	0.4
FEV1/FVC	0.09	0.3
HADS Anxiety	-0.32	0.0002***
HADS Depression	-0.26	0.002***
BMQ Medication Necessity	0.31	0.0003 ***
BMQ Medication Concerns	-0.37	<.0001 ***
BMQ Medication overuse	-0.31	0.0003 ***
BMQ Medication Harm	-0.37	0.000 ***
Daily dose of corticosteroids	0.08	0.33
Corticosteroid side effect inventory	-0.17	0.0524***
Number WASOG Organs	0.54	0.05***
Time between first use of prednisone and enrollment	0.27	0.0021***
Time between diagnosis and study enrollment	-0.02	0.7833

*** indicates significance at a .01 level

Poster

Feasibility of a mHealth App intervention to improve sarcoidosis-associated fatigue

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Background: Sarcoidosis is a multisystem inflammatory disease that can result in significant morbidity. Sarcoidosis associated fatigue (SAF) is the most reported symptom by sarcoidosis patients, is strongly associated with stress and negative mood states and has a significant negative impact on quality of life (QOL). Pulmonary rehabilitation and breathing awareness meditation can improve fatigue, but access to in-person programs is limited by cost and availability in the U.S. where sarcoidosis disproportionately impacts minorities and underserved populations. The use of mHealth has emerged as a viable method of deploying self-management techniques to improve a patient's quality of life.

Methods: We developed the Sarcoidosis Patient Assessment and Resource Companion (SPARC) App as a self-management tool to improve stress and fatigue using education modules and breathing awareness meditation (BAM) and investigated its feasibility in a 3-month randomized control trial comparing use of the SPARC App versus controls in patients with SAF. Usability and Feasibility were assessed using utilization rates, standardized usability scales, and key informant interviews.

This project was supported by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health under award number 5R21EB025525-02.

Results: A total of 49 patients with SAF, defined as a fatigue assessment scale (FAS) score ³ 22 were randomized (25 to SPARC and 24 to control). Baseline FAS and stress (PSS-10) scores were similarly elevated in both groups. Only 40% of those in the SPARC group were considered adherent (predefined as completing ³70% of daily BAM sessions). Nonadherent patients were younger and more likely to be black, employed full time, and have lower education levels. Usability scores were generally favorable (uMARS functionality 3.7, engagement 3.1), and facilitators/barriers to app use were explored. FAS, PSS-10, and overall quality of life (KSQ) scores improved in the SPARC group compared to controls, and there was a dose-response observed in those who were adherent versus nonadherent.

Discussion: Our data suggests that SPARC App may be effective in reducing fatigue and stress and improving QOL in sarcoidosis patients, but deployment of such mHealth tools still faces some barriers in underserved populations.

Poster

Fibrotic Sarcoidosis Associated PH on Inhaled Treprostinil: A Descriptive Study

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Background: Sarcoidosis associated pulmonary hypertension (SAPH) is multifactorial and often complicated by significant parenchymal disease. There is limited data on pulmonary vasodilator therapy and no approved pulmonary vasodilators for management of SAPH. Inhaled Treprostinil has been approved for fibrotic ILDs and data is suggestive of some improvement in FVC in that group on therapy. We describe a case series of 21 patients on Inhaled Treprostinil in fibrotic SAPH.

Methods: Retrospective, single center, study with an inclusion criterion of a diagnosis of fibrotic SAPH and had been treated with inhaled Treprostinil. Descriptive statistics were performed.

Results: Twenty one patients met our inclusion criterion. The majority of patients were on other vasodilators in addition to Treprostinil. Mean age was 63.8. There were 10 males to 11 females with a predominance of 16 African American patients. Regarding hemodynamics, the pulmonary vascular resistance (PVR) on diagnosis was 6.8 Woods Units (WU) and increased to 7.8 WU at follow-up. The average FVC at diagnosis was 58.2% predicted and increased to 61.3% predicted at follow-up. The average 6MWD at diagnosis was 236.9m and increased to 242m at follow-up . Quantification of lung fibrosis by a radiologist revealed an average fibrosis score of 11/18 points. Regarding outcomes, 4 patients passed away and one was transplanted.

Discussion: Patients with fibrotic SAPH treated with pulmonary vasodilators including inhaled Treprostinil had an improvement in their 6-minute walk distance and FVC similar to the findings found in the INCREASE trial. Patients had severe PH with an average PVR greater than 5 WU. These findings should prompt a prospective study of fibrotic SAPH to further assess role of inhaled Treprostinil in SAPH.

Variables	Average (SD)
Gender	
Male	10
Female	11
Race	
Caucasian	3
AA	16
Unidentified	1
Hispanic	1
Comorbidities	
Cardiac disease (excluding cardiac sarcoidosis)	8
CKD	10
Liver Disease	6
Former smoker	14
Diabetes	7
Outcome	
Exacerbation	17
Death	4
Transplanted	1
Right heart catheterization at diagnosis	
mPAP	41 mmHg (10.7)
Pulmonary Vascular Resistance	6.8 WU (3.2)
PCWP	12.5 mmHg (5.6)
Cardiac Output	4.7 L/min (1.3)
Cardiac Index	2.4 L/min/m2 (0.7)
BNP @ RHC	312 pg/mL (291.3)
Right heart catheterization after initiation of treatment	
mPAP	44.1 mmHg (11.3)
Pulmonary Vascular Resistance	7.8 (4.6)
PCWP	12.2 mmHg (5.1)
Cardiac Output	4.6 L/min (1.2)
Cardiac Index	2.3 L/min/m2 (0.5)
BNP @ Repeat RHC	1171 pg/mL (1800)
Pulmonary Function Testing at Diagnosis	
FEV1	54.8 % (21.5)
FVC	58.2 % (25.3)
FEV1/FVC	69.5 (13)
TLC	66.5 % (11.5)
DLCO	27.1 % (9)
6 MWD	236.9 m (72.2)
O2 requirements	6.1 L (4.2)
Pulmonary Function Testing after initiation of treatment	
FEV1	52.2% (20.4)
FVC	61.3% (16)
FEV1/FVC	65.8 (12.7)
TLC	65.2% (11.9)
DLCO	24.5 % (10.5)
6 MWD	242 m(138)

Oral

Gut Microbiota Induces Pulmonary CD4+ IL-6+ Expression Through PD-1/HIF-1α Signaling in Mice

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Background: Sarcoidosis is an interstitial lung disease (ILD) characterized by increased systemic interleukin 6 (IL-6) expression in patients with worse clinical outcomes. In addition, increased expression of programmed death 1 (PD-1) and hypoxia inducible factor 1 alpha (HIF-1α), both known inducers of IL-6 expression, are also associated with poor prognosis in sarcoidosis subjects. Recent independent investigations demonstrate that dysbiotic gut microbiota drive pulmonary CD4+ IL-6+ expression in murine models of ILD; however, there has been limited further investigation into the mechanism underlying, and possibly connecting, these correlates of severity.

Methods: We conducted flow cytometric analysis, immunohistochemical and molecular analysis of human peripheral blood mononuclear cells from healthy controls and sarcoidosis patients to determine the role of PD-1 signaling on IL-6 expression. To further define the molecular mechanisms driving pulmonary IL-6 expression in CD4 T cells, we conducted fecal material transfer on germ-free mice, using stool with diverse microbial communities or dysbiotic stool, followed by intranasal bleomycin installation. This was followed by immunoblot analysis of lung specimens for HIF-1α expression.

Results: Immunohistochemistry showed elevated IL-6 levels in sarcoidosis lymph nodes compared to normal tissue samples. Flow cytometric analysis of sarcoidosis patients with poor outcomes demonstrate high levels of PD-1+IL-6+ CD4+ T cells, as well as in the murine model of bleomycin-induced pulmonary fibrosis. Blockade of the PD-1 signaling pathway using anti-PD-1 antibodies resulted in a significant reduction in IL-6 expression from sarcoidosis CD4+ T cells. Additionally, PD-1 knockout mice exhibit significant reductions in IL-6 expression from pulmonary CD4+T cells. Lastly, gavage of dysbiotic stool prior to intranasal bleomycin instillation into germ free mice showed increased pulmonary HIF-1α expression.

Discussion: Taken together, this work identifies a critical, previously unrecognized mechanism by which gut microbiota can induce IL-6 expression, specifically through PD-1/HIF-1α signaling, and ultimately modulate the lung phenotype and outcome during ILD.

Poster

Higher Area Deprivation Index is associated with decreased access to a pulmonologist among patients with an ICD diagnosis of sarcoidosis in a single-center retrospective cohort

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Background: Among cohorts established with a sarcoidosis specialist, Black and female patients are more likely to present to care with multiorgan involvement and patients with lower socioeconomic status (SES) are more likely to face barriers to care. However, barriers to accessing care contribute to health disparities and limited data exist regarding how sociodemographic factors affect referral or access to specialty care for sarcoidosis.

Methods: We retrospectively identified all adult patients with a new ICD diagnosis of sarcoidosis between 10/30/2011 and 10/30/2021 at a large tertiary care center. We excluded patients who did not have requisite data or were seen by pulmonary medicine prior to diagnosis. Chi-squared test, Wilcoxon rank sum test, or Fisher's exact test were performed to examine demographic differences between (1) patients referred versus not referred to pulmonary medicine and among those referred (2) patients seen versus not seen by a pulmonologist within 1 year of diagnosis. We used Area Deprivation Index (ADI), derived from patients' home addresses, as a surrogate for SES.

Results: 1027 patients were identified with a new ICD diagnosis of sarcoidosis. The cohort was 55% (569) male, 34% (349) Black or African American, and had an average ADI of 67 (48, 84). 27% (279) of patients were referred to pulmonary medicine. Insurance type and younger age were associated with increased referral while sex, race, and ADI were not associated with referral status. Among patients referred, 22% (61) did not see a pulmonologist. Among those referred, patients with private insurance were more likely to see a pulmonologist. The average ADI of patients who did not see a pulmonologist was 72 (58, 91), significantly higher than the ADI of patients who saw a pulmonologist.

Discussion: Although sex, race, and ADI were not associated with receiving a referral to pulmonary medicine, our results suggest that a higher ADI, a surrogate for lower SES, is a barrier to transitioning from primary to specialty care among patients with a new ICD diagnosis of sarcoidosis. Additional research and interventions are needed to mitigate this healthcare disparity and ensure sociodemographic factors such as SES do not limit access to specialty care among patients with sarcoidosis.

Poster

Investigation of Sarcoidosis-associated Neuropathy: Challenges with Diagnosis of Small Fiber Neuropathy

Kristen Caldwell[1], *Huzaefah Syed*[1], *Kelly Gwathmey*[1], *Sindhuja Koppu*[1]
[1]Virginia Commonwealth University School of Medicine

Background: Small fiber neuropathy (SFN) is an under recognized complication of sarcoidosis which can significantly impair individuals' physical functioning and quality of life. Diagnosis includes both clinical and histologic testing; however, diagnosis can be difficult in this patient population due to lack of gold standard diagnostic criteria and variable presentations. This study seeks to evaluate potential screening tools and histologic data in the assessment of patients with sarcoidosis-associated SFN.

Methods: This is a cross-sectional study comparing 20 patients with biopsy-confirmed sarcoidosis with and without a physician impression of neuropathy (PIN and non-PIN, respectively). The cohort was evaluated according to the Utah Early Neuropathy Scale (UENS) for small and large fiber sensory and distal motor function on exam, Toronto Consensus Criteria (TCC) for SFN, electromyography (EMG) for large fiber involvement, and skin biopsy for small fiber involvement.

