The Rheumatism Society of the District of Columbia

Presents...

The 15th Annual Rheumatology Fellows Forum

Saturday, May 13th, 2017

MedStar Washington Hospital Center
True Auditorium
Washington, DC
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David Pisetsky is Professor of Medicine and Immunology, Duke University Medical Center and Chief of Rheumatology, Durham Veterans Administration Medical Center. Dr. Pisetsky has conducted basic and translational research in the field of autoimmunity, focusing on the pathogenesis of SLE and the immunological properties of nuclear macromolecules, including DNA. From 2000-2005, he served as Editor of Arthritis and Rheumatism and, from 2006-2011, he was the first Physician Editor of The Rheumatologist. In 2016, he was awarded the ACR Presidential Gold Medal - the highest award the ACR can bestow in recognition of outstanding achievements over an entire career. He is currently the President of the United States Bone and Joint Initiative.

The title of his talk is “Antibodies as Diagnostic and Theranostic Markers in SLE”
Award Winners

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• David R. Amici - NIAMS (student/research post-bac) - Autoantigen upregulation in myositis muscle is driven by muscle regeneration and does not determine autoantibody specificity (pages 8-9)

• Shubhasree Banerjee – NIAMS - Vascular Inflammation Assessed by 18F-Fludeoxyglucose Positron Emission Tomography (FDG-PET) is Modified by Treatment in Patients with Large Vessel Vasculitis (page 12)

• Amit K. Dey – NIH (post doc) - Small Dense Low-density Lipoprotein Particle Number Relates to Coronary Plaque Burden Independent of Traditional Cardiovascular Risk Factors in Patients with Psoriatic arthritis (pages 17-18)

• Sara Faghihi-Kashani - NIEHS (post doc) - HLA-DQA1*05 is Associated with Interstitial Lung Disease in Caucasian Patients with Polymyositis and Dermatomyositis Independent of Autoantibody Status (pages 20-21)

Poster Awards

• Paloma Alejandro – WHC - Belimumab Use in African-American Patients in an U.S. Academic Medical Center (page 7)

• Blas Betancourt – NIAMS - Relapsing Polychondritis with Ulcers: A Little Rheumatology Prestidigitation (pages 13-14)

• Jeffery Eickhoff – WRNMMC - Efficacy of Coagulation Pathway Inhibitors in Attenuating Secondary Lung Injury in Lupus Ischemia/Reperfusion (IR) Murine Model (page 19)

• Elisabeth Kramer – GUH - Outcomes of African Americans with Scleroderma (page 31)

• Nancy Sein - WRNMMC - An Unusual Case of Human Parvovirus B19 Associated Arthritis (page 39)
Title: Intravenous Immunoglobulin in Combination with Intravenous Methylprednisolone in the Treatment of Calcinosis Associated with Juvenile Dermatomyositis (JDM)

Authors: Yaseen Aleatany1, Marc Phillpotts1, Olcay Y Jones1, 2, Gulnara Mamyrova1, Lisa G Rider1, 3, Rodolfo V Curiel1

1George Washington University, Washington, DC, 2Walter Reed National Military Medical Center, Bethesda, MD, 3Environmental Autoimmunity Group, NIEHS, NIH, DHHS, Bethesda, MD,

Background: Calcinosis is one of the hallmark complications of juvenile dermatomyositis (JDM), and is associated with long-term damage, functional disability, and poor quality of life. There is no known effective treatment of calcinosis and current treatment protocols have been limited to anecdotal retrospective studies. Few published case reports showed improvement of calcinosis in JDM patients treated with Intravenous Immunoglobulin (IVIG). We assessed the response of IVIG in five JDM patients with calcinosis.

Methods: Retrospective medical record review of over 200 JDM patients seen from 2008-2016 at The George Washington Myositis Clinic was performed. 53 (26.5%) of JDM patients developed calcinosis, 15 had at least one follow-up visit and 5 were identified that received IVIG treatment for calcinosis. The number of anatomic areas (bilateral upper extremities, lower extremities, axilla, chest, back, abdomen, head, and buttocks), limitation of joint range, type of calcinosis (plaque, nodular), consistency, extent, signs of inflammation, and progression were used to assess response to treatment.

Results: The median age at baseline was 14.8 years [13.7-17.7], 4 patients were male, and 3 were Caucasian, 2 Hispanic. Median disease duration at baseline was 5.5 years [2.9-10.0]. The median duration of IVIG treatment from baseline to clinical improvement in calcinosis was 9.0 months [5.0-13.0], with a dose ranging between 1g/kg- 2g/kg per month. Patients also received IV Methylprednisolone ranging from 100 mg to 1,000 mg at the time of the IVIG infusion; 4 patients also received oral prednisone and MTX, 1 pt infliximab and 1 pt rituximab, among other therapies. The median Childhood Assessment Questionnaire score (CHAQ) was 1.6 [0.17-2.6] pre-treatment and 0.0 [0.0-1.1] at follow-up after treatment. Median Childhood Myositis Assessment Scale score (CMAS) was 48.5 [20.8-50.8] pre- and 51.0 [38.0-51.5] post-treatment, median Manual Muscle Testing (MMT) was 138.0 [127.0-145.0] pre- and 150.0 [128.0-150.0] post-treatment. Median number of anatomic areas involved with calcinosis was 6.0 [1.5-7.5] pre- and 6.0 [1.0-8.0] post-treatment, the median number of restricted joints was 5.0 [1.5-8.0] pre- and 0.0 [0.0-6.5] post-treatment.

Conclusion: Major clinical benefit was seen after the initiation of IVIG and IV methylprednisolone in this small case series of JDM patients with refractory calcinosis. All patients exhibited a late response to IVIG therapy. Larger, controlled studies are needed to determine the effectiveness of immunosuppressive and immunomodulatory therapies for treatment of calcinosis associated with JDM.
Title: Belimumab Use in African-American Patients in an U.S. Academic Medical Center

Authors: Paloma Alejandro, Anjani Pillarisetty, Christopher Collins

MedStar Washington Hospital Center/Georgetown University Medical Center, Washington DC

Background/Purpose: Belimumab is an anti-BAFF monoclonal antibody approved for the treatment of auto-antibody positive patients with SLE. This study examines the effect of belimumab on clinical outcomes and disease activity in a cohort of African-American patients with SLE being treated at an academic medical center.

Methods: Data was analyzed for up to 24 months of therapy. Patient demographics, disease manifestations, medication usage, and labs were recorded for visits at Day 0 (day of initial belimumab infusion), and at months 3, 6, 12, 18, and 24. Whenever all appropriate labs, clinical exam and history were available, a SLEDAI was calculated. For any patient who discontinued belimumab therapy at any time point prior to 24 months, additional information as to reason was recorded.

Results: 23 African-American SLE patients were identified; mean age 38.9 years (22-58), 87% female, with a mean duration of disease of 12.7 years (4-31). At the time of their initial belimumab infusion, 91.3% of the patients were on prednisone at an average dose of 20 mg/day (5-60), 78.3% of patients were taking lupus DMARDs, and 91.3% were on HCQ. The mean SLEDAI score was 8.5 (2-20) with 39% of patients having a score ≥10. 65% of patients were hypocomplementemic (low C3/C4) at baseline, 60% had elevated anti-dsDNA titers, and 47% had both. The most common clinical disease manifestation at belimumab initiation was arthritis (56.5%) followed by cutaneous (47.8%). Over the subsequent observation period, 5 patients (22%) discontinued belimumab therapy at a mean duration of 8.4 months, 2 due to inefficacy, 1 secondary to abnormal LFTs, one patient moved away, and 1 patient self-discontinued secondary to feeling well. For the remainder of the patients, by month 3 the mean SLEDAI had decreased 3.6 points (8.5 to 4.9) and by month 24 the mean SLEDAI was 3.5 (p < 0.001). Prednisone dose among those still taking the medication also decreased, going from a mean of 20 mg/day to 8.06 mg/day by month 24 (p < 0.001). Four patients came off of prednisone completely. 53.8% of those patients with low C3/C4 normalized their levels and 25% of those with elevated anti-dsDNA titers became undetectable. One patient was hospitalized for community acquired pneumonia during the observation period but no other major infections were noted.

Conclusion: Belimumab is well tolerated and may be effective in African-American patients with SLE. Prednisone doses as well as SLEDAI scores decreased significantly and were maintained through 2 years of treatment in most patients.
Title: Autoantigen Upregulation in Myositis Muscle is Driven by Muscle Regeneration and Does Not Determine Autoantibody Specificity

Authors: David R. Amici1, Iago Pinal-Fernandez1*, Cassie A Parks1, Assia Derfoul1, Richard Yeker1, Katherine Pak1, Julie Paik2, Jemima Albayda2, Andrea M Corse2, Tom Lloyd2, Lisa Christopher-Stine3, Andrew L Mammen1,2,3

1National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, 2Johns Hopkins Department of Rheumatology, Baltimore, MD, 3Johns Hopkins Myositis Center, Baltimore, MD,

Purpose/Methods: In myositis, autoantibodies define unique phenotypes, and individual patients typically produce only one autoantibody. It has been suggested that selective overexpression of a given myositis autoantigen may drive autoantibody production against that protein. To test this hypothesis, RNA-sequencing was performed on muscle biopsies from 82 myositis patients, including those with autoantibodies recognizing HMGCR (n=22), SRP (n=5), Jo1 (n=5), NXP2 (n=8), Mi2 (n=3) and TIF1γ (n=5), as well as on non-myositis control biopsies (n=10), normal mouse muscle, and regenerating mouse muscle.