Results: Twenty patients were recruited, ages 30 – 70 years old, and 70% female. There were 13 participants with PIN and 7 with non-PIN. Of those with PIN, 76.9% were positive for SFN according to the TCC compared to 14.3% with non-PIN (p =0.02). On the UENS, those with PIN had a higher mean score (M=8.23, SD 5.33) compared to those with non-PIN (mean=4.86, SD=5.73, p=0.22). With skin biopsy,1 of 11 with PIN had an abnormal skin biopsy compared to 3 of 7 with non-PIN (p=0.25). Finally, 30.8% of participants with PIN had an abnormal EMG compared to 28.6% of those with non-PIN (p=1.00).

Discussion: Participants with PIN were more likely to test positive for SFN using the TCC and have a higher UENS score, though a statistically significant difference was found only with TCC. By contrast, there was no statistically significant difference in those with PIN or without PIN on EMG and skin biopsy, though these results are almost certainly confounded by small sample size. Although skin biopsy remains the histologic gold standard for SFN, our findings suggest this may be an inadequate diagnostic tool in this condition. We recommend future studies with a larger sample size to evaluate for correlation of UENS scoring and graded TCC classification as potential alternative screening tools for sarcoidosis-associated SFN.

Poster

Longitudinal Assessment of Pulmonary Sarcoidosis Using Quantitative Parenchymal CT Texture

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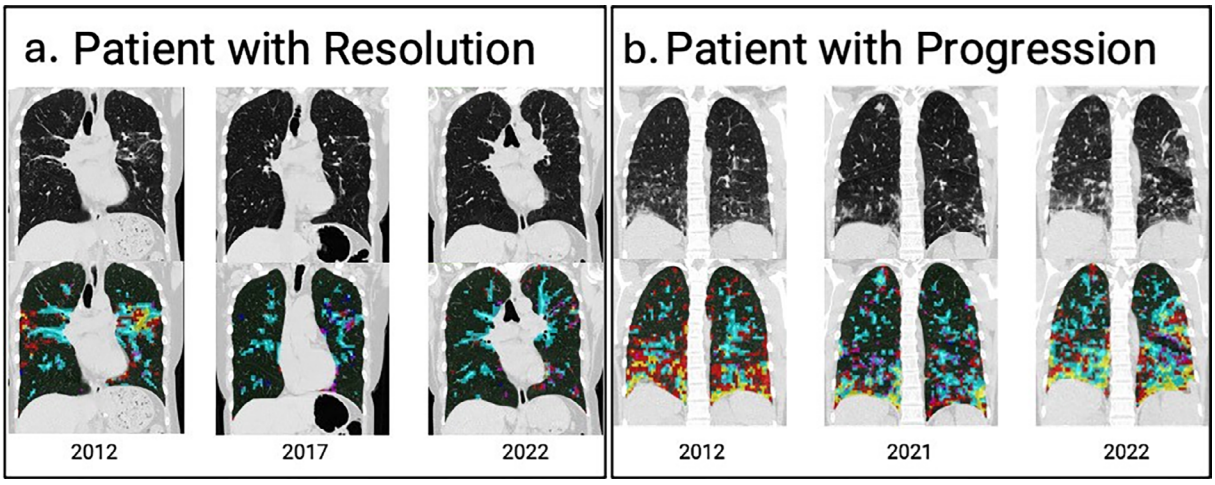
[1]University of Iowa

Background: Computed tomography (CT) is the preferred modality in the clinic to assess pulmonary sarcoidosis. However, current radiographic assessments rely on qualitative scoring methodologies that are labor intensive, subject to reader expertise, and largely focus on identification of opacities and lung fibrosis. Advanced parenchymal assessment using texture analysis can provide robust, quantitative metrics that provide greater insights into the extent of disease and in tracking regional progression.

Methods: Clinical non-contrast, inspiratory CT scans, from three time points, were retrospectively selected from five patients with varying disease trajectories, diagnosed with pulmonary sarcoidosis, for an initial methodological assessment. Patients were enrolled in a larger research study and provided informed consent for clinical data access. Datasets were selected based on optimal acquisition and reconstruction parameters (end-inspiratory, thin-slice, Q30f reconstruction kernel). Analysis involved the Adaptive Multiple Feature Method (3D-AMFM), which utilizes a Bayesian classifier and 24 volumetric texture features, to label lung regions as either: Normal, ground glass, reticulation, Emphysematous, Broncho Vascular bundle, Honeycombing, or consolidation.

Results: CT texture analysis shows marked changes between timepoints in each patient. Spatially matched (to the extent possible) coronal slices from two patients (three timepoints) can be seen in Figure 1. The first patient (Figure1a) demonstrates inflammation (ground glass) in 2012, which resolves in 2017, and does not recur at follow-up (2022). This patient's quantitative analysis suggests an increase in normal lung from 78% to 85%. In contrast, another patient (Figure1b) initially experiences decreased ground glass and reticulation between the first and second timepoints, followed by significantly increased lung abnormalities in the subsequent year. The percent of normal lung increased from 51% to 61% from 2012 to 2021 and fell to 49% in 2022, demonstrating the efficacy of image analysis tools to identify potential exacerbating agents to deliver better patient outcomes.

Discussion: Parenchymal texture analysis using AMFM provides robust metrics to track disease progression or resolution. Previously AMFM-defined texture demonstrated prediction of IPF progression (Salisbury ML et al. PMCID: PMC5387708). Here, we demonstrate that texture analysis can be extended to spatially match longitudinal datasets and potentially track progression of lobar and sub-lobar segments, to objectively and quantitatively evaluate the impact of therapeutic interventions.


a. Patient with Resolution
2012
2017
2022
b. Patient with Progression
2012
2021
2022

Poster

Mimicking the Great Mimicker: Poorly Differentiated Adenocarcinoma Mimicking Extrapulmonary Sarcoidosis

Bijal Patel[1], *Dr. Christopher Izzo*[1], *Dr. Leela Krishna Teja Boppana*[1], *Dr. Kristyn Lewis*[1], *Dr. Nimeh Najjar*[1]
[1]UF Health Jacksonville

Background: Sarcoidosis is a multisystemic illness characterized by the presence of noncaseating granulomas that can radiographically mimic malignancy. However, patients with sarcoidosis also have an increased risk of developing hematologic malignancies (particularly lymphoma), solid tumors (melanoma, nonmelanoma skin cancer, neoplasms of the cervix, liver, uterus, testicles, and lung) and paraneoplastic syndromes. Diagnosis of malignancy in these patients is often delayed due to a misdiagnosis of progressive sarcoidosis.

Results: A 63-year-old female with biopsy confirmed pulmonary sarcoidosis presented to the hospital with a 3-week duration of left lower back and abdominal pain. Computed tomography (CT) of the abdomen/pelvis revealed a 3 cm soft tissue density within the extrahepatic biliary system, a soft tissue pelvic mass adjacent to the cul-de-sac, soft tissue deposits within the right external oblique, peripancreatic and periaortic region, and a 2 cm soft tissue nodule at the left renal pelvis causing moderate to severe left hydronephrosis. Chest CT angiography demonstrated perilymphatic pulmonary nodules, bilateral mediastinal and hilar lymphadenopathy with mass effect on the right upper lobe pulmonary artery, and non-specific deposits within the thoracic soft tissues. These findings were new compared to CT imaging 8 years prior. Additionally, the patient endorsed adherence with her sarcoidosis treatment of 10 mg prednisone daily and methotrexate 15 mg weekly. Due to a suspicion for a secondary disease process, endobronchial ultrasound fine needle aspiration (EBUS-FNA) was performed of the subcarinal and left internal lobar lymph nodes (LN) which revealed benign bronchial cells in a background of lymphocytes. A right upper lobe endobronchial biopsy was also benign. FNA of a right retroperitoneal LN was pursued and showed a poorly differentiated adenocarcinoma. Immunostaining was diffusely positive for calretinin, MOC31, AE1/AE3, and p53 and focally positive for CDX-2 and CK 5/6. Flow cytometry from lymph node biopsies did not demonstrate immunophenotypic lymphocyte abnormalities. She is pending outpatient oncology evaluation at the time of writing this report.

Discussion: It is crucial that practitioners consider coexistent malignancy in patients with sarcoidosis to allow timely diagnosis and treatment. Currently, there is scant literature regarding management of sarcoidosis in these situations and a multidisciplinary approach is encouraged.

Poster

Multi-Omic Signatures of Sarcoidosis and Progression in Bronchoalveolar Lavage Cells

Dr. Nancy Lin[1], Dr. Iain Konigsberg[2], Dr. Shu-Yi Liao[1], Ms. Cuining Liu[2], Ms. Kristyn MacPhail[1], Ms. Margaret Mroz[1], Ms. Elizabeth Davidson[2], Dr. Clara Restrepo[1], Dr. Sunita Sharma[2], Dr. Li Li[1], Dr. Lisa Maier[1], Dr. Ivana Yang[2]
[1]National Jewish Health, [2]University of Colorado

Background: Sarcoidosis is a heterogeneous granulomatous disease with no accurate biomarkers of disease progression. Therefore, we profiled and integrated the DNA methylome, mRNAs, and microRNAs to identify molecular changes associated with sarcoidosis and disease progression that might illuminate underlying mechanisms of disease and potential biomarkers.

Methods: Bronchoalveolar lavage cells from 64 sarcoidosis subjects and 16 healthy controls were used. DNA methylation was profiled on Illumina HumanMethylationEPIC arrays, mRNA by RNA-sequencing, and miRNAs by small RNA sequencing. Linear models were fit to test for effect of diagnosis and phenotype, adjusting for age, sex, smoking, and principal components of the data. We built a supervised multi-omics model using a subset of features from each dataset.

Results: We identified 1,459 CpGs, 64 mRNAs, and 5 miRNAs associated with sarcoidosis versus controls and 4 mRNAs associated with disease progression. Our integrated model emphasized the prominence of the PI3K/AKT1 pathway, which is important in T cell and mTOR function. Novel immune related genes and miRNAs including *LYST*, *RGS14*, *SLFN12L*, and hsa-miR-199b-5p, distinguished sarcoidosis from controls. Our integrated model also demonstrated differential expression/methylation of *IL20RB, ABCC11, SFSWAP*, *AGBL4*, miR-146a-3p, and miR-378b between non-progressive and progressive sarcoidosis.

Discussion: Leveraging the DNA methylome, transcriptome, and miRNA-sequencing in sarcoidosis BAL cells, we detected widespread molecular changes associated with disease, many which are involved in immune response. These molecules may serve as diagnostic/prognostic biomarkers and/or drug targets, although future testing is required for confirmation.