Results: Compared with control biopsies, myositis biopsies from all clinical and autoantibody groups displayed elevated expression of most myositis autoantigens (Figure 1A, B). There were no differences in expression patterns for antigens considered myositis-specific (e.g. MDA5) vs. myositis-associated (e.g. Ro52), and increased expression of a given autoantigen did not correlate with the presence of autoantibodies recognizing that autoantigen. To explore the mechanisms underlying this broad upregulation of many myositis autoantigens in myositis muscle, we assessed the correlation of myositis autoantigen expression with transcript levels of genes upregulated with chronic muscle damage (e.g. LIPE, FSP1), inflammation (e.g. CD19, CD3G), and muscle regeneration (e.g. NCAM1, MYOG). Autoantigen expression correlated most highly with expression of markers of muscle regeneration (Figure 1C, D). Additionally, most autoantigens were upregulated in regenerating mouse muscle after experimental injury (Figure 1E), suggesting a causal link between muscle regeneration and autoantigen expression.

Conclusion/Significance: Most myositis autoantigens are broadly upregulated in regenerating muscle, which may relate to propagation of autoimmunity. However, factors other than specific antigen induction govern the development of unique autoantibodies in individual patients.
Figure 1A: Heatmap displaying expression (log fold-change) of myositis autoantigens in myositis-specific autoantibody groups and IBM. B: Representative box-and-whisker plots of an upregulated autoantigen (Mi2) and an unchanged antigen (NT5C1A) in myositis subgroups. C: Heatmap displaying the Pearson correlation of autoantigen expression with transcripts indicative of chronic muscle damage, acute inflammation, and muscle regeneration. D: Representative scatterplot, color-coded by disease subtype, of Mi2 expression as a function of NCAM1 (indicative of muscle regeneration) and LIPE (indicative of fatty replacement and chronic damage). E: Expression of myositis autoantigens in regenerating mouse muscle at three time points after a day 0 (D0) cardiotoxin injury.
Title: Improving Gout Outcomes in the Primary Care Setting

Authors: CPT Wayne T. Bailey, MC, USA, LT Jeffrey C. Eickhoff, MC, USN, CAPT Michael P. Keith, MC, USN

Walter Reed National Military Medical Center, Department of Rheumatology, Bethesda, MD

Background: Gout affects up to twelve million Americans annually with significant morbidity and higher healthcare costs. Gout is generally managed with urate-lowering therapy (ULT) in the primary care setting. Studies have demonstrated inadequate titration of ULT to obtain a goal serum uric acid (sUA) level <6.0mg/dL.

Project Initiative/Objectives: This Quality Improvement (QI) project was designed to assess the comfort level of providers managing gout, provide education (gout management) for primary care resident physicians, provide patient educational materials to stimulate patient-initiated discussion about their gout management, and identify barriers to obtaining a goal sUA.

Methods: Pre- and post-intervention surveys were provided to WRNMMC Internal Medicine PGY-2 and PGY-3 cohorts. Educational interventions included a 30-minute lecture with accompanying laminated cards outlining approach to monitoring/treatment of chronic gout, and patient education (posters, National Institutes of Health educational pamphlets in waiting areas). Gout patients empaneled to each resident were identified via CarePoint with ICD-10 codes (M10.XXX). From this sample size, the goal was to increase sUA checked per primary care visit by 25% from baseline.

Results: 26/31 residents were included in the pre-interventional survey and 19/31 were included in the post-intervention survey. 60 resident-empaneled gout patients were included. Provider comfort level adjusting ULT was assessed (0=least comfortable,10=most comfortable) and was statistically significant for both PGY-2 and PGY-3 cohorts with a p-value of 0.011 and 0.012 respectively, corresponding to an increase from 4 to 6 and 5.25 to 7.5 on the Likert scale. All patient charts were reviewed. The rate of sUA/visit drawn increased from 20% to 38.5%. This was not statistically significant and likely due to small sample size.

Conclusion: Residents were subjectively more comfortable adjusting ULT post-educational intervention. We are unable to draw conclusions regarding objective improvement in sUA levels after only 3 months of post-intervention lab data.
Title: Atypical Presentation of Polymyalgia Rheumatica: A Case of Puffy Arms Unraveled with Novel Advanced Imaging

Authors CPT Wayne T. Bailey, MC, USA, Lt. Col. Angelique N. Collamer, USAF, MC

Walter Reed National Military Medical Center, Department of Rheumatology, Bethesda, MD

Introduction: Polymyalgia rheumatica (PMR) is a disease of elderly onset affecting 2% of the population. Classically presentation is bilateral shoulder and hip girdle pain, stiffness, or limited range of motion. Degenerative arthritis is prevalent in this patient population, making the initial diagnosis of PMR difficult, especially if classic features are absent. Experts advocate low-dose corticosteroid trial in ambiguous cases as rapid improvement is characteristic of PMR. Prompt corticosteroid response can be seen in conditions such as elderly onset rheumatoid arthritis (EORA) and remitting seronegative symmetrical synovitis with pitting edema (RS3PE). We describe a patient who presented with symptoms concerning for malignancy, PMR and RS3PE with a diagnosis of PMR was supported by fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT).

Case: 85 year old female with Sjogren’s Syndrome (SjS) presented with three weeks of marked bilateral arm non-pitting edema. Swelling was noted on both hands and forearms extending proximal to her elbows without synovitis or subjective pain. No lower extremity involvement was present. Physical exam revealed bilateral shoulder pain and fatigue on internal rotation and extension. ESR was 86 mm/hr, CRP was 13.6 mg/dL (normal <0.5) and rheumatoid factor was 16 IU/mL (normal <14). Differential diagnosis included occult malignancy, venous thromboembolism (VTE), RS3PE, PMR and EORA. Upper extremity ultrasound was negative for VTE. Occult malignancy was considered and FDG-PET/CT was obtained. Radiotracer uptake was present within her shoulders, sternoclavicular joints, hips, cervical and lumbar spine. Findings were consistent with bursitis in classic PMR areas. Prednisone was started and arm swelling resolved within 72 hours.

Conclusion: Advanced imaging has been used recently in the diagnosis of patients with uncharacteristic features of rheumatic diseases. PMR typically presents with constitutional symptoms and proximal girdle bursitis. However, dramatic limb swelling is unusual, prompting alternative diagnosis considerations. Moderate dose corticosteroids improve symptoms related to many conditions. Standard PMR treatment is one to two years of tapering steroids. A correct diagnosis is paramount to minimize iatrogenic injury, particularly in the elderly. To our knowledge, this is the first reported case of PMR manifesting as limb edema confirmed with FDG-PET/CT.
Title: Vascular Inflammation Assessed by 18F-Fludeoxyglucose Positron Emission Tomography (FDG-PET) is Modified by Treatment in Patients with Large Vessel Vasculitis

Authors: Shubhasree Banerjee1, Sara Alehashemi1, Ali Cahid Civelek2, Elaine Novakovich3, Armin A. Bagheri3, Ashkan A. Malayeri3, Mark A. Ahlman3, Peter C. Grayson3

1Rheumatology Fellowship and Training Branch, NIAMS, 2Radiology and Imaging Sciences, Clinical Center, NIH, 3Vasculitis Translational Research Program, NIAMS, Bethesda, MD

Background: Disease activity in large vessel vasculitis (LVV) is traditionally assessed by clinical and serological (ESR, CRP) parameters. Imaging assessment may also be useful to monitor LVV, and vascular inflammation can be detected by FDG-PET. The study objective was to determine if currently available therapies for LVV impact disease activity as assessed by clinical, serologic, and imaging-based parameters.

Methods: Patients with giant cell arteritis (GCA) or Takayasu’s arteritis (TAK) were recruited into a prospective, observational cohort. All subjects in this study underwent ≥2 FDG-PET/CT scans at 6-month intervals. Serologic assessment [ESR, CRP], clinical assessment [physician global assessment (PGA)] and imaging assessment (PETVAS) was determined at each visit. PETVAS is a global summary score of arterial FDG uptake measured qualitatively in 9 vascular beds (range 0- 27). Clinical and imaging assessments were performed blinded to each other. Treatment status between visits was categorized as increased, decreased, or unchanged. Treatment change was defined as change in daily prednisone by ≥5mg or addition/50% dose change of a DMARD or biologic therapy.

Results: FDG-PET/CT was performed in 33 patients with LVV (GCA=21; TAK=12) over 91 visits. Interval treatment changes involved glucocorticoids (n=28), methotrexate (n=17), tocilizumab (n=7), TNF inhibitors (n=5), or another DMARD/ biologic (n=10). Increased, decreased, or unchanged therapy was recorded over 26, 11, and 20 visit intervals respectively. There was simultaneous glucocorticoid reduction with DMARD increase over 1 interval, which was excluded from analysis. PETVAS differed among the 3 treatment categories (p<0.0001) with significant reduction in PETVAS score in increased versus decreased treatment and increased versus unchanged treatment groups. A significant change in ESR was observed among the 3 treatment groups (p=0.01) with a significant decrease in ESR in the increased versus unchanged treatment groups. Similar findings were observed for CRP (p=0.03). Change in PGA did not differ significantly among the 3 treatment categories (p=0.2). PETVAS decreased significantly with the addition of tocilizumab (25 to 20, p=0.01) and to a lesser degree with TNF inhibitor therapy (19 to 17, p=0.06). Methotrexate did not significantly affect PETVAS (24 to 19.5, p=0.3).

Conclusion: Changes in treatment in patients with LVV are more consistently associated with changes in imaging-based assessments rather than serologic or clinical parameters. Specific medications can reduce vascular inflammation as measured by arterial FDG uptake. Assessment of disease activity in LVV should incorporate serologic, clinical, and imaging based parameters.
Title: Relapsing Polychondritis with Ulcers: A Little Rheumatology Prestidigitation

Authors: Blas Betancourt, Marcela Ferrada, James Katz, and Peter Grayson

National Institutes of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, MD

Case Description: A 48-year-old female presented with a 20-year history of recurrent subglottic and bronchial stenosis requiring tracheostomy and airway stenting. The most recent episode occurred 5 months ago with acute respiratory distress status post tracheostomy. She was treated with a prednisone taper to discontinuation along with Rituximab. Her history included recurrent oral and genital ulcers coinciding with the respiratory problems. She reported pain in fingers, wrists, elbows, shoulders, knees, and ankles. She noted morning stiffness for 2 hours, sharp chest wall pain exacerbated by cough and trunk movement, and bilateral ear pain (outer part) that interrupted sleep. Physical examination revealed 2 small white based ulcers < 2mm inside of the upper lip. Multiple joints were tender without redness or effusion including fingers, wrists, elbows, shoulders, knees, and ankles. The left sternoclavicular joint and multiple costochondral joints also on the left were tender. Pelvic examination demonstrated an area of vaginal scarring from an old ulcer.

Investigations showed CRP = 60.60 mg/L (0-4.99 mg/L) with normal erythrocyte sedimentation rate. Anti-myeloperoxidase antibody levels were borderline at 0.04 units (<0.04 units). Antinuclear antibodies (ANA), anti-extractable nuclear antigens (ENA), anti-double-stranded DNA antibody, lupus anticoagulant, anti-cardiolipin antibodies (IgM and IgG), and anti-Proteinase-3 antibody were all negative. Serology for syphilis, HIV, hepatitis B and C were negative as well. C3, C4, and urinalysis were normal. Screening for tuberculosis (QuantiFERON) was negative. PET/CT showed signs of activity of the ascending aorta, aortic arch, and descending thoracic aorta (see figure). PET/MRI revealed active vasculitis with mild to moderate increased FDG activity involving major branches of the aortic arch. The patient was diagnosed with Mouth and Genital Ulcers with Inflamed Cartilage (MAGIC syndrome) owing to the overlapping features of Behçet’s disease and relapsing polychondritis. The patient was started on prednisone 40 mg daily along with Rituximab infusion.

Case Discussion: MAGIC syndrome is a rare multisystem disease with overlapping features of Behçet’s disease and relapsing polychondritis. This condition can be associated with inflammatory aortitis and ultimately aneurysmal aortitis. The use of advanced images studies such as PET/CT and PET/MRI can be used to help in the clinical diagnosis and identify patients with active vascular involvement. We were able to identify the presence of inflammatory aortitis in our case and thus justify intensified immunosuppression.

Conclusion: This case highlights the danger of attributing complaints of chest pain in MAGIC syndrome solely to the clinical finding of costochondritis. Close monitoring for the possible development of inflammatory aortic aneurysms, including the use of advanced image studies, should be considered in patients with MAGIC syndrome who have persistently high levels of inflammatory markers. Moreover, inflammatory markers may be misleading if only the ESR is measured. We recommend that the CRP be measured in conjunction with the ESR in cases of MAGIC syndrome.
Figure: PET/CT demonstrating an increased activity of the aortic arch.
Title: Patient Assistance Program Outcomes in a Community Clinic Setting

Authors: Stephanie Cerritos1, Yani Ruiz-Perdomo1, Natalie Tobar1, Ann Biehl2, James D. Katz1

1National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, 2Clinical Center Pharmacy Department, NIH, Bethesda, MD

Background: Under and uninsured patients are at risk for inadequate treatment of rheumatic disease due to issues related to access to care. One barrier is the cost of medications. We previously showed that medication costs in our patient population averaged $1659/patient/10 weeks (and higher in the case of rheumatoid arthritis). Patient assistance programs (PAPs) offered by pharmaceutical companies are one mechanism by which this financial barrier to care may be addressed.

Aim: To understand one aspect of the direct cost of care upon a community health clinic.

Methods: We created a team to aid clients in the process necessary for seeking approval for high-cost biological therapy. We then followed all patients who required assistance with access to such treatment over the course of one year. Our analysis identified individuals with barriers to care and the subsequent rates of success in procurement of high-cost medications through the assistance programs. We stratified the analysis based upon a diagnosis of Rheumatoid Arthritis (RA) or Other Autoimmune diseases (OTHER).

Results: For the total number of patients there is a 93.9% success rate for patients who apply to the PAP programs and get accepted. Patients diagnosed with RA have a 92.3% of getting assistance and patients diagnosed with other autoimmune diseases have a 100% acceptance rate. The patients that are denied assistance are those that can’t provide proper documentation of income or are eligible for government assistance like Medicaid or Medicare.

Discussion: This study asks the question, what is the impact of a dedicated effort within a community clinic setting aimed at expediting access to medications through a streamlined Patient Assistance Program? A disadvantage of this study is that clinical outcomes are not analyzed. We have previously demonstrated that outpatient drug costs for rheumatic diseases are important to target when looking to contain overall direct health care costs. Our observations take this further to demonstrate that a high proportion of limited-resource individuals may succeed in attaining access to high cost medications when aided by a health care team dedicated to stream-lining the PAP process. At the same time because rheumatology trainees are all involved in the program, they learn about health disparities. Finally, we determined that the program yields downstream benefits as it enables the clinical pharmacist to spend more time on teaching, clinical oversight and academic scholarship. In conclusion, investing resources in a support program to aid patients in the PAP process may reap both financial and educational benefits.
**TABLE 1.**

**BIOLOGICAL THERAPY ACCESS RATES**

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<td>RA</td>
<td>52</td>
<td>48</td>
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<tr>
<td>Other Autoimmune</td>
<td>14</td>
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Success Rate for Patients: 93.9%
Success Rate for Patients with other Autoimmune Diseases: 100%
Success Rate for Patients Diagnosed with RA: 92.3%
Title: Small Dense Low-density Lipoprotein Particle Number Relates to Coronary Plaque Burden Independent of Traditional Cardiovascular Risk Factors in Patients with Psoriatic arthritis

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1National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, US. 2Arthritis and Rheumatism Associates, Rockville, MD

Introduction: Psoriatic arthritis (PsA) and psoriasis (PSO) are chronic inflammatory diseases that are associated with increased risk of cardiovascular disease (CVD) and lipoprotein dysfunction. Moreover, CCTA-derived coronary plaque burden is a reliable marker of subclinical atherosclerosis. Furthermore, atherogenic small dense LDL-particle (sdLDL-p) is now recognized as an important predictor of CVD risk. Here we aim to determine the difference in coronary plaque burden and sdLDL-p levels in patients with psoriatic arthritis when compared to psoriasis only patients and healthy controls.

Methods: 47 consecutive PsA patients, 105 consecutive PSO only (with no diagnosis of PsA) patients and 61 age/sex matched controls underwent cardiometabolic profiling and CCTA (Toshiba, 320-detector row) for coronary plaque characterization. Total (TB) and non-calcified (NCB) coronary plaque burden were quantified using semi-automated software (QAngio Medis). Lipoprotein profiling was done using NMR spectroscopy. The association of NCB and sdLDL-p was analyzed using multivariable regression models (STATA 12).

Results: PsA as well as PSO only patients were middle-aged, predominantly male, had a moderate cardiovascular risk by Framingham risk score and had moderate-to-severe skin disease (Table 1). PsA patients had higher TB (1.24±0.54 vs. 0.99±0.34, p<0.001) and NCB (1.21±0.50 vs. 0.98±0.34, p<0.001) when compared to healthy controls. Moreover, PsA patients also had increased TB (1.24±0.54 vs. 1.10±0.39, p=0.003) and NCB (1.21±0.50 vs. 1.07±0.39, p=0.002) in comparison to PSO only patients. This difference in NCB between PsA and PSO only group persisted independent of traditional risk factors (Beta=0.16, p=0.002). In addition, sdLDLp levels were also higher in the PsA group when compared to the PSO only group (585.54±327.04 vs. 529.75±301.75, p=0.04) as well as controls (585.54±327.04 vs. 401.36±343.78, p=0.005). Furthermore, sdLDL-p levels associated with increased NCB in the PsA group (Beta=0.30, p=0.003) and the PSO only group (Beta=0.21, p=0.001) which remained robust beyond adjustment for traditional cardiovascular risk factors, BMI, Statin use and systemic/biologic therapy in both PsA (β=0.29, P=0.012) and PSO only group (β=0.20, P=0.004).