Poster

Multi-organ Sarcoidosis-like Reactions Associated with TNF-alpha Inhibition Therapies: A Case Series

Dr. Jana Lovell[1], Dr. Danya Waqfi[2], Dr. Joban Vaishnav[1], Dr. Nancy Lin[2], Dr. Edward Chen[2], Mrs. Kayla Nyakinye[2], Mrs. Victoria Wotorson[2], Ms. Cherie Livingston[1], Dr. Michelle Sharp[2], Dr. Nisha Gilotra[1]

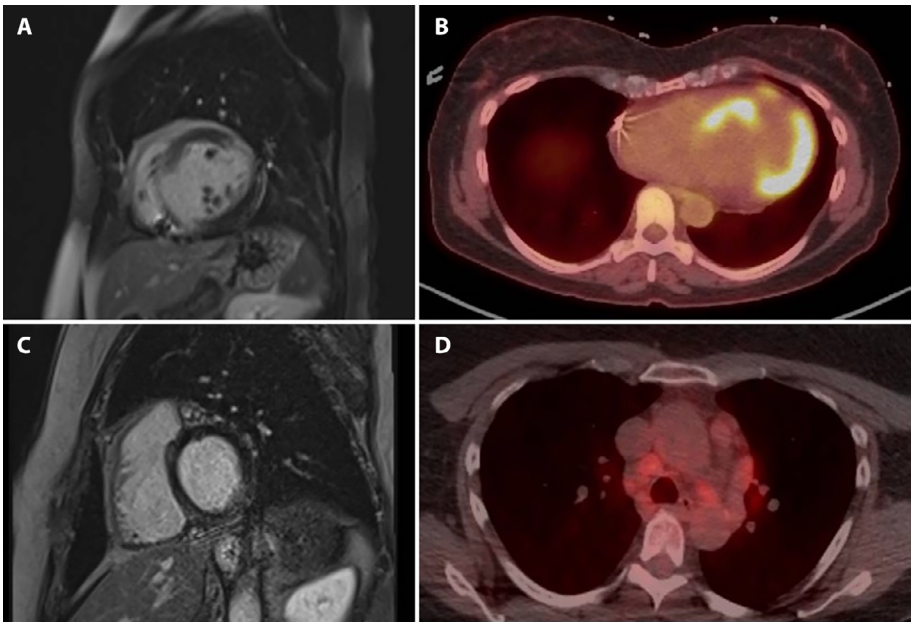
[1]Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA., [2]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Johns Hopkins University, Baltimore, MD

Background: Sarcoidosis is characterized by multi-organ granulomatous inflammation. While tumor necrosis factor-α inhibitors (TNFαi) have a well-established role in the treatment of sarcoidosis, specific TNFαi have been associated with sarcoidosis-like granulomatous reactions. Here, we report three cases of TNFαi-associated multi-organ sarcoidosis-like reactions.

Results: A 57-year-old patient with psoriasis treated with etanercept for three years presented with dyspnea and complete heart block. Echocardiography revealed reduced left ventricular systolic function. She had mild non-obstructive coronary artery disease on coronary angiography. Cardiac MRI (CMR) showed transmural late gadolinium enhancement (LGE) in the basal septal and mid-lateral left ventricle (LV) (Figure 1A). Cardiac FDG-PET showed multifocal patchy LV (Figure 1B) and hilar/subcarinal nodal FDG uptake. Etanercept was discontinued and she was initiated on prednisone and mycophenolate mofetil. Follow-up FDG-PET showed resolution of FDG uptake.

1. A 55-year-old patient with ankylosing spondylitis presented with cough eight months after starting certolizumab. Chest imaging revealed mediastinal adenopathy and mediastinal lymph node biopsies revealed non-necrotizing granulomatous inflammation with negative cultures. Given palpitations and right bundle branch block, she underwent CMR that showed LGE in the basal inferior/inferolateral LV (Figure 1C). On FDG-PET, FDG uptake was seen in the basal lateral/inferolateral LV, mediastinal lymph nodes, and spleen (Figure 1D). Certolizumab was discontinued and she was initiated on prednisone, methotrexate, and infliximab with improvement in respiratory symptoms. Follow-up FDG-PET is pending.
2. A 67-year-old patient with rheumatoid arthritis on etanercept for five years presented with atypical chest pain. CT chest showed mediastinal lymphadenopathy and scattered pulmonary nodules. Pulmonary function tests revealed mild restrictive pattern with reduced diffusion capacity. Bronchoscopy with lymph node biopsy revealed non-necrotizing granulomatous inflammation and negative cultures. Etanercept was stopped with improvement in lung function testing and resolution of pulmonary nodules.

Discussion: We describe three cases of TNF-αi-induced sarcoidosis-like disease that improved with removal of the presumed offending TNF-αi, with two patients also transitioning safely to alternative TFN-αi agents. Etanercept and certolizumab do not induce cytotoxic complement-induced cell lysis, which may indicate a potential mechanism underlying these sarcoidosis-like reactions. Further studies are needed to understand the complex role of TNFα inhibition in granulomatous inflammation.


A
B
C
D

Poster

Navigating Diagnostic Complexity: An Unusual Presentation of Cardiac Sarcoidosis

Dr. Do Park[1], Dr. Elizabeth Hardin[1]
[1]University of Texas Southwestern

Background: An enigmatic disease, sarcoidosis is a multi-system, granulomatous inflammatory disease that can involve any organ system but most commonly affects the lungs, eyes, and skin. Clinically manifest cardiac sarcoidosis (CS) is prevalent in only 5% of patients who have systemic sarcoidosis. However, based on autopsy and imaging studies, 25% of patients with sarcoidosis have subclinical or asymptomatic cardiac involvement. Cardiac involvement is a leading cause of morbidity and mortality in patients with sarcoidosis. The most common clinical manifestations of CS include heart block, malignant ventricular arrhythmias including sudden cardiac death, and heart failure.

Results: A 19-year-old woman with no prior medical history presented after a pre-syncopal episode. She was found to have sustained, monomorphic ventricular tachycardia and underwent electrical cardioversion with successful restoration of sinus rhythm. Workup was notable for large soft tissue "mass" in the right ventricle attached to the interventricular septum with extensive late gadolinium enhancement on cardiac magnetic resonance imaging with additional soft tissue mass encasing the inferior vena cava and in the right paratracheal region. PET-CT showed FDG avidity of the soft tissue abnormality in the interventricular septum and inferior vena cava with involvement of both the right atrium and right ventricle. Additionally, there were FDG avid lymph nodes in the thorax. Endomyocardial biopsy was pursued and notable for scattered interstitial T-cells and macrophages, negative for amyloid deposits, and overall non-diagnostic. Transbronchial biopsy of the mediastinal lymph nodes revealed non-caseating granulomas and multinucleated giant cells without evidence of malignancy or infection on extensive staining. The diagnosis of sarcoidosis with cardiac involvement was made.

Discussion: CS presenting as cardiac tumor is atypical and can be challenging to diagnose definitively. The yield of endomyocardial biopsy for the definitive diagnosis of CS is highly specific but not sensitive with a yield of around 25%. Therefore, clinicians rely heavily on clinical criteria based on expert consensus guidelines. These guidelines recommend an extra-cardiac biopsy suggestive of sarcoidosis as well as evidence of underlying cardiac pathology. Experts emphasize the use of multimodal imaging as these have high diagnostic accuracy and can help differentiate between different types of cardiac masses through characteristic features.

Poster

Neurological Emergencies in Neurosarcoidosis: A Series of Illustrative Cases

Dr. Susana Carolina Dominguez Penuela[1], Dr. David Acero-Garces[1], Dr. Michelle Sharp[2], Dr. Nisha Gilotra[3], Dr. Edward Chen[2], Dr. Barney Stern[1], Dr. Carlos Pardo-Villamizar[1]
[1]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, [2]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, [3]Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

Background: Neurological manifestations of sarcoidosis are reported in 5-20% of patients, either as the presenting syndrome or during disease evolution. Involvement of the central nervous system (CNS) typically progresses insidiously and can lead to significant morbidity. However, presentations with acute, life-threatening emergencies are also observed. We aim to explore the spectrum of neurological emergencies encountered in sarcoidosis with four illustrative cases.

Results:

Case #1: Stroke

A 29-year-old man with probable neurosarcoidosis (myelopathy and meningeal disease) presented with bilateral lower extremity numbness, tingling, and chest pain. He was diagnosed with a pericardial effusion and subsequently experienced a large right middle cerebral artery (MCA) territory infarction followed by a left MCA infarct consistent with intracranial large artery vasculitis. Despite treatment with intravenous corticosteroids and infliximab, there was a progressive worsening of his condition due to stroke-associated edema and increased intracranial pressure, prompting a transition to comfort measures.

Case #2: Acute Hydrocephalus

A 46-year-old man with biopsy-proven pulmonary sarcoidosis presented with worsening headache, nausea/vomiting, and gait disturbance. MRI findings revealed acute communicating hydrocephalus due to sarcoidosis-associated meningitis. The patient received IV corticosteroid treatment and an endoscopic third ventriculostomy, with dramatic improvement in symptoms.

Case #3: Seizures

A 42-year-old woman with biopsy-proven untreated cutaneous sarcoidosis presented to the ED due to unprovoked seizures and altered mental status. A brain MRI showed nodular leptomeningeal enhancement with multifocal vasogenic edema, and CSF studies were consistent with aseptic meningitis. She was diagnosed with sarcoidosis-associated meningoencephalitis and treated with corticosteroids and anti-seizure medication, with a satisfactory response.

Case #4: Cryptococcal Meningitis

A 62-year-old woman with biopsy-proven sarcoidosis involving the lung, skin, and CNS, treated with prednisone, azathioprine, and adalimumab, presented with progressive unsteadiness and new cognitive impairment. A brain MRI showed brainstem and cervical cord leptomeningeal enhancement. CSF analysis revealed lymphocytic pleocytosis and CSF studies established a diagnosis of cryptococcal meningitis. She was treated with amphotericin B and flucytosine, followed by fluconazole with clinical improvement.

Discussion: We aim to raise awareness about the need for early recognition and diagnosis of neurological emergencies in sarcoidosis to facilitate rapid and appropriate treatments. Importantly, emergent presentations often require an urgent multi-disciplinary team approach.

Poster

Objective Cognitive and Neuroimaging Assessment in Sarcoidosis

Dr. Nabeel Hamzeh[1], *Dr. Jacob Simmering*[1], *Ms. Carinda Linkenmeyer*[1], *Mr. Jacob Hampton*[1], *Ms. Taylor Titterington*[1], *Ms. Tara Lanning*[1], *Ms. Brenda Werner*[1], *Dr. Vincent Magnotta*[1], *Dr. Karin Hoth*[1]
[1]University of Iowa

Background: Perceived cognitive difficulties are common in patients with sarcoidosis, which can contribute to reduced quality of life and disability. However, the underlying neurobiology of cognitive impairment in sarcoidosis remains unknown. We hypothesize that higher sarcoidosis disease burden is associated with altered cerebral metabolism and decreased white matter structural integrity and a corresponding reduction in cognitive function.

Methods: Thirty-two patients with sarcoidosis and 12 age-, sex-, and education matched healthy controls (HC) underwent objective cognitive testing utilizing the NIH Toolbox Cognition Battery and brain magnetic resonance imaging (MRI). The MRI protocol included T1-T2 structural imaging and diffusion weighted imaging (DWI) to assess white matter structural integrity for 12 patients and 12 matched controls. Additionally, 5 patients and 7 controls underwent magnetic resonance spectroscopy (MRS) and t1rho to assess alterations in neurobiology. We defined higher sarcoidosis disease burden using three measures: disease duration >= 5 years, >= 2 organ systems involved, any history of immunosuppressive use. All three measures were coded via medical record review.

Results: Patients with sarcoidosis, particularly those with higher disease burden, consistently demonstrated worse cognitive performance than HC, most pronounced for the cognitive processing speed domain (sarc vs HC, T=2.3, p=.01). Participants with sarcoidosis also demonstrated lower fractional anisotropy (FA) on DWI indicating disorganization of white matter that was present across all regions examined with large effect sizes (Cohen's d all >1.4). In the subset of participants who completed neurometabolic imaging, we observed group differences for Glutamate-Glutamine peak ratio to creatine+phosphocreatine in white matter (forceps minor) with a large effect size (T=3.1, p=.006; Cohen's d=1.8). T1rho signal was consistently higher in patients than controls across regions of the cerebrum and most pronounced in the thalamus (T=-2.7, p=.02). Concentrations of cerebral metabolites and T1rho were strongly correlated with objective cognitive performance in processing speed and executive function domains (betas >0.5).