Conclusion: PsA patients have higher coronary plaque burdens when compared to PSO only group and healthy controls beyond traditional cardiovascular risk factors. Furthermore, sdLDL-p levels independently associated with subclinical atherosclerosis beyond traditional cardiovascular risk factors in both PsA and PSO only patients.
**Significance:** These findings suggest that PsA patients may have increased cardiovascular risk than PSO only patients suggesting that patients with PsA should receive aggressive cardiovascular risk factor profiling. Whether advanced lipid testing offers an advantage over NMR based sdLDL-P needs testing in larger, prospective studies.

Table 1: Comparison of Parameters between Psoriatic arthritis (PSA), Psoriasis only (PSO) and Controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PSA</th>
<th>PSO</th>
<th>Controls</th>
<th>P (PSA vs PSO)</th>
<th>P (PSA vs Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic and Clinical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Characteristics</td>
<td>(N=47)</td>
<td>(N=105)</td>
<td>(N=61)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>50.72±11.27</td>
<td>49.69±13.09</td>
<td>40.00±13.44</td>
<td>0.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Males</td>
<td>28 (50)</td>
<td>65 (62)</td>
<td>44 (71)</td>
<td>0.79</td>
<td>0.21</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (30)</td>
<td>25 (24)</td>
<td>9 (15)</td>
<td>0.44</td>
<td>0.07</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>21 (45)</td>
<td>53 (51)</td>
<td>16 (27)</td>
<td>0.51</td>
<td>0.05</td>
</tr>
<tr>
<td>Type-2 Diabetes</td>
<td>8 (17)</td>
<td>10 (10)</td>
<td>4 (7)</td>
<td>0.19</td>
<td>0.09</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>30.88±6.69</td>
<td>29.20±6.37</td>
<td>26.00±4.87</td>
<td>0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>6 (13)</td>
<td>12 (11)</td>
<td>2 (3)</td>
<td>0.81</td>
<td>0.07</td>
</tr>
<tr>
<td>Clinical and Lab Values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol, mg/dl</td>
<td>184.09±42.86</td>
<td>182.66±37.48</td>
<td>177.75±35.78</td>
<td>0.42</td>
<td>0.20</td>
</tr>
<tr>
<td>High-density Lipoprotein, mg/dl</td>
<td>53.85±11.60</td>
<td>55.51±18.09</td>
<td>57.08±18.05</td>
<td>0.29</td>
<td>0.16</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>100 (76-181)</td>
<td>106 (78-141)</td>
<td>87 (74-129)</td>
<td>0.89</td>
<td>0.31</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>4 (1-9)</td>
<td>2 (1-3)</td>
<td>1 (1-3)</td>
<td>0.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Framingham Risk Score</td>
<td>3 (1-6)</td>
<td>2 (1-7)</td>
<td>1 (1-3)</td>
<td>0.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NMR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>105.63±36.09</td>
<td>105.63±36.09</td>
<td>96.86±35.07</td>
<td>0.46</td>
<td>0.10</td>
</tr>
<tr>
<td>LDL particle number</td>
<td>1217.86±423.8</td>
<td>1196.26±409.0</td>
<td>1034.28±440.0</td>
<td>0.39</td>
<td>0.02</td>
</tr>
<tr>
<td>LDL particle size</td>
<td>20.67±6.66</td>
<td>20.67±6.63</td>
<td>20.99±0.78</td>
<td>0.36</td>
<td>0.04</td>
</tr>
<tr>
<td>Small LDL particle</td>
<td>529.75±301.75</td>
<td>529.75±301.75</td>
<td>401.36±343.78</td>
<td>0.04</td>
<td>0.005</td>
</tr>
<tr>
<td>Large LDL particle</td>
<td>355.96±239.96</td>
<td>355.96±239.96</td>
<td>374.26±30.02</td>
<td>0.47</td>
<td>0.32</td>
</tr>
<tr>
<td>Psoriasis Characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriasis area severity index</td>
<td>6.5 (4.9-10.1)</td>
<td>7.9 (4.9-13.5)</td>
<td>---</td>
<td>0.12</td>
<td>---</td>
</tr>
<tr>
<td>Systemic/Biologic therapy</td>
<td>23 (49)</td>
<td>27 (26)</td>
<td>---</td>
<td>0.005</td>
<td>---</td>
</tr>
<tr>
<td>Coronary Burdens</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Burden(X100)</td>
<td>1.24±0.54</td>
<td>1.10±0.39</td>
<td>0.003</td>
<td>0.99±0.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Calcified Burden(X100)</td>
<td>1.21±0.50</td>
<td>1.07±0.39</td>
<td>0.002</td>
<td>0.98±0.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dense-Calcified Burden(X100)</td>
<td>0.01 (0.003-0.030)</td>
<td>0.009 (0.003-0.030)</td>
<td>0.99</td>
<td>0.009 (0.003-0.020)</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as Mean±SD or Median (IQR) and categorical variables as N (%). P-value<0.05 deemed significant.
Title: Efficacy of Coagulation Pathway Inhibitors in Attenuating Secondary Lung Injury in Lupus Ischemia/Reperfusion (IR) Murine Model

Authors: LT Jeffrey C. Eickhoff, MC, USN1, COL Jess Edison, MC, USA1, S. Peng2, Chantal M. Moratz3

1Walter Reed National Military Medical Center, Bethesda, MD, 2Food and Drug Administration, Silver Spring, MD, 3Uniformed Services University School of Health Sciences, Bethesda, MD

Background: Systemic lupus erythematosus (SLE) is a complex disease characterized by tissue damage in multiple organ systems. Defective regulation of the coagulation cascade plays an important role in the pathogenesis, through impaired fibrinolysis and tissue ischemia. Previous work has demonstrated the effectiveness of inhibiting other inflammatory mediators, including activated complement components, chemotactic signals, or the sphingosine-1-phosphate (S1P) signaling pathways, in attenuating primary tissue injury. However their ability to inhibit secondary systemic sites of tissue injury in inconsistent. Other work has suggested that activated platelets from the initial site of tissue injury may play a critical role in the secondary systemic injury. We hypothesize that thrombin released from these platelets may act at remote sites to cause ischemic injury through activation of the coagulation cascade as well as through protease-activated receptor 1 (PAR-1) on endothelial cells. PAR-1 activation decreases barrier function in the lungs, leading to exacerbation of the baseline lung damage seen in lupus-prone mice. Using an ischemia/reperfusion model of the intestine in MRL/lpr lupus-prone mice, the current work explores the efficacy of extrinsic coagulation cascade inhibition to mitigate secondary lung injury compared to other inflammatory inhibitors.

Methods: Using a superior mesenteric artery IR model, we induced tissue injury in both immune competent (C57BL/6) and autoimmune prone (B6.MRL/lpr) mice. Various inhibitors were assessed for efficacy in reducing remote lung injury, including FTY720 (S1P receptor agonist), PTX (Gαi signaling inhibitor) and TFPI (coagulation inhibitor). The pathology was assessed by H&E, with further evaluation ongoing including immunohistochemistry/immunofluorescence analysis (comparing baseline PAR-1 levels in C57BL/6 vs B6.MRL/lpr lung tissue), and western blot analysis of coagulation components.

Results: Tissue Factor Pathway Inhibitor (TFPI), a coagulation inhibitor targeting the intrinsic and extrinsic pathways, was found to reduce lung injury (pneumonitis scores) after IR to below sham levels, with improved alveolar architecture and vascular structure. Inhibition of the S1P receptor signaling pathways, or Gαi linked signaling pathways (chemotactic factors) were not effective in attenuating secondary lung injury. Current work is evaluating the mechanism of inhibition.