Discussion: Objective cognitive assessment suggests that impairments in sarcoidosis are most pronounced in cognitive processing speed and executive functioning domains., Higher sarcoidosis disease burden was associated with neurometabolic alterations assessed by MRS and t1rho neuroimaging, which were in turn associated with cognitive performance.

Poster

Outcomes of Patients with Cardiac Sarcoidosis Managed with Cardiac Resynchronization Therapy

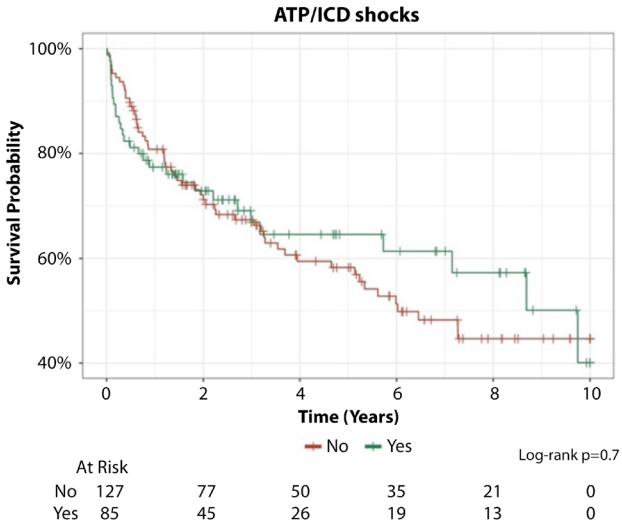
Maryam Mojarrad Sani[1], James Flynn[2], Ashkan Abdollahi[1], Nisha Gilotra[3], Jonathan Chrispin[3]
[1]Division of Cardiology, Department of Medicine, Johns Hopkins University, Baltimore, MD, [2]Department of Medicine, Johns Hopkins University, Baltimore, MD, [3]Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

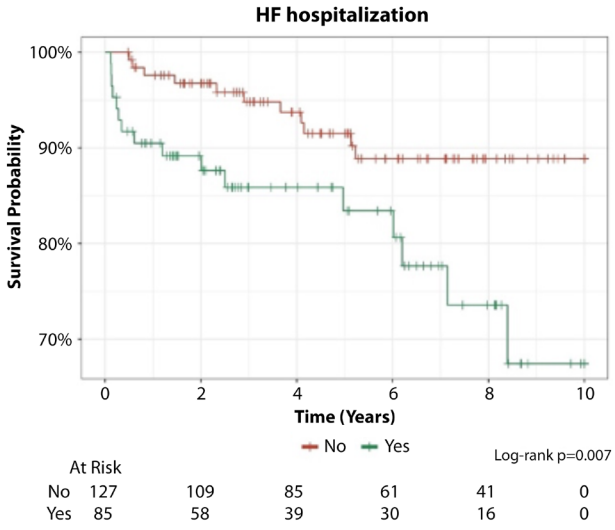
Background: Patients with cardiac sarcoidosis (CS) can have both cardiomyopathy and electrical manifestations. Cardiac resynchronization therapy (CRT) is indicated in patients with symptomatic systolic left ventricular function who may have other indications for pacing or meet QRS duration criteria. The role of CRT in patients with sarcoidosis, who frequently have other indications for cardiac implantable electronic devices (CIED), however has not been fully investigated. Therefore, we aimed to evaluate cardiac outcomes in CS patients undergoing CIED with or without CRT.

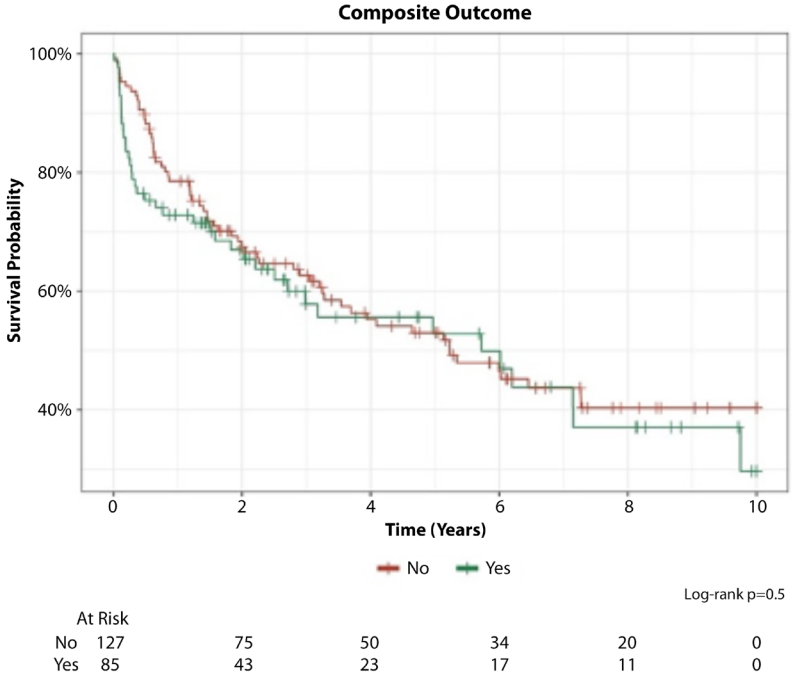
Methods: Patients with a clinical or histological diagnosis of CS who underwent CIED (implantable cardiac defibrillator (ICD), or Permanent Pacemaker (PPM)) with or without CRT therapy at Johns Hopkins between 2004 and 2024 were included. Baseline characteristics, heart failure hospitalization, the frequency of ATP (Anti-Tachycardia Pacing) or ICD shocks and all-cause mortality were assessed.

Results: The study cohort consisted of 212 patients (40.1% female) with an average age of 52.8 ± 11.1 years. Ultimately, 85 patients underwent CRT implantation (n=82 CRT-D, n=3 CRT-P), whereas the rest received either an ICD (n=117) or a PPM (n=7) without CRT therapy. The majority of CRT recipients (58.8%) initially underwent PPM or ICD implant with subsequent upgrade to CRT. During the follow-up period (6.15 ± 4.43 years), 27 (12.7%) patients were hospitalized for HF, and 86 (40.6%) experienced ATP or ICD shocks. The composite outcome of all-cause mortality, HF hospitalization, and ATP/ICD shocks was observed in 103 patients (48.5%) with no significant differences between CRT and non-CRT groups ($P = .51$). Survival analysis indicated significantly reduced freedom from HF hospitalizations in the CRT group compared to non-CRT group ($P = .01$). However, ATP/ICD shocks did not have a significant difference.

Discussion: We found that CRT upgrade does not appear to affect ATP/ICD shock and mortality in CS patients, although it is associated with significantly higher rates of heart failure (HF) hospitalizations compared to CS patients with an ICD or PPM alone. These findings warrant further investigation, including the optimal timing of CRT in CS associated conduction disease and heart failure to improve outcomes.


ATP/ICD shocks
Survival Probability
100%
80%
60%
40%
0
2
4
6
8
10
Time (Years)
No
Yes
Log-rank p=0.7
At Risk
No 127 77 50 35 21 0
Yes 85 45 26 19 13 0


HF hospitalization
Survival Probability
100%
90%
80%
70%
0
2
4
6
8
10
Time (Years)
No
Yes
Log-rank p=0.007
At Risk
No 127 109 85 61 41 0
Yes 85 58 39 30 16 0


Composite Outcome
Survival Probability
100%
80%
60%
40%
0
2
4
6
8
10
Time (Years)
No
Yes
Log-rank p=0.5
At Risk
No 127 75 50 34 20 0
Yes 85 43 23 17 11 0

Poster

Patient-reported quality of care and access to care in patients with sarcoidosis

Hassan Perera Mesa[1], Jason Cory Brunson[2], Arthur Perez[3], Diana Gomez Manjarres[4], Johnny Jaber[4], Divya Patel[4]

[1]Department of Internal Medicine, University of Florida, Gainesville, Florida, [2]Laboratory for Systems Medicine, College of Medicine, University of Florida, Gainesville, Florida, USA., [3]University of Florida, Gainesville, Florida, [4]Division of Pulmonary, Critical Care and Sleep Medicine, University of Florida, Gainesville, Florida.

Background: Sarcoidosis is a chronic, multisystem granulomatous disease with heterogeneous presentation requiring multispecialty care. Despite the under recognized nature of the disease, patients' access to care, and their perceptions of care have not been examined in the United States. We aimed to assess patients' perceptions of their access to care for sarcoidosis treatment and self-perceived barriers leading to disparities in health outcomes.

Methods: Anonymous surveys were distributed to patients living in the United States using the Foundation for Sarcoidosis Research contact list from February 2020 to July 2020. Responses were stratified by race-ethnicity, region, and employment status. Data was analyzed in correlation to Penchansky and Thomas's definition of care and its five dimensions: availability, accessibility, accommodation, affordability, and acceptability. We fit linear regression models to each grouping variable and used t-tests to compare pairs of groups.

Results: Overall response rate was 46.3% with 1,390 responses received. When stratified by race, Hispanics reported the greatest access to care along most dimensions. Black and mixed-race patients reported similar access to care to white patients. When stratified by region, rural and suburban patients reported greater acceptability and availability than urban patients. Patients of all three region types reported similar affordability. Finally, when stratified by employment status, no consistent differences emerged. Pairwise differences were greater among racial-ethnic groups (0.04–0.11) than among employment statuses (0.04–0.07), and especially region types (0.01–0.05), suggesting a greater impact on access to care. While some t-tests yielded evidence with $p < 0.05$, these would be expected by chance given the number of comparisons. Statistical evidence was stronger where dimensions were measured using composites of larger numbers of survey items.

Discussion: Using self-reported survey data, patients diagnosed with sarcoidosis may have differences in their access and perception of care based upon their social determinants of health. The strongest disparities appear to exist when stratified by race-ethnicity. However, these differences were small (10% or less on each subscale) and evidence from this sample was lacking for systemic differences. While disparities in access to care may still exist for sarcoidosis patients, more work needs to be done to identify those demographic groups or communities in greatest need.

Poster

Prednisone Dose and Duration in the Treatment of Pulmonary Sarcoidosis

Matthew Freedman[1], Naima Farah[1], Michael Andrew Schmidt[1], Allyson Timm[1], Imre Noth[1], Cathy Bonham[1]
[1]University of Virginia

Background: Since the early 1950s, corticosteroids have been considered a first-line agent in the treatment of Sarcoidosis. While current guidelines give a general overview for corticosteroid use in the management of pulmonary sarcoidosis, practice patterns widely vary across different providers and institutions. Recent studies have demonstrated initial treatment with lower steroid doses to be equally effective as higher. Despite this, patients often receive longer courses and/or larger doses than suggested, increasing the risk for the well-described adverse effects of long-term steroid use in this population. We aim to demonstrate the prednisone practice patterns of in our center over the past decade for the treatment of pulmonary sarcoidosis.

Methods: We performed a retrospective study of patients of a single academic center who were started on prednisone monotherapy for pulmonary sarcoidosis between January 2014 and January 2024. All patients assessed were greater than 18 years old, had not received sarcoidosis treatment within three years of starting prednisone, started therapy for pulmonary symptoms, were treated for a minimum of four weeks, and eventually weaned off prednisone. Measurements include duration of prednisone use, starting prednisone dose, and time to starting a secondary agent if began while still on initial steroid wean.

Results: Patients started on prednisone monotherapy for pulmonary sarcoidosis received it for an average of 269.6 days (SD=273.7). The majority (61.5%) were Scadding Stage II at the time of therapy initiation. 34.6% required a secondary agent before weaning off prednisone, which was started an average of 91.0 days (SD=81.1) after beginning corticosteroids. 100% of patients started on <40mg/day identified as white compared to 55.6% of those started on ≥40mg/day.

Discussion: Patients started on prednisone monotherapy for pulmonary sarcoidosis demonstrated a wide range of treatment durations, with the average spanning nearly three-quarters of a year. With the field trending towards more conservative steroid strategies, understanding current practice patterns is imperative for best guiding future treatment protocols. Further research is needed to analyze the interaction of race and barriers to care with dose and duration of planned treatment for sarcoidosis.

Poster

Rates of Antibody Mediated Rejection and Acute Cellular Rejection in African Americans with Sarcoidosis Undergoing Immunosuppression After Lung Transplantation

Tanya Bronzell-Wynder[1], *Megan O'Rourke*[1], *Rohit Gupta*[1], *Kevin Carney*[1]
[1]Temple University

Background: Sarcoidosis is a multi-system inflammatory disease characterized by the formation of granulomas in various organs. It is more common among African Americans than in other racial or ethnic groups. Sarcoidosis can affect any organ in the body, but it most often affects the lungs. In terms of organ transplantation, sarcoidosis patients may require immunosuppression to prevent organ rejection. However, there are different types of rejection that can occur post-transplantation: antibody-mediated rejection (AMR) and acute cellular rejection (ACR). AMR is caused by antibodies that attack the transplanted organ, while ACR is caused by T cells attacking the transplanted organ. As of now, there is limited data available on the comparative rates of AMR and ACR in African Americans with a diagnosis of sarcoidosis who are on immunosuppression. Further research is required to understand the exact rates and the factors that may influence them. Potential factors that could influence these rates include the level of immunosuppression, single versus double lung transplantation, the presence of other health conditions, and individual genetic factors. It is clear that further research is needed in this area to improve patient outcomes and to ensure that African American patients with sarcoidosis receive the most appropriate and effective treatment.

Methods: This descriptive study was conducted using retrospective data from African American patients diagnosed with sarcoidosis and undergoing immunosuppressive therapy in lung transplantation. The study population was divided into two groups based on the type of organ rejection experienced: AMR and ACR.

Results: The study found that the rate of AMR and ACR among African Americans with sarcoidosis on immunosuppression was 5.1% and 7.7% respectively. Several factors including age, gender, type of organ transplanted(single versus double), and level of immunosuppression were found to be associated with the type of rejection.

Discussion: The study provides valuable insights into the rates of AMR and ACR in African Americans with sarcoidosis on immunosuppressive therapy. Further research is needed to understand the underlying mechanisms and to develop strategies to reduce the rates of rejection in this population.

Poster

Sarcoidosis and Risk of Nephrolithiasis in The Black Women's Health Study

Theresa McAllister[1], Praveen Govender[2], Shaun Wason[3], Yvette Cozier[4]
[1]Boston University School of Public Health, [2]Boston University Chobanian & Avedisian School of Medicine Medicine, [3]Beth Israel Deaconess Medical Center - Needham, [4]Slone Epidemiology Center at Boston University

Background: Sarcoidosis has been linked to dysregulation of Vitamin D and subsequently calcium metabolism, theoretically increasing the risk of nephrolithiasis or kidney stones. Both sarcoidosis incidence and kidney stone risk factors (e.g., hypertension, type-2 diabetes) are common among US Black women, yet little has been reported about the relation between sarcoidosis and stone formation. We sought to assess the association between existing sarcoidosis and the development of kidney stones in a cohort of US Black women.

Methods: We conducted a cross-sectional analysis using data from the Black Women's Health Study (BWHS), a national study of US Black women begun in 1995. Diagnoses of sarcoidosis and data on covariates were obtained from baseline (1995) and biennial follow-up questionnaires through 2005. The 2005 follow-up questionnaire asked women if they had ever been diagnosed with kidney stones. Prevalence odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression adjusting for age, education, alcohol consumption, cigarette smoking, calcium supplementation, history of gallstones, and history of metabolic conditions: body mass index ≥ 30 kg/m^2, type 2 diabetes, hypertension, hyperlipidemia. We repeated analyses within strata of number of metabolic conditions.

Results: A total of 43,718 women completed the 2005 BWHS questionnaire of which 832 also reported a sarcoidosis diagnosis (1995 - 2005). Among sarcoidosis cases, 3.9% reported a history of nephrolithiasis, compared to 1.9% among non-sarcoidosis participants. The OR for nephrolithiasis was 1.80 (95% CI: 1.25, 2.59) among women with sarcoidosis, compared to those without. When we explored the association within strata of number of metabolic conditions (none, 1-2, 3-4), the association was slightly increased for women with 3-4 co-occurring conditions: 1.96 (95% CI: 1.09, 3.52).

Discussion: Our results indicate that U.S. Black women with sarcoidosis have an increased risk of developing kidney stones. The findings highlight the importance of monitoring for signs of vitamin D and calcium dysregulation in the management of sarcoidosis, especially among those with co-occurring metabolic conditions. Future analyses are needed to explore incidence and recurrence of nephrolithiasis among patients with sarcoidosis.

Poster

Sarcoidosis myopathy: a diagnosis with little blaCK and white

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Background: Introduction: Sarcoidosis myopathy is an elusive manifestation of sarcoidosis. Three major disease phenotypesacute, chronic, and nodular have been described. The acute and chronic subtypes present with weakness, while the nodular subtype presents with soft-tissue masses typically without associated weakness. We present a unique case of sarcoidosis myopathy that is not consistent with any of these predefined phenotypes. Additionally, our case is distinct from inflammatory myopathies, which typically feature weakness and abnormal EMG and muscle MRI.

Results: Case Report: A 42-year-old woman with a history of highly probable cardiac sarcoidosis presented to Rheumatology clinic for ten years of myalgias and elevated creatine kinase (CK). She endorsed myalgias in her proximal arms and thighs that limited her daily activities and improved substantially after initiation of methotrexate and prednisone for cardiac sarcoidosis two years prior. She denied weakness. Physical examination showed 5/5 strength in the upper and lower extremity muscles. Laboratory evaluation was notable for peak CK of 732 U/L (29 - 143 U/L) before initiation of immunosuppression with gradual decrease to 193 U/L at evaluation. Complete blood count and comprehensive metabolic panel were normal. Myositis autoantibody panel was negative. Electromyography of the right deltoid, biceps, vastus lateralis/medialis, and iliopsoas was normal. MRI of the left lower extremity showed no muscle edema or atrophy. She was ultimately diagnosed with probable sarcoidosis myopathy given that her myalgias and CK elevation responded to immunosuppression. In the years following this diagnosis, she had episodes of worsening myalgias accompanied by elevated CK that improved with increases in immunosuppression.

Discussion: Conclusion: Skeletal muscle inflammation has been previously found to be a pathologic feature in nearly half of sarcoidosis patients; however, less than 5% of sarcoidosis patients exhibit symptoms consistent with myopathy. It is unclear if this disparity between pathologic and clinical disease is driven in part by underrecognition of atypical but symptomatic disease, as CK is not routinely checked in sarcoidosis evaluation, nor is its monitoring recommended by sarcoidosis guidelines. Consideration of screening CK in patients with sarcoidosis reporting muscle dysfunction and further phenotyping of individuals with abnormal CK may help us better understand the scope of muscle disease in sarcoidosis.

Poster

Sarcoidosis Specialty Center Use of Multidisciplinary Team Meetings in Diagnosis and Management of Cardiac Sarcoidosis

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[1]Northwestern Memorial Hospital

Background: Diagnosis and management of patients with cardiac sarcoidosis (CS) are often clinically challenging. The recent American Heart Association Scientific Statement on CS (Circulation 2024;149:e1197-e1216) emphasizes the importance of a multi-disciplinary team (MDT) approach for patients with suspected or confirmed CS. MDT meetings are commonly utilized for other medical conditions, but the degree to which this approach has been adopted in CS care is unknown. Thus, we surveyed sarcoidosis specialty centers to identify those that employ MDT meetings in the diagnosis and management of CS, and to assess the characteristics and outcomes of such meetings as they currently exist.

Methods: A 27-point survey was sent to World Association of Sarcoidosis and Other Granulomatous Diseases (WASOG) Sarcoidosis Centers of Excellence and Foundation for Sarcoidosis Research Global Sarcoidosis Clinic Alliance (FSRGCSA) members. Questions called for open- and close-ended responses regarding meeting logistics, specialty participants, changes in diagnosis and management, and recommendations for further diagnostic testing and/or treatment. Data collection began April 2024 and is ongoing.

Results: Of 63 WASOG and FSR-GCSA centers, 22 responded by June 1, 2024. 15 of 22 (68%) responding centers conduct MDT meetings specifically for diagnosis and management of CS. Advanced heart failure cardiologists and pulmonologists participate in MDT meetings at 93% of centers and most frequently comment during meeting discussions, followed by imaging specialists and electrophysiologists. Cardiac PET-CT and cardiac MRI are the most frequently recommended tests in cases of diagnostic uncertainty. Notably, based on MDT consensus recommendations, 6 of 15 centers (40%) altered treatment plans in >50% of cases, and 8 of 15 centers (53%) altered treatment plans in 25-50% of cases.

Discussion: The majority of responding sarcoidosis specialty centers employ MDT meetings for evaluation and management of patients with suspected or confirmed CS. MDT meeting discussions lead to additional advanced imaging studies in cases of diagnostic uncertainty and alterations in treatment in a large proportion of cases. Limitations include the small number of centers responding to date and the fact that only process outcomes were assessed. Further studies are needed to assess the impact of MDT meetings on clinical outcomes in patients with suspected or confirmed CS.

Oral

Spatial transcriptomics reveals structurally organized and distinct immune polarization in inflammatory cutaneous granulomatous disorders

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[1]Yale University, [2]Royal College of Surgeons in Ireland, [3]University of Wisconsin-Madison, [4]New York University

Background: Non-infectious inflammatory cutaneous granulomatous disorders include cutaneous sarcoidosis (CS), granuloma annulare (GA), necrobiosis lipoidica (NL), and necrobiotic xanthogranuloma (NXG). These disorders share macrophage predominant inflammation and granuloma formation in tissue, but their inflammatory architecture and clinical presentation varies. The molecular explanations for the overlapping yet distinct features of these disorders has not been fully elucidated.

Methods: To understand spatial gene expression patterns in these disorders, we performed spatial transcriptomics using skin biopsies of CS (n=2), GA (n=4), NL (n=5), NXG (n=1), and control unaffected skin (n=3) with the 10X Genomics Visium platform. Immunohistochemical and RNA in situ hybridization staining was performed on a larger series of biopsies from patients with these disorders to validate patterns observed with spatial transcriptomics.

Results: We found that CS is characterized by a spatially organized T helper (Th) 1 response with classical macrophage activation programs predominating. GA was characterized by a mixed, but spatially organized pattern of Th1 and Th2 polarization with both classical and alternative macrophage activation evident. NL showed concomitant activation of Th1, Th2, and Th17 immunity with a mixed pattern of macrophage activation. NXG showed upregulation of CXCR4-CXCL12/14 chemokine signaling and exaggerated alternative macrophage polarization. Areas of necrobiosis typical of GA, NL, and NXG were characterized by a hypoxia signature. Increased IL-32 expression was noted across all granulomatous disorders.