Conclusion: The coagulation cascade plays an important role in lung injury after remote ischemia/reperfusion injury. Inhibition prior to prothrombin activation with TFPI is the most effective point to inhibit tissue injury, and suggests potential future targets for therapeutic interventions. Of particular importance is the reduction of edema/injury below sham group levels. This indicates a baseline defect in the coagulation cascade in the Lupus prone mice.
Title: HLA-DQA1*05 is Associated with Interstitial Lung Disease in Caucasian Patients with Polymyositis and Dermatomyositis Independent of Autoantibody Status

Authors: Sara Faghihi Kashani, Fredrick W. Miller, Terrance P. O’Hanlon, Willy A. Flegel, Sharon D. Adams, Ira N. Targoff, Chester V. Oddis, Rohit Aggarwal, Lisa G. Rider, Steven R. Ytterberg, Lisa Christopher-Stine, Sonye K. Danoff, Paul F. Dellaripa, Eijaz A. Shamim, Andrew Mamman, Adam Schiffenbauer

1Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 2Department of Transfusion Medicine, NIH Clinical Center, National Institutes of Health, Bethesda, MD, 3Veterans Affairs Medical Center, University of Oklahoma Health Sciences Center, and Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Myositis Center, University of Pittsburgh School of Medicine, Pittsburgh, PA, 5Division of Rheumatology, Mayo Clinic, Rochester, MN, 6Johns Hopkins Myositis Center, Johns Hopkins University School of Medicine Baltimore, MD, 7Division of Pulmonary and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD, 8Division of Rheumatology, Immunology, and Allergy, Brigham and Women’s Hospital, Boston, MA, 9Department of Neurology, Mid-Atlantic Permanente Research Institute, Kaiser Permanente, Rockville, MD, 10National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD

Background: Interstitial lung disease (ILD) is a frequent complication and a major contributor to mortality and morbidity in polymyositis and dermatomyositis (PM/DM). Previous studies have linked the presence of anti-synthetase autoantibodies (ASA) and part of the HLA 8.1 ancestral haplotype (AH8.1 = HLA-A*01, B*08, Cw*07, DRB1*0301, DQA1*05) to ILD in PM/DM patients. This study aimed to evaluate the contribution of HLA-DQA1*05 to the presence of ILD in Caucasian PM/DM independent of ASA.

Methods: Caucasian patients with adult-onset PM/DM per Bohan and Peter criteria and with HLA class I (A, B and Cw) and class II (DRB1 and DQA1) were included. ILD status was determined by retrospective chart review based on imaging results and/or treating specialist’s diagnosis. ASA were determined by standard immunoprecipitation methods. Pearson chi-square (Fisher exact when appropriate), multiple logistic regression tests and forward stepwise logistic methods were applied. P<0.05 was considered statistically significant.

Results: Overall, 27 (33%) had ILD, 29 (36%) were positive for the presence of ASAs and 29 (36%) carried the AH8.1. ILD was associated with ASA (OR=7.82, 95%CI: 2.77-22.09, P<0.001) and with the AH8.1 (OR=3.57, 95%CI: 1.35-9.45, P=0.010) as expected. Of the five AH8.1 alleles, HLA-DQA1*05 was the only locus significantly associated with ILD after adjusting for the presence of ASA (OR=5.81, 95%CI: 1.43-23.57, P=0.014). This association remained significant after additionally adjusting for the presence of the other alleles of the AH8.1 (OR=11.94, 95% CI: 1.75-81.54, P=0.011). Chi-squared tables, categorizing the cohort based on the presence of AH 8.1 allele, were used to assess the independent effect of HLA-DQA1*05 on risk of ILD conditioned on ASA status. Frequency of ILD was higher in DQA1*05 carriers, however, due to limited power, not all comparisons met statistical significance. Additionally, forward stepwise logistic analysis was performed while keeping ASA in the model regardless of step, DQA1*05
was the only HLA allele that remained in the best fit model for risk of ILD (OR=5.81, 95% CI: 1.43-23.57, P=0.014). Figure 1 shows the risk of ILD in Caucasian PM/DM patients based on the ASA and DQA1*05 status.

**Conclusion:** Our results show that HLA-DQA1*05 is associated with an increased risk of ILD in Caucasian PM/DM patients, independent of ASA and other AH8.1 alleles. HLA-DQA1*05 seems to be a useful test for evaluating the risk of ILD in ASA negative PM/DM patients. This suggests HLA-DQA1*05 has diagnostic, prognostic and pathogenic implications for myositis-associated ILD, that should be further assessed in additional cohorts.

**Figure 1.** ILD risk in Caucasian PM/DM patients based on anti-synthetase autoantibody (ASA) and HLA DQA1*05 allele status

### Presence of ILD in PM/DM patients

- **ASA negative**
  - [9/52 (17%)]
- **DQA1*05 negative**
  - [0/22 (0%)]
- **ASA positive**
  - [18/29 (62%)]
- **DQA1*05 positive**
  - [15/23 (65%)]

### Comparison of ILD risk

- **ASA negative** vs. **ASA positive**
  - OR=7.82, P<0.001
- **DQA1*05 negative** vs. **DQA1*05 positive**
  - OR=19.88, P=0.007 (OR is calculated using Woolf-Haldane Correction method)
- **ASA negative** vs. **DQA1*05 negative**
  - OR=1.87 P=0.50

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*a Numbers in the brackets represent those positive for the presence of ILD over the total number in that study group. Percentages are shown in parenthesis.
*a comparison between these groups has yielded OR=7.82, P<0.001.
b comparison between these groups has yielded OR=19.88, P=0.007 (OR is calculated using Woolf-Haldane Correction method).
*c comparison between these groups has yielded OR=1.87 P=0.50.
Title: Airway Findings in Patients with Relapsing Polychondritis

Authors: Marcela A. Ferrada, Peter Grayson, James Katz

National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, MD

Purpose/Methods: Relapsing polychondritis (RP) is a rare multiorgan disease. Involvement of the upper and lower airway is associated with significant morbidity and mortality. Isolated airway involvement can be seen even without obvious ear swelling. The study objective was to determine the prevalence of airway inflammation and damage in patients with RP who endorse clinical symptoms suggestive of airway disease. Patients described in this cohort were selected from a prospective natural history protocol. All patients met McAdams or Damiani’s diagnosis criteria for relapsing polychondritis. Patients were selected if they reported voice changes, choking sensation, shortness of breath or cough. All patients underwent laryngoscopy and dynamic computed tomography (CT) scanning.

Results: 10 adult patients were identified out of our cohort of 20 for inclusion in this report. Demographics of these individuals were: age 48.9 (SD 7.6) and 90% of the patients were female, 90% of the patients were white; All of the patients reported voice changes, cough, choking sensation and shortness of breath. On laryngoscopy, 90% of the patients had arytenoid swelling (image 1), 80% of the patients had nasal ulcers, 10% septal perforation, and no patient had a saddle nose deformity. On dynamic CT scan, 30% of the patients had tracheomalacia, 20% had tracheobronchomalacia, and 20% had alveolar infiltrates. 30% of the patients had tracheal thickening and 30% had peribronchial thickening.

Conclusion: Airway symptoms such as voice changes, cough, choking sensation and shortness of breath in patients with relapsing polychondritis should be further investigated with laryngoscopy and dynamic CT to assess for airway inflammation and damage. Arytenoid swelling is a common finding in RP and may be indicative of active disease.
**Title:** *Children with Relapsing Polychondritis are Likely to be Seen in the Emergency Room Prior to Establishing the Diagnosis*

**Authors:** Marcela A. Ferrada, Ninet Sinaii, Keith Sikora, Peter C Grayson, Thomas Christie, Robert Colbert, James Katz

National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, MD

**Background/Methods:** Relapsing polychondritis (RP) is a rare immune-mediated disease characterized by recurrent episodes of chondritis. Clinical manifestations can be variable resulting in a delay of diagnosis, especially in children. We sought to explore the various patterns of early disease presentation in children by way of an international survey. A questionnaire based on known clinical symptoms and several possible clinical presentations associated with RP was developed. The Relapsing Polychondritis Awareness and Support Foundation administered the survey by posting the link to it on the Relapsing Polychondritis pediatric support group. The survey was anonymous and met criteria for exemption from IRB review and was approved by the Office of Human Subjects Research Protections.

**Results:** The data of 13 surveys is included in this analysis. The mean current age was 14.6 years (SD=6), with mean age at diagnosis of 9.9 years (SD=5). 62% (n=8) of the patients were male. 69% (n=9) of the patients saw more than 3 doctors prior to diagnosis, and 30% (n=4) were diagnosed by a rheumatologist. The most common painful joints were ankles and knees (each 38%; n=5). 77% of the patients went to an emergency room due to RP symptoms prior to diagnosis with the top two reasons of ear pain 38% (n=5) and shortness of breath 31% (n=4). 38% (n=5) of the patients were diagnosed with asthma prior RP diagnosis. 62% (n=8) of the patients reported that weather changes were symptom triggers. In females, 80% (n=4) had worsening of symptoms with menses. 77% (n=10) of the patients missed school for more than a week and 69% (n=9) missed more than a month of school due to their disease.

**Conclusion:** In this cohort of pediatric patients with RP, we found that there were possible environmental and personal triggers such as weather and menstruation. Our data suggest that establishing a diagnosis was difficult as evidenced by the fact that the majority of patients saw more than 3 doctors prior to establishing a diagnosis. The majority of doctors making the diagnosis were not rheumatologists. The data reported in this small cohort of patients provides important descriptions of presenting features and the burden of RP in children including missed school, emergency room visits, dependent joint arthritis, and pulmonary symptoms.
Title: Opportunistic Autoimmune Diseases

Authors: Suneetha Jasty and Anastasia Markopoulou

MedStar Washington Hospital Center, Washington, DC

Purpose: Immune checkpoint inhibitors (ICIs) targeting the programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) pathways are increasingly used as therapy in multiple advanced cancers. Though they have demonstrated improved survival, they can also lead to new challenges with immune-related adverse events (IRAE). IRAEs such as colitis, pneumonitis, and thyroiditis have been reported to occur during, or weeks to months after therapy but arthritis are less reported. Herein, we report the case of a patient without a history of arthritis who developed inflammatory arthritis after 9 cycles of pembrolizumab.