Discussion: Our study demonstrates that inflammatory cutaneous granulomatous disorders show distinct and spatially organized immune activation patterns. These patterns begin to help us to understand molecular differences in these disorders and imply multiple avenues for novel therapeutic intervention in each.

Poster

Specific lesions of cutaneous sarcoidosis are associated with cardiac sarcoidosis: A multi-center retrospective review

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Background: Sarcoidosis is a multi-system granulomatous disease with cutaneous involvement observed in approximately 30% of cases.[1,2] Sarcoidosis-specific skin lesions, characterized by noncaseating granulomas, may be the presenting sign of sarcoidosis. Certain lesions, such as lupus pernio, may hold prognostic information regarding internal organ involvement.[1,3] Cardiac sarcoidosis is an uncommon, potentially fatal disease manifestation.[4-8] Research suggests a higher risk of cardiac sarcoidosis among Black patients; however, data is limited. Furthermore, associations between specific skin lesions and cardiac disease remain unexplored.[7] We aimed to investigate the epidemiology of cutaneous and cardiac sarcoidosis at two New York City hospitals, to characterize skin lesions and assess potential associations with cardiac sarcoidosis.

Methods: An IRB-approved multi-center retrospective review analyzed patients with systemic sarcoidosis at NYU Langone Health and NYC H+H Bellevue Hospital from 2000-2022. Inclusion criteria required tissue confirmation of sarcoidosis from at least one organ and involvement of at least two organs, including skin. Patients were stratified by diagnosis of cardiac sarcoidosis. Data analysis included chi-squared tests, Fisher's exact tests, and independent t-tests.

Results: 221 patients were identified with cutaneous sarcoidosis, of which 31 patients also had cardiac sarcoidosis. Cardiac sarcoidosis patients were significantly more likely to have cutaneous lesions on the head/face ($p<0.001$), nose ($p=0.002$), and scalp ($p=0.040$) compared to non-cardiac patients. Significant differences were seen in morphologies of cutaneous sarcoidosis among patients with and without cardiac sarcoidosis. Macules ($p=0.002$) and papules ($p=0.003$) were more common among patients with cutaneous and cardiac sarcoidosis. No significant association between race and cardiac sarcoidosis ($p=0.677$) was observed. Patients with cardiac involvement were significantly more likely to have multiple affected organs ($p=0.001$).

Discussion: Significant differences in lesion distribution and morphology were observed between groups, particularly on the scalp and central face. As opposed to prior research, there was no difference in cardiac involvement between Black and non-Black patients.[7] Limitations include a small sample size, retrospective methodology, and cases with limited exam descriptions. Dermatologists should ensure that patients with cutaneous sarcoidosis receive a cardiac evaluation, regardless of lesion type and extent, though patients with facial and scalp sarcoidosis may require additional screening. Further research is needed to confirm these findings.

Table 1. Cutaneous Lesion Location

Location	Cardiac (n=31)	Non-cardiac (n=190)	P-value
Head/Face	61.3% (19)	26.8% (51)	**<0.001**
Neck	16.1% (5)	8.4% (16)	0.187
Chest	6.5% (2)	6.3% (12)	1
Abdomen	0% (0)	14.2% (27)	**0.018**
Back	12.9% (4)	22.1% (42)	0.341

Table 2. Cutaneous Manifestations

Manifestation	Cardiac (n=31)	Non-cardiac (n=190)	P-value
Macules	32.3% (10)	10% (19)	**0.002**
Papules	54.8% (17)	26.8% (51)	**0.003**
Plaques	38.7% (12)	24.2% (46)	0.121
Patches	9.7% (3)	13.2% (25)	0.774
Nodules	16.1% (5)	19.5% (37)	0.807
Subcutaneous	6.5% (2)	5.3% (10)	0.678
Lupus Pernio	9.7% (3)	7.4% (14)	0.714
Erythema Nodosum	6.5% (2)	6.3% (12)	1
Atrophy	9.7% (3)	5.3% (10)	0.401
Erythema	12.9% (4)	24.7% (47)	0.173
Hyperpigmentation	12.9% (4)	22.1% (42)	0.341
Hypopigmentation	6.5% (2)	6.8% (13)	1
Annular	6.5% (2)	6.8% (13)	1
Alopecia	3.2% (1)	3.7% (7)	1
Panniculitis	3.2% (1)	2.6% (5)	1
Scar Sarcoidosis	0% (0)	1.6% (3)	1
Tattoo Sarcoidosis	0% (0)	7.4% (14)	0.227
Unspecified Rash	41.9% (13)	51.1% (97)	0.439
Scaling	6.5% (2)	7.4% (14)	1
Arciform	0% (0)	0.5% (1)	1
Flesh-colored	6.5% (2)	3.7% (7)	0.617

Table 3. Comparison of the Number of Organs Affected in Patients with Concomitant Cardiac and Non-cardiac Sarcoidosis

	No. (%)			
	All cases (n = 221)	**Cardiac (n = 31)**	**Non-cardiac (n = 190)**	**P-value**
Number of organ involvement				
< 5	97.7 (216)	87.1 (27)	99.5 (189)	**0.001**
≥ 5	2.3 (5)	12.9 (4)	0.5 (1)	

Poster

Specific recruitment of type 1 innate lymphoid cells to mature tertiary lymphoid structures in human sarcoidosis

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[1]University of Pennsylvania School of Medicine

Background: Sarcoidosis is a multiorgan granulomatous disease that lacks diagnostic biomarkers and targeted treatments.

Methods: We performed single-cell RNA-sequencing, spatial transcriptomics, flow cytometry, immunohistochemistry, migration assays on sarcoidosis and non-sarcoidosis skin samples and blood. We also used in vivo mouse models of granuloma formation.

Results: Here, using single-cell sequencing on blood and skin from sarcoidosis and non-sarcoidosis skin granuloma patients, we report that sarcoidosis granulomas are specifically enriched for type 1 innate lymphoid cells (ILC1s). Moreover, spatial transcriptomics and immunohistochemistry confirmed a sarcoidosis-specific immune cell composition and molecular programs associated with mature tertiary lymphoid structures (TLS) that were not observed in non-sarcoidosis granulomas. Sarcoidosis patient samples had an 8-fold increase in circulating ILC1s, which correlated with the effects of treatment. Consistently, granuloma formation was attenuated in mice lacking ILCs, uncovering their role in non-infectious granuloma formation. Mechanistically, sarcoidosis-activated ILC1s were dependent on increased CXCR4 expression for migration, and granuloma formation was attenuated in mice treated with a pharmacologic CXCR4 inhibitor.

Discussion: We therefore propose ILC1s are a novel tissue and circulating biomarker that distinguishes sarcoidosis from other skin granulomatous diseases. Repurposing existing CXCR4 inhibitors may offer a new targeted treatment for this devastating disease.

Poster

The Use of EMG as a Screening Tool in Sarcoidosis-associated Neuropathy

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Background: Small fiber neuropathy (SFN) is the most common peripheral nervous system manifestation of sarcoidosis. Diagnosis of SFN includes clinical evaluation, occasionally skin biopsy to evaluate intraepidermal nerve fiber density, and electrodiagnostic studies. The utility of these tests to aid in diagnosis of sarcoidosis-associated SFN is unclear. This study evaluates the yield of normal electromyography (EMG) in diagnosing SFN.

Methods: This is a cross-sectional study comparing 19 patients with biopsy-confirmed sarcoidosis with and without normal EMG. Participants were evaluated for SFN according to the Toronto Consensus Criteria (TCC) with possible, probable, or definite SFN; the Utah Early Neuropathy Scale (UENS) that captures both small and large sensory fiber function; physician impression of neuropathy (PIN); and skin biopsy.

Results: In total, 19 patients ranging age 30-70 years were recruited, including thirteen participants with normal EMG and 6 participants with abnormal EMG. Of this cohort, 66.7% of participants with abnormal EMG had PIN compared to 33.3% of those without PIN (p=1.00). Those with normal EMG had a lower mean UENS score (M=5.69, SD 4.50) compared to those with abnormal EMG (M=7.83, SD=5.49, p=0.43). When evaluated by TCC, 46.2% with normal EMG tested positive for SFN compared to 66.7% of those with abnormal EMG (p =0.63). In addition, 15.4% with normal EMG had positive biopsy suggesting pure SFN compared to 33.3% (p=0.59).

Discussion: Though this study aimed to correlate normal EMG data with clinically suspected SFN, surprisingly 4 of 12 participants with clinically suspected SFN had abnormal EMG and 2 of 7 participants without suspected SFN had incidental EMG abnormalities. Notably, those with alternative causes of neuropathy (e.g., diabetes) were excluded. Participants with an abnormal EMG were more likely to have a higher UENS score, consistent with impaired large fiber function. Skin biopsy suggesting small fiber dysfunction was present in some patients with normal EMG (likely pure small fiber neuropathy) and some with abnormal EMG (likely mixed neuropathy). Although these findings were not statistically significant, there are clinically significant correlates. Despite a small sample size, our findings suggest that EMG studies may not be an adequate screening instrument for sarcoidosis-associated polyneuropathy.

Poster

Treatment of Cardiac Sarcoidosis with Mycophenolate Mofetil and Steroids: Clinical and Radiographic Outcomes

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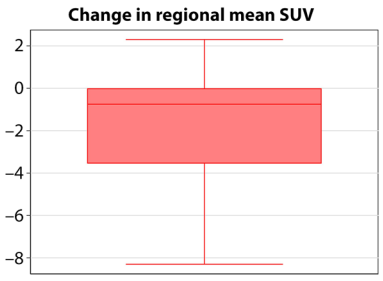
Background: Long-term immunosuppression is the mainstay of treatment for cardiac sarcoidosis (CS). While steroids are the cornerstone of therapy, steroid-sparing alternatives are considered second-line or adjunctive in the management of CS. We aimed to evaluate the efficacy of mycophenolate mofetil and steroids on the clinical and radiographic outcomes of patients with CS.

Methods: A retrospective chart review at a single academic medical center of patients with CS that were treated with prednisone or combination therapy with prednisone and MMF was conducted between 2019-2021. Baseline demographics, clinical data, echocardiography, and PET data were collected pre and post-treatment. Improvement in disease was based on improvement in left ventricular ejection fraction (LVEF), reduction of arrhythmia burden, and regional maximum Standardized Uptake Value (SUV) and percentage of inflammation on 18F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Results: There were 17 total patients (65% male and 53% black) who were found to have CS and were treated with combination therapy consisting of prednisone and MMF. Seven of these had a positive cardiac or extra cardiac biopsy. The median follow-up between scans was 154 days. There was an improvement in EF with a median of 6.5 (p 0.22), regional max SUV decreased by 1.35 ($p < 0.05$) and percent inflammation decreased by a median of 22 percentage points (p 0.11). Of the 14 patients that had an underlying arrhythmia, 11 (78%) had a mitigated or absent arrhythmia burden after treatment.