Case Description: A 63 year-old female with a history of stage IIIC malignant melanoma who had recurrence of disease twice after initial surgical management was started on Immunotherapy with pembrolizumab. The patient had a total of 9 cycles of treatment with pembrolizumab. She presented to the rheumatology clinic with chronic joint pains which started after she received cycle 2 of pembrolizumab. She noticed bilateral knee pain and right knee swelling. Her symptoms gradually progressed to involve her wrists, MCP and PIP joints. She was initially treated with Prednisone starting at 60mg daily. However she was unable to taper her prednisone to less than 10 mg a day. Physical exam revealed mild synovitis of MCP and PIP joints and tenderness in the knees. Laboratory work up demonstrated elevated CRP with normal ESR, negative RF and anti-CCP. MRI of Right knee showed synovitis within the knee joint as seen in the figure below. MRI of the hands showed synovitis in the carpal bones and tenosynovitis of the flexor and extensor compartments. She was started on Methotrexate 15mg q weekly along with low dose prednisone of 5mg daily. She is off pembrolizumab for over 9 months now but she continues having arthritis with some improvement on Methotrexate and low dose steroids.

Conclusion: IRAEs in the setting of ICIs have been recognized and well described including their management algorithms but inflammatory arthritis and other rheumatologic disorders due to ICI use have been less commonly reported. Use of ICIs will be expanding in the coming years for several reasons, so is the recognition of these IRAEs and developing treatment strategies. The rheumatologist plays a critical role in evaluating and treating these patients. Collaboration between oncology and rheumatology for clinical care will enhance understanding and treating these new disease entities.
Title: Unusual Cause of Swollen Face

Authors: Deborah Kim and Florina Constantinescu

MedStar Washington Hospital Center, Washington, DC

Background and Objective: IgG4-related disease (IgG4-RD) is a rare yet increasingly recognized fibro-inflammatory disorder characterized by tumefactive lesions and characteristic histopathological features, and frequently, but not always elevated serum IgG4 concentrations.

Case Description: A 47 year-old-woman with chronic sinusitis and asthma was referred from ENT with five-year history of undiagnosed persistent bilateral lacrimal and parotid gland swelling. Previously, she had a negative serologic work up for systemic lupus erythematosus (SLE) and Sjogren’s syndrome and multiple lymph node biopsies including the biopsy from open right parotidectomy showed no evidence of malignancy or sarcoidosis. Review of systems was notable for 3-year history of loss of smell and taste, blurry vision, and persistent sinus symptoms but otherwise negative for rash or joint symptom. Physical exam was remarkable for marked lacrimal, parotid and submandibular gland swelling. CT of the chest, abdomen and pelvis revealed no pathologic lymphadenopathy. Orbit MRI with contrast showed extraocular muscle infiltration. Additional labs revealed elevated IgG4 serum concentration. Staining for IgG4 and IgG on her previous lymph node biopsy (Figure 1: IgG4 and IgG staining) showed tissue IgG4/IgG of greater than 40%. Based on these findings, a diagnosis of IgG4-RD was made. She was promptly started on high dose steroids with subsequent rapid resolution of gland swelling as well as restoration of smell and taste. She is currently on rituximab infusion as a steroid sparing therapy to prevent recurrence of her disease.

Discussion: The differentials for persistent salivary gland enlargement are broad from Sjogren’s syndrome, IgG4-related sialadenitis, sarcoidosis, MALT to tuberculosis. As this case illustrates, prompt referral to rheumatology, ENT for tissue biopsy, and possibly hematology referral to evaluate for underlying malignancy are crucial. Otherwise, untreated IgG4-RD may progress from lymphoplasmacytic inflammation to extensive fibrosis which could lead to decreased response to therapy. It is with thorough and careful correlation with the histopathological and radiographic findings as well as sound clinical judgment that we can be certain that we do not miss this important diagnosis.
**Title:** Prevalence of Clinical Gout and Subclinical Gout in Patients with Severe Heart Failure

**Authors:** Deborah Kim\(^1\), Anastasia Markopoulou\(^1\), Raj Nair\(^2\), Florina Constantinescu\(^1\), Arthur Weinstein\(^1\)

\(^1\)MedStar Washington Hospital Center, Washington, DC, \(^2\)Food And Drug Administration, Silver Spring, MD

**Purpose:** Hyperuricemia is a frequent finding in congestive heart failure (CHF) occurring in over 50% of patients with severe CHF (NYHA Class III-IV). 11% of patients with CHF also have gout. Musculoskeletal ultrasound has emerged as an important imaging modality for diagnosis of gout which can detect monosodium urate (MSU) crystal deposition in joints and periarticular structures even in patients who have no history of clinical gout (subclinical gout). Ultrasound lesions specific to MSU crystal deposition are the double contour sign, tophi and aggregates, based on current OMERACT (Outcome Measures in Rheumatology) definition. We performed a pilot study to determine the prevalence of clinical and subclinical gout in patients with NYHA Class III-IV.

**Methods:** Patients with severe HF were screened at MedStar Washington Hospital Center Heart Failure Unit. 19 patients were included in the study. Extensive clinical data was collected including history of gout, co-morbidities, medications, diet, and uric acid levels. Joint examination was also performed. An ultrasound examination was performed by a rheumatologist certified in musculoskeletal US, blinded to the patient’s clinical history. A Sonosite X-porte machine was used for all the studies. Two anatomical sites were scanned: bilateral knees and first MTPs. Findings specific to MSU deposition were recorded.

**Results:** Hyperuricemia was defined as serum uric acid level above 6 mg/dl. 84% (16/19) of patients with severe CHF had hyperuricemia. 58% (11/19) of patients had history of clinical gout. Of those patients with clinical gout, 10 out of 11 had ultrasound evidence of gout. The only gout patient with no ultrasound evidence of gout has been on allopurinol for 5 years and his uric acid is well controlled at below 6 mg/dl. 3/19 (16%) patients had no clinical history of gout but had ultrasound evidence of MSU deposition. These 3 patients with subclinical gout had hyperuricemia. Only 5/11 (45%) patients with history of gout were on any urate lowering therapy. 5/19 (26%) patients had no history of gout and no ultrasound evidence of gout.

**Conclusion:** Although this is a small study, our data again demonstrates high prevalence of hyperuricemia and gout in HF patients. We found that 16% patients with no history of gout had ultrasound evidence of MSU crystal deposition (subclinical gout) and all of them had hyperuricemia. Over 50% definitive gout patients were not on any urate lowering therapy (ULT) although it was clearly indicated. This pilot study is a work in progress.
Figure 1: Plantar longitudinal (LEFT) and plantar transverse (RIGHT) views showing double contour sign.
Title: *Secondary Large Vessel Vasculitis: A Case Report*

Authors: Sumit Kunwar¹, Christopher Collins¹, Peter C. Grayson²

¹MedStar Washington Hospital Center, Washington, DC, ²National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, MD

Purpose/Method: Large vessel vasculitis (LVV) is defined as inflammation of the aorta and its primary branches. Secondary forms of LVV are associated with specific multi-systemic diseases. We present a case report of sarcoidosis with secondary LVV to highlight the diagnostic value of vascular imaging. Whole body magnetic resonance (MR) angiography with black blood, STIR, and VIBE sequences were done to evaluate the aorta and branch vessels. 18F-fluorodeoxyglucose (FDG) PET –MR was performed at 60 minutes uptake time and findings on PET were registered to corresponding MR angiography.

Results: A 27-year-old female diagnosed with sarcoidosis in 2011 (granulomatous scleritis, steroid responsive pulmonary symptoms, and a right conjunctival biopsy showing a rare poorly formed granulomas) was referred to rheumatology clinic for evaluation of recurrent mild chest and neck pain. Her sarcoidosis was previously treated by her pulmonologist with glucocorticoids; however, prednisone tapering below 10mg/day was unsuccessful due to recurrent episodes of chest and neck discomfort. She otherwise had no recent pulmonary symptoms and a recent pulmonary function test was normal. She reported fatigue but denied other constitutional symptoms, rash, headache, visual changes, joint or abdominal pain, and limb claudication. There were no bruits, peripheral pulse abnormalities, or carotid artery tenderness on peripheral vascular examination. Blood pressures were equal in upper and lower extremities. Laboratory assessment was notable for elevated inflammatory markers (ESR 52mm/hr, CRP 43.1 mg/L). Angiography revealed a dilated ascending aorta and severe wall thickening and edema of the proximal left common carotid artery. FDG-PET was notable for moderate FDG uptake in the wall of the ascending aorta and aortic arch with intense uptake in the wall of left common carotid artery at the corresponding site of angiographic abnormalities. She was diagnosed with LVV likely related to sarcoidosis. She was started on methotrexate at 20mg/week as a steroid sparring agent and bone protective measures were instituted. At her most recent office visit, she had no pain and inflammatory markers had normalized.

Conclusion: LVV is a known complication of sarcoidosis. This patient had mild symptoms of chest and neck discomfort without corresponding findings on physical examination; however, vascular imaging studies revealed profound abnormalities. The case highlights the diagnostic value of angiography and PET scan to identify LVV. Vascular imaging should be considered in treatment refractory diseases known to be associated with secondary forms of LVV.
Figure 1. FDG PET MR showing intense uptake in the left common carotid corresponding to area of edema on STIR image.
Title: A Case Report of Rheumatoid Arthritis with Secondary Renal Amyloidosis

Authors: Sumit Kunwar, Christopher Collins, Florina Constantinescu, Konstantinos Loupasakis

MedStar Washington Hospital Center, Washington, DC

Purpose/Method: Secondary amyloidosis can be a rare complication of long standing rheumatoid arthritis (RA). The incidence seems to be decreasing likely due to improved RA treatments. Here we present a patient with long standing untreated RA who presented with renal failure and anasarca due to serum A amyloidosis.

A 77 year old male with no known prior medical history was admitted to MedStar Washington Hospital Center with generalized body aches, fatigue and joint pain for 1 month duration. He was taking OTC Ibuprofen with minimal relief. He denied fever, weight loss, Raynaud’s phenomenon, oral ulcer and skin rash. Examination was notable for anasarca and synovitis of both elbows and wrists, 1st and 2nd MCPs bilaterally, a moderate effusion in the right knee and right ankle tenderness. Work up revealed renal failure (BUN 52mg/dl, creatinine 6.37mg/dl), high inflammatory markers (ESR>85mm/hr, CRP 162mg/L), severe hypoalbuminemia (0.6mg/dl) and massive proteinuria (15.6 gm/day). Further work up included negative serum and urine electrophoresis for monoclonal proteins, nonreactive HIV and hepatitis tests, and a normal echocardiogram. Further rheumatologic workup revealed high titer RF (428) and anti-CCP (>250). Xrays of hands and feet demonstrated erosions and changes consistent with long standing RA. He subsequently underwent a kidney biopsy which stained positive for congo red in the glomeruli and vessel walls. Electron microscopy revealed abundant amyloid like fibrillary material in the mesangium, capillary wall and subepithelial areas. Amyloid typing was positive for serum amyloid A.

Results: Based on the laboratory results, radiographic findings and histopathology of the kidney, he was diagnosed with Seropositive Erosive Rheumatoid Arthritis with secondary Renal Amyloidosis. He was initially started on oral steroids, diuretics and hemodialysis. He was subsequently placed on tocilizumab (anti IL-6) infusion in the outpatient setting.

Conclusion: Serum A amyloidosis (SAA) is a rare complication of untreated RA and most commonly involves kidneys resulting in nephrotic range proteinuria and renal failure. Since IL-6 has a role in SAA production, blocking it has the potential to help these patients. Indeed, anti IL-6 therapy has been used and shown to decrease serum amyloid level and improve proteinuria as well as renal failure in multiple case reports.

Figure 1: Kidney Biopsy: (Congo red stain). Glomerulus and vessel walls are stained with congo red.
Title: Outcomes of African Americans with Scleroderma

Authors: Elisabeth G. Kramer1*; Duncan F. Moore1*; Rami ElTaraboulsi1*; Carolyn Fridley1, Maia Zulmatashvili2, Virginia Steen1, 2

1Department of Medicine, Georgetown University Hospital, Washington, DC, 2Department of Rheumatology, Georgetown University Hospital, Washington DC
*should be considered co-first authors

Purpose: Systemic Scleroderma (SSc) is an autoimmune disease that affects different populations with variable severity; particularly the African-American population, where diagnosis is often delayed and mortality is significantly increased. Ethnicity, genetic factors as well as socioeconomic level have been found to affect disease outcomes. The goal of this study was to compare characteristics and outcomes of African-American (AA) patients and non-African American patients with Systemic Scleroderma

Methods: An 8-year retrospective study of patients with scleroderma was performed comparing African Americans to non-Caucasian patients. Patients included in the study were evaluated by the senior author (VS) at our institution between 2008 and 2016. A comparison of demographic, serological and clinical features was performed using data obtained from each patient's medical record starting from the time of first visit at our institution. Clinical characteristics were compared between groups based on gender, serological profile, scleroderma subtype, and other related factors.

Results: A total of 385 patients were included in the analysis. African Americans (AA) comprised 182 (47.3%) of the population. Women comprised 87% of the study population. The average age at diagnosis was 55 years in AAs versus 56 years for the non-AAs. The disease duration at the time of the first visit was not significantly different between the AA group and the non-AA group. There was a significant difference in mortality between the populations with mortality in AA being 22.5% versus 10.73% in the non-AA population (P 0.008). Mortality among patients with diffuse disease was 22.2% versus 11.8% of the patients with limited disease (P 0.022). There was no significant difference in skin score between the AAs and the non-AAs, however there was a significant difference with regards to DLCO(46.3% vs 63.7%) and FVC(67.9% vs 83.7%) in both groups. Severe Fibrosis was diagnosed on CT Chest in 9.9% of the AA patients as opposed to 3% of the non-AA patients.

Conclusion: This retrospective study reports data consistent with previously published reports of increased mortality and severe burden of SSc in African Americans in comparison to non-African Americans which is not fully accounted for by socioeconomic factors alone but reflected by organ system damage and disease characteristics.
Title: Isolated HLA-B27+ Associated Aortitis vs Tertiary Syphilis: A Diagnostic Dilemma

Authors: Rachel Lu-Do¹, Suneetha Jasty², Anastasia Markopoulo², Christopher Collins²

¹Medstar Harbor Hospital, Baltimore, MD, ²MedStar Washington Hospital Center, Washington, DC

Purpose: Cardiac involvement, especially aortitis, is a well described feature of some patients with seronegative spondyloarthropathies. There are also numerous case reports of isolated non-infectious aortitis in HLA-B27+ individuals. Several other causes of aortitis also exist however, including tertiary syphilis, which can create a diagnostic dilemma. We herein describe a case of a 46-year-old African American man who presented with severe aortitis in the setting of HLA-B27 positivity and evidence of past syphilis exposure.

Case Description: a 46-year-old African American man was admitted for elective valve repair due to severe aortic insufficiency and dilated ascending aorta, and proximal aortitis, confirmed on histopathology with myxoid degeneration and chronic inflammation with lymphoid aggregates. His past medical history was notable for known HLA-B27+ status, a history of recurrent uveitis, and a diagnosis of “rheumatoid arthritis” at the age of 18, transiently treated with MTX. Confounding the picture however was the discovery that he was T. pallidum particle agglutination (TP-PA) positive, but RPR negative. He denied every having been treated for syphilis, but had been treated for gonorrhea in the past. The patient denied having any symptoms of arthritis for decades as well as morning stiffness, low back pain, enthesitis, nor any neurologic problems. On labs, he was confirmed to be HLA-B27 positive, RF was low titer at 17 IU/mL, anti-CCP negative, HIV negative, and ANA 1:80. There was no active uveitis at the time of admission, and his MSK exam was completely benign. An MRI of his pelvis and spine were performed and read as normal with no evidence of sacroiliitis or other radiographic evidence of axial disease.

Case Discussion: This case presents a challenging diagnostic dilemma: is this patient’s aortitis a consequence of tertiary syphilis, or a rare manifestation of HLA-B27+ associated disease? While the presence of TP-PA strongly suggests a previous exposure to syphilis, the absence of RPR (indeed, high titer RPR) in tertiary syphilis is extremely rare. Alternately, isolated aortitis in HLA-B27+ individuals garners only a few case reports in the literature. While a history of possible inflammatory arthritis in this patient’s remote past, as well as reports of episodic uveitis, is compelling evidence for non-infectious aortitis, the complete lack of any skeletal manifestations of AS create uncertainty in this case. Currently, additional studies are underway to try to clarify the clinical picture, including PET imaging of the vasculature and staining of the aortic tissue for spirochetes. Meanwhile, he has been placed on empiric penicillin only and is doing well.

Conclusion: This case is unique in that no cases of aortic disease in setting of concomitant HLA-B27 positivity and prior syphilis infection have been reported to our knowledge. It offers us a clinically challenging feat to determine the true etiology of this patient’s severe aortic disease and more importantly, the implications for appropriate management and therapy.
Title: Faces of the Wolf: A Case of Systemic Lupus Erythematosus Presenting with Hypoalbuminemia Secondary to Lupus Protein Losing Enteropathy


Walter Reed National Military Medical Center, Department of Rheumatology, Bethesda, MD

Case Description: Systemic Lupus Erythematosus (SLE) is a relatively common rheumatic condition with a prevalence rate of between 20-150 cases per 100,000. Hypoalbuminemia is a common manifestation of SLE most frequently attributable to renal involvement and lupus nephritis. However there can be multiple causes for hypoalbuminemia in the SLE patient and this case describes the presentation of Lupus Protein Losing Enteropathy (LUPLE).