Discussion: CS patients treated with combination therapy consisting of prednisone and MMF appeared to have radiographic and clinical evidence of improvement. MMF may be considered an effective adjunctive therapy to prednisone alone.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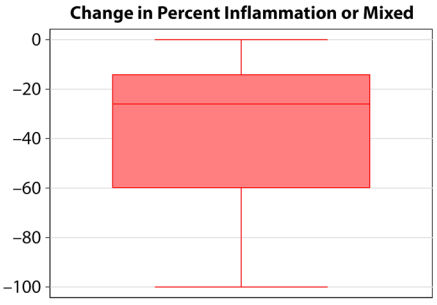
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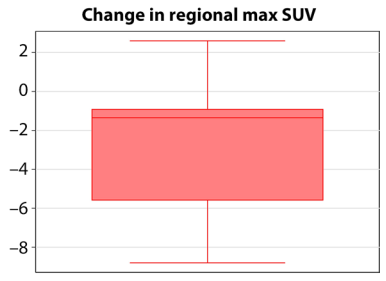
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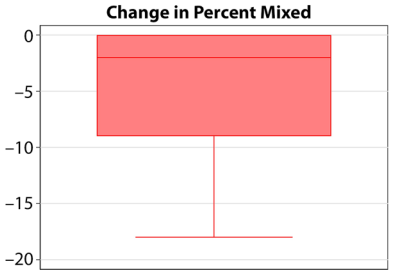
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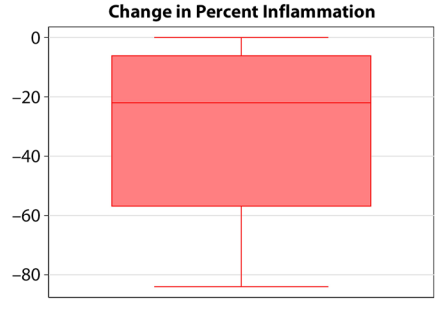
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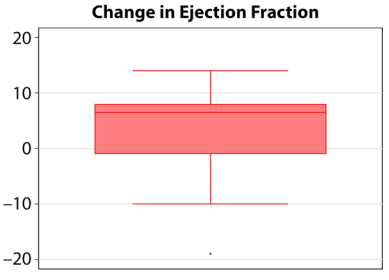
−40
−60
−80


Change in Ejection Fraction
20
10
0
−10
−20

Poster

Treatment of isolated cardiac sarcoidosis with tumor necrosis factor-alpha inhibitors at a tertiary referral sarcoidosis center

Jasmine Malhi[1], Jana Lovell[2], Kayla Nyakinye[3], Victoria Wotorson[3], Cherie Livingston[1], Edward Kasper[1], Jonathan Chrispin[2], Michelle Sharp[4], Edward Chen[3], Nisha Gilotra[1]

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Background: Tumor necrosis factor-alpha inhibitors (TNFai) have an established role in treating sarcoidosis, with increasing use in cardiac sarcoidosis (CS). However, in patients with non-histologically diagnosed isolated CS, diagnostic uncertainty and concern for worsening cardiomyopathy, may result in hesitancy to treat with TNFai. We describe our center's experience treating such patients with TNFai.

Methods: Patients were evaluated at a Sarcoidosis Center of Excellence by multiorgan sarcoidosis specialists and diagnosed based on clinical (non-histologic) criteria for isolated CS (Japanese Circulation Society guidelines). TNFai indication, treatment, sarcoidosis activity and safety monitoring were performed using center protocol. Baseline characteristics and clinical outcomes were retrospectively adjudicated and descriptive statistical analyses performed.

Results: Six patients (50% female, 16% Black, 55.1±9.6 years old) with clinical, isolated CS treated with TNFai were identified (Table). Alternative causes of cardiomyopathy were evaluated and excluded. Endomyocardial (n=4) or lymph node (n=2) biopsy were nondiagnostic for sarcoidosis. Five patients had reduced LVEF (41.6±7.9%) and 1 had RV dysfunction All patients had cardiac FDG uptake despite immunosuppression with prednisone (19.2 ± 12 mg) and an oral steroid sparing agent, and had experienced steroid side effects.

Patients were initiated on TNFai (5 infliximab, 1 adalimumab) 1.9±0.8 years after CS diagnosis. On first follow-up FDG-PET (median 6 months), 2 (33%) had complete resolution and 4 (67%) had ongoing cardiac FDG uptake. Ultimately, 5 patients achieved complete resolution (mean 10.1±6.1 months); however, 1 of these patients had recurrent inflammation after dose reduction of prednisone requiring escalating doses of infliximab. One patient was switched from adalimumab to infliximab due to persistent cardiac FDG, and 1 from infliximab to adalimumab due to infliximab antibody formation. Prednisone dose was substantially lower at time of cardiac FDG resolution (4±4.1 mg). There was one episode of bacteremia in 1 patient while on TNFai.

Discussion: We found that among patients with clinical, isolated CS, TNFai was effective in most patients to control cardiac inflammation but may require frequent dose changes and take nearly one year for complete resolution. Prospective trials are needed to identify optimal treatment strategies using biologics in CS, including timing, dosing, patient selection, and endpoints specific to isolated CS.

Patient	1	2	3	4	5	6
Sex	F	F	M	F	M	M
Race	White	White	White	White	White	Black
Cardiac Manifestations	HF	HF, AVB	HF, AVB	HF, AVB, VT	HF, VT	AVB
Max prednisone (mg)	40	40	40	40	40	40
SSA	MMF	MMF	MMF, MTX	MMF	MMF	AZA
Oral IS at time of TNFαi	prednisone 40 mg, MMF 1.5g BID	prednisone 5 mg, MMF 1.5 g BID	prednisone 20 mg, MMF 1g BID	prednisone 10 mg, MMF 1 g BID	prednisone 20 mg, MMF 1g BID	prednisone 20 mg, AZA 150 mg/d
Initial TNFαi regimen	infliximab 5 mg/kg q8wk	infliximab 5 mg/kg q6wk	infliximab 5 mg/kg q8wk	infliximab 5 mg/kg q8wk	adalimumab 40 mg q2wk	infliximab 10 mg/kg q8wk
Nadir LVEF pre TNFai (%)	20	30	30	40	20	55
Pre-treatment LVEF (%)	45	30	35	45	40	55
Pre-treatment NYHA Class	2	1	2	1	2	1
Follow up LVEF (%)	40	40	35	60	35	55
Pre-TNFai cardiac FDG	+ LV	+ LV	+ LV	+ LV	+ LV	+ LV
First post-TNFai PET	Resolved	Partially Resolved	Ongoing	Partially Resolved	Resolved	Partially Resolved
Resolved cardiac FDG at any follow up PET	Yes	Yes	No	Yes	Yes	Yes
Time to FDG resolution (m)	4.1	8.4	Not achieved	18.4	5.4	14.4
TNFai regimen at time of resolution	infliximab 10 mg/kg q6wk	infliximab 5 mg/kg q6 wk	NA	infliximab 5 mg/kg q8wk	infliximab 5mg/kg q8wk	adalimumab 40 mg qwk
Oral IS at FDG-PET resolution	prednisone 5 mg, MMF 1g BID	prednisone 5 mg, MMF 0.5g BID	NA	MMF 1g BID	MMF 1g BID	prednisone 10 mg, AZA 50 mg/d
Status at follow up	Resolved inflammation	Recurrent inflammation, increasing TNFai dose	Ongoing inflammation	Resolved inflammation	Resolved inflammation	Resolved inflammation, switched TNFai due to antibody formation

Poster

Unmasking The Masquerade: Tuberculosis Infection Masquerading As Lofgren's Syndrome Of Sarcoid

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[1]Suny Upstate Medical University, Department of Pulmonary and Critical Care medicine, [2]Suny Upstate Medical university, Department of Pulmonary and Critical Care Medicine

Background: *Introduction:* The Lofgren syndrome of sarcoid, consisting of erythema nodosum, bihilar lymphadenopathy (LAP), and polyarthralgia, is typically considered highly specific for sarcoid. It is crucial to recognize that tuberculosis (TB) can present similarly.

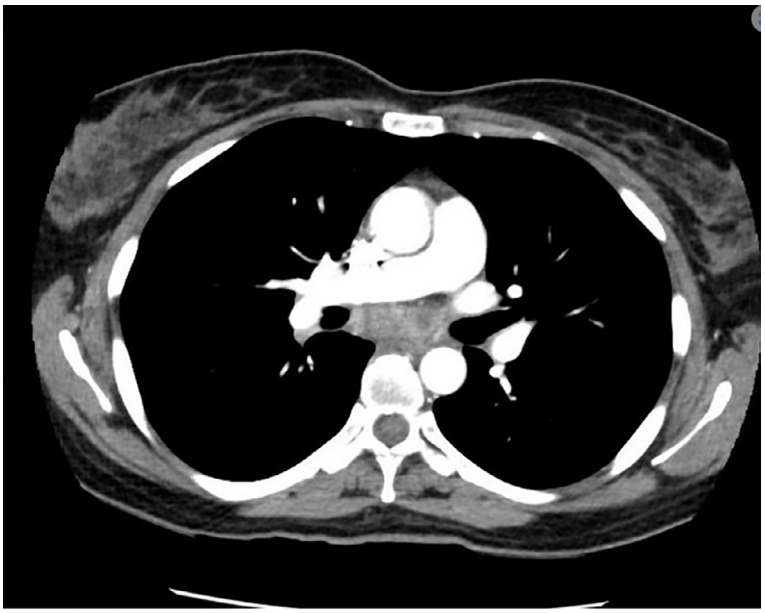
This case report emphasizes the importance of ruling out TB infection in Lofgren syndrome. It challenges current guidelines that diagnose sarcoid without tissue biopsy in Lofgren's triad due to its high specificity for sarcoid. we present a patient who has been experiencing fever, joint pain, and erythema nodosum. CT chest imaging demonstrated mediastinal LAP, and lymph node biopsy resulted in caseating necrotizing granulomatous inflammation and identified acid-fast bacilli (AFB).

Results: *Case Report:* A 48-year-old female from India, reports few months of dry cough, fatigue, low-grade fever, ankle pain, and pretibial painful skin nodules. She had a positive QuantiFERON test but no abnormal chest X-rays in the past. Following the discovery of mediastinal adenopathy on CT chest, she underwent endobronchial ultrasound-guided fine needle aspiration of the subcarinal lymph node and bronchial washing was sent for culture. While awaiting culture results, she was started on low-dose prednisone and rifampin for latent TB, which improved her symptoms.

Pathology showed caseating necrotizing granulomatous inflammation and AFB were identified. Bronchial washing and sputum culture resulted in positive AFB and the detection of Mycobacterium tuberculosis complex DNA by PCR. Fungal cultures were negative. She was advised to stop prednisone and start a 4-drug anti-TB regimen.

Discussion: *Conclusion:* This case report emphasizes the significance of recognizing TB as a potential masquerader in patients who present with the Lofgren Syndrome. While the Lofgren Triad is typically considered highly specific for sarcoid, it can create a diagnostic challenge when TB manifests with similar clinical features. The current guidelines suggest diagnosing sarcoid without a tissue biopsy in cases of the Lofgren Triad. However, this case challenges that approach, as TB can mimic sarcoid and lead to misdiagnosis.

Clinicians should maintain a high level of suspicion for TB in patients who present with Lofgren syndrome, especially in regions with a high burden of TB. A thorough evaluation, including imaging, tissue biopsy, and microbiological testing, should be conducted to differentiate between sarcoid and TB.



Subcarinal lymph node measuring 1.5 cm

Poster

Use of High Dose Infliximab in the Treatment of Multi-Organ Sarcoidosis

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Background: Sarcoidosis is a granulomatous disease often with multi-organ involvement. Case reports have described infliximab as potential treatment. We report four cases where patients received high doses of infliximab. These doses of infliximab have not been previously described in the literature for sarcoidosis.

Results: Patient 1 is a 41-year-old female with biopsy-proven pulmonary sarcoidosis. She developed right arm burning pain with normal neurologic work-up. Given suspicion for neurosarcoidosis, she was started on infliximab 5mg/kg every 8 weeks. Patient then developed similar symptoms in lower extremities. Infliximab dose was changed to 15mg/kg every 4 weeks. Prednisone was stopped.

Patient 2 is a 45-year-old male with history of presumed monomelic amyotrophy. He developed new neurologic symptoms. MRI of the spine demonstrated changes concerning for an inflammatory process. Imaging showed thoracic lymphadenopathy with biopsy confirming sarcoidosis. Treated with prednisone and dose of infliximab 5mg/kg. Given persistent symptoms, Infliximab was increased to 15mg/kg every 4 weeks. MRI spine no longer showed enhancing lesions and symptoms abated. Prednisone was tapered off.

Patient 3 developed renal and liver failure secondary to sarcoidosis and underwent transplant. She subsequently developed painful skin nodules and shortness of breath. Skin biopsy showed sarcoidosis associated small-vessel vasculitis. CT chest demonstrated interstitial lung disease. Was started on steroids and infliximab 5mg/kg every 8 weeks. She developed acute kidney injury with biopsy showing sarcoidosis. Infliximab was titrated to 10mg/kg every 6 weeks. Her renal function improved and remained stable. Currently on steroids for adrenal insufficiency. Patient 4 is a 54-year-old female with biopsy-proven lupus pernio treated with prednisone. Hydroxychloroquine and methotrexate were self-discontinued due to side effects. She was started on infliximab 3.5mg/kg every 6 weeks. Rash improved, although experienced mild flares. Infliximab was increased to 12 mg/kg every 4 weeks until complete resolution of lupus pernio. She has been off prednisone.

Discussion: The pathogenesis of sarcoidosis is complex. Given variable presentations, no standard of care currently exists. Our literature review revealed infliximab doses ranging from 3-7.5mg/kg. We demonstrated that high-dose infliximab resulted in improvement of sarcoidosis symptoms. Infliximab should be considered when steroids or other treatments have failed to adequately control this multi-organ disease.

Poster

Variograms: A more robust quantitative approach to summarizing texture in sarcoidosis?

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Background: Expert visual assessment scoring (VAS) of chest high resolution computed tomography (HRCT) in patients with pulmonary sarcoidosis have high inter- and intra-rater variation and are often not clinically available. Reproducible quantitative texture measures associated with VAS as well as with pulmonary function testing (PFT) are desirable. Variograms are a geostatistical tool for quantifying spatial covariance within an image. Variograms may be an alternative to standard radiomics, which are known to be sensitive to pre-processing pipelines and acquisition. In support of generalizable research, we desire measures which can be reasonably obtained in typical clinical contexts, are robust to image processing and acquisition factors, and exhibit strong association with disease.

Methods: We computed location-specific empirical variograms via 48 different preprocessing approaches on the deciles of axial images, ensuring pipelines investigated are applicable to clinically obtained images. Preprocessing factors of interest included whether variograms were computed before or after image registration to a disease-specific lung template and whether features were harmonized for scanner model prior to further analysis. Unsupervised clustering was used to obtain quantitative imaging phenotypes of disease and logistic and linear regression was used to map clusters to VAS and PFT. We assessed how these associations changed according to image processing pipeline to better identify appropriate, generalizable approaches to image quantification in the study of sarcoidosis.

Results: Variogram-based phenotypes showed consistency across the 48 approaches (typical pairwise Cramér's V>0.5). Strength of Variogram-based phenotypes were strongly associated with many expert visual assessments (optimistic AUC~0.9, $p<0.0001$ in models for architectural distortion, conglomerate mass, fibrotic abnormality, and traction bronchiectasis) and PFT (R-squared comparable with other studies, $p<0.0001$ in models of spirometry and diffusion capacity of the lungs for carbon monoxide). Phenotype associations with disease were robust to processing approach and variogram data were less associated with image acquisition than traditional radiomic measures.

Discussion: Variogram-based feature sets considered here are more interpretable, of lower dimension, and less distorted by scanner model than radiomics. Variogram-based phenotypes also showed strong association with disease features. This work suggests variograms are a promising alternative to classic radiomics for generalizable research and imaging biomarker development in sarcoidosis.

Poster

Why am I crying blood? A unique case of hemolacria in a patient with multisystemic sarcoidosis and the importance of multispecialty involvement

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Background: Sarcoidosis is known as the "great pretender" due to its ability to mimic diseases. (1,2) Extrapulmonary manifestations can affect different organs such as the skin and eyes. (3) Conjunctival granuloma causing hemolacria is extremely rare but can be caused by inflammatory disorders. (4) The diagnosis of sarcoidosis continues to be challenging and requires appropriate management by a multidisciplinary team. (1,5) We aim to present a case of a young man with multisystemic sarcoidosis, who benefited from multispecialty care after presenting with hemolacria.

Results: A 39-year-old male with a past medical history of sarcoidosis, presented to the rheumatology clinic after presenting positive antinuclear antibodies (ANA). In 2016, he developed a keloid-type scar in his forearm tattoo. A biopsy confirmed the diagnosis of skin sarcoidosis. X-ray chest was ordered revealing bilateral mediastinal adenopathy, biopsy confirmed non-necrotizing granulomatous lymphadenitis. He remained asymptomatic, undergoing yearly monitoring with chest X-rays. In 2023, the patient reported severe fatigue to his primary care physician (PCP). Laboratory investigations revealed low morning testosterone levels and ANA titers 1:160. Testosterone replacement therapy resulted in symptom improvement. Five months later, he began having bloody tears during physical exertion. Ophthalmology diagnosed conjunctival non-necrotizing granuloma, managed successfully with topical corticosteroids. After the diagnosis of hemolacria due to granuloma, the PCP referred the patient to rheumatology, pulmonology, and ophthalmology for continuous monitoring. Upon referral to rheumatology clinic for new symptoms and positive ANA, further investigations revealed elevated-angiotensin-converting enzyme levels, and normal vitamin D. A multidisciplinary consensus determined that continued monitoring was the appropriate management strategy.

Discussion: We reported a case that highlights the importance of multidisciplinary collaboration in achieving optimal clinical outcomes, particularly in addressing rare manifestations such as hemolacria in sarcoidosis. As a chronic inflammatory disease with multi-organ involvement, sarcoidosis mandates comprehensive evaluation and treatment strategies Unfortunately, our patient's prolonged asymptomatic period led to discontinued monitoring, emphasizing the need for vigilant follow-up even in stable cases. Each specialty brings unique expertise crucial for addressing different facets of the disease. Collaboration among specialists ensures early detection, accurate diagnosis and more importantly helps to optimize patient outcomes and enhance quality of life.

Poster

Working Together in Sarcoidosis: Experience and Outcomes of a formalized Multidisciplinary Discussion

Ali Mustafa[1], Michelle Sharp[1], Kristen Mathias[2], Jasmine Malhi[3], Susana Carolina Dominguez Penuela[4], Kayla Nyakinye[1], Victoria Wotorson[1], Paula Barreras[4], Edward Chen[1], Steve Mathai[1], Carlos Pardo-Villamizar[4], Barney Stern[4], Abby Hubbard[5], Cherie Livingston[5], Edward Kasper[5], Jonathan Chrispin[5], Nisha Gilotra[5]

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Background: Sarcoidosis, a systemic illness that impacts multiple organs, has traditionally been managed by one or more physicians with varying degrees of care coordination. Given the complexity of patients with sarcoidosis, multidisciplinary discussions (MDD) involving a panel of subspecialist sarcoidosis experts may be valuable for patient management. MDD are becoming the standard of care for challenging illnesses, where they have been shown to improve diagnostic accuracy, care delivery, and clinical management. However, the value of MDD has not been evaluated in sarcoidosis.

Methods: The Johns Hopkins Sarcoidosis Center's MDD meeting was formalized in October 2019 and consists of physicians and advanced practice providers from pulmonology, cardiology, neurology, rheumatology, dermatology, hepatology, ophthalmology, and transplant medicine. We reviewed MDD held at our Center to evaluate its effectiveness. Weekly MDD were documented from June 2020 to December 2023. Goals and outcomes for each discussion were determined through chart review with a focus on diagnosis, sarcoidosis disease activity, and treatment changes.

Results: Of the 321 documented discussions, 207 unique patients were the subject of MDD. A majority of MDD were initiated by members of the group, however inpatient teams referred 14 (4%) cases. Sixty-six (21%) discussions questioned the diagnosis of sarcoidosis, 9 (14%) led to an alternate diagnosis. Ascertaining disease activity and additional organ involvement was a goal of 190 (59%) MDD; further evaluation was recommended in 68 (35%) instances of which 51 (75%) were recommended to undergo subspecialty consultation, facilitated by the MDD team. Imaging studies crucial to medical decision making, such as cardiac PET/CT, chest CT, and MRI, were reviewed in 84 (27%) MDD. Treatment decisions were discussed in 171 (55%) MDD, leading to medication changes in 123 (72%) of cases.

Discussion: We describe the results of 3 years of MDD for complex patients with sarcoidosis. Among patients discussed, the goals of discussion typically included diagnosis, disease activity, and treatment. The presence of a sarcoidosis-focused MDD resulted in significant changes in evaluation and management. Our work highlights the importance of a MDD approach in sarcoidosis, but more work is needed to understand their impact on patient outcomes.

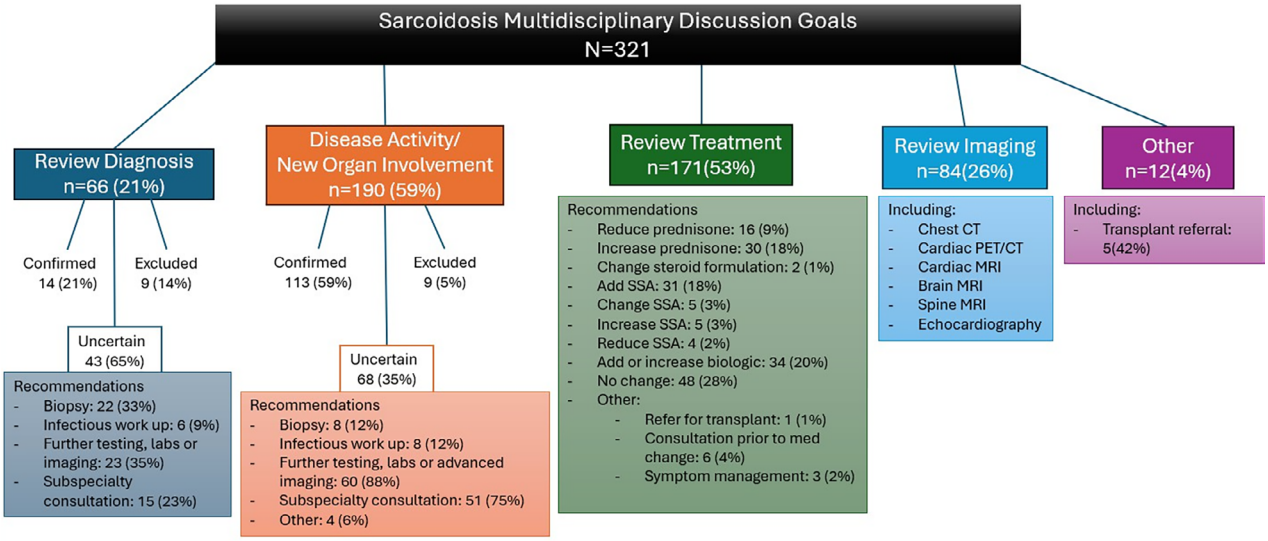

Figure 1:
Summary of goals for MDD and outcomes of discussion. Several MDD had multiple goals of discussion. If infectious work up was recommended, this could include blood or respiratory cultures or more invasive testing including bronchoscopy.
SSA – Steroid sparing agent
MDD – Multidisciplinary discussion

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