Case Discussion: A 34-year-old African American female presented with 3 months of new onset arthralgia, Raynaud’s phenomenon, lower extremity edema, watery diarrhea and progressive dyspnea on exertion that acutely worsened ultimately causing her to present to the emergency department. A CT of the chest was obtained and she was found to have bilateral subsegmental pulmonary emboli, large bilateral pleural effusions, abdominal ascites and a pericardial effusion. Her laboratory evaluation demonstrated a positive ANA at 1:640, positive anti-Smith antibody, hypocomplimentemia, hypoalbuminemia, an active urine sediment and non-nephrotic range proteinuria. A thoracentesis was performed demonstrating an exudative effusion and serial blood, urine and pleural fluid cultures for bacterial, fungal, clostridium difficile and mycobacterial infections were negative. Additionally there was no evidence of a chronic infection to include hepatitis B/C, HIV or parasites. She was diagnosed with new onset SLE given her clinical and laboratory findings. Her demonstrated level of hypoalbuminemia was out of proportion to her proteinuria and a gastrointestinal source was suspected given her otherwise unexplained diarrhea. A renal biopsy was obtained demonstrating class II lupus nephritis and a stool α-1-antitrypsin was found to be elevated confirming the diagnosis of LUPLE.

Conclusion: LUPLE is an uncommon manifestation of SLE with an overall prevalence of 3.2-7.5%. It is characterized by diarrhea, peripheral edema, ascites, pleural and pericardial effusions in a hypoalbuminemic patient for whom other causes of protein loss have been ruled out. The diagnosis is supported by the presence of an elevated fecal α-1-antitrypsin and an abnormal 99m Tc-labeled human serum albumin scintigram. The primary treatment modality consists of the use of corticosteroids with or without additional immunosuppressive therapy. It is important to consider LUPLE as a potentially unrecognized cause of protein loss in a SLE patient and to recognize that there may be multiple contributing factors for hypoalbuminemia in a single patient.
Title: *Interstitial Pneumonia with Autoimmune Features (IPAF): Are There Definable Subsets?*

Authors: Sepehr Mesdaghinia and Virginia Steen

MedStar Georgetown University Hospital, Washington, DC

**Background:** Interstitial lung disease (ILD) commonly occurs in the context of a connective tissue disease (CTD), but it may be the first, early or the sole manifestation of an occult CTD. Although there are specific diagnostic criteria for idiopathic pulmonary fibrosis (IPF), it can be difficult to distinguish CTD related ILD from idiopathic interstitial pneumonia (IIP). It is important to sort this out since there are new treatment options for IPF which are very different from the ones for ILD associated with CTDs.

Many patients with an IIP have features of autoimmunity but do not meet criteria for a CTD although they may have some of its clinical, laboratory, radiographic or histopathologic manifestations. There has been a lack of consensus over nomenclature and classification of this patient population. In 2016, a task force from the American Thoracic Society and the European Respiratory Society, proposed a unified name, Interstitial Pneumonia with Autoimmune Features (IPAF) to such patients and provided a set of criteria which included clinical, serologic and radiographic components.

We feel that additional retrospective experience will add important information. It is our feeling that although many of these patients do not fulfill official criteria for a specific CTD, that they may be close enough to one of the CTDs that they should be treated as such. We proposed to look at the ILD patients at Georgetown rheumatology and pulmonary divisions who do not fulfill the criteria for IPF, to determine the features of the IPAF patients, and perhaps determine outcomes based on treatment.

**Methods and Analysis:** We have identified patients through electronic medical records who have been seen for ILD at rheumatology and pulmonary clinics at MedStar Georgetown University Hospital. The EMR will be reviewed for the demographic, clinical, laboratory, radiographic and histopathologic features and entered into Excel database for analysis. Patients who meet criteria for a rheumatologic disease will be excluded from the study. We will try to determine if patients fit into subgroups, ie scleroderma like, myositis like, etc or whether there is a unique subset of just IPAF.

**Results:** Data collection ongoing.

**Conclusion:** We hope to be able to categorize those patients to different groups based on the “flavor” of their autoimmune features. This way, we may be able to predict prognosis, or complications based on their category. We think this also will help determining the best approach to treatment of these patients.
**Title:** Scleroderma Renal Crisis: Challenges in Diagnosis of SRC in 5 Patients

**Authors:** Romy Abou Mrad and Virginia Steen

**MedStar Georgetown University Hospital, Washington, DC**

**Introduction:** Scleroderma renal crisis (SRC) occurs in 5-20% of patients with systemic sclerosis. It typically presents with malignant hypertension, micro-angiopathic hemolytic anemia (MAHA) and acute kidney injury. RNA polymerase III (RNA Pol3) and SCL 70 antibodies are associated with SRC, but anti-centromere (ACA) antibody is not. A delay in the diagnosis and treatment can lead to significant morbidity, hemodialysis, (HD) and mortality.

**Methods:** We identified 5 cases of scleroderma renal crisis seen in the rheumatology clinic at Georgetown University Hospital within the past year. We describe their initial clinical features, antibodies, the diagnosis of SRC and outcomes.

**Results:**

- **Case 1** had long standing Raynaud’s/Sjogren’s and was misdiagnosed as having CREST syndrome because of a Direct ANA showing low value ACA, despite a nucleolar pattern ANA. She developed malignant hypertension, MAHA and AKI. Kidney biopsy was consistent with SRC. Repeat serology showed a negative ACA and + PM-SCL. She remains HD dependant.

- **Case 2** had rapidly progressing puffy hands, dyspnea and hemoptysis. He was diagnosed with ILD and treated with high dose of steroids for possible vasculitis. Our evaluation showed diffuse scleroderma, ILD and a + RNA pol 3. He was then admitted with worsening SOB and AKI. Kidney biopsy showed SRC. The patient refused dialysis and died.

- **Case 3** presented with 4 months of arthritis and swollen leg. She was diagnosed with RA and CREST syndrome, again because of a low value ACA on Direct ANA, despite a nucleolar pattern ANA. She was then admitted for AKI requiring dialysis and kidney biopsy was consistent with SRC. Our evaluation showed subtle skin findings and repeat labs showed a negative ACA and a strongly + RNA pol 3. She did not tolerate dialysis and had a sudden death.

- **Case 4** presented with accelerated hypertension thought to be secondary to renal artery stenosis. Our evaluation showed diffuse SSc with + RNA pol 3. She was readmitted with AKI but no RAS was found. ACEi was initiated but she remains HD dependent.

- **Case 5** had new diffuse SSc with known + RNA Pol 3. On routine visit she was found to have new hypertension. On admission, she had AKI and MAHA. ACEi therapy was promptly initiated and her kidney function improved.

**Conclusion:** SRC needs to be promptly recognized and treated. RNA-Pol 3 antibody should always be tested especially in patients with rapidly progressing symptoms, AKI and those with a nucleolar ANA pattern. Although HTN, MAHA, pericardial effusions are common presentation, their absence should not rule out SRC in the appropriate clinical setting.
## Table: This table describes the SSC features, laboratory, renal crisis presentation and outcomes.

<table>
<thead>
<tr>
<th>Cases</th>
<th>SSc clinical features upon our evaluation</th>
<th>Antibodies</th>
<th>Scleroderma renal crisis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>62 year old Caucasian female</td>
<td><strong>Initial serology:</strong> Direct ANA positive ACA 1.2</td>
<td><strong>4/2016 hospitalization:</strong> BP=220/100 H/H 8.9/29.1 (baseline 11.2/34) LDH=541 Creatinine 3.5 (baseline 1.2) Bilirubin 4.2 Kidney biopsy consistent with SRC ACEI initiated immediately</td>
<td>Dialysis initiated on 4/18/2016, still HD dependant</td>
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<td></td>
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<td><strong>Subsequent serology:</strong> ANA 1:1280 nucleolar Positive PM-SCL Negative ACA</td>
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<td><strong>11/2016 hospitalization:</strong> BP=150/91 systolic, (on amiodipine) No MAHA, Hemoptysis, Creatinine 2.7 Kidney biopsy consistent with SRC</td>
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<td></td>
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<td><strong>Progressive renal failure, in spite of ACEi therapy</strong></td>
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<td></td>
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<td></td>
<td><strong>Death (refused dialysis and opted for comfort care)</strong></td>
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<td>Case 2</td>
<td>58 year old Caucasian male</td>
<td><strong>Initial serology:</strong> Negative Direct ANA, SCL70, PMSCL and ACA</td>
<td><strong>10/2016 hospitalization:</strong> BP=150/85 (on Losartan) No MAHA Cr 3.5 Kidney biopsy consistent with SRC</td>
<td>Dialysis initiated on 10/17/2016 but she didn’t tolerate it and had sudden death at home (unclear etiology)</td>
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<td></td>
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<td><strong>Subsequent serology:</strong> Negative ANA by IFA Anti-RNA polymerase III strongly positive</td>
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<td>Case 3</td>
<td>83 Caucasian female</td>
<td><strong>Initial serology:</strong> ANA: 1:1280 nucleolar and speckled pattern Direct ANA with Anti-centromere antibody 1.2</td>
<td><strong>12/2016 hospitalization:</strong> BP=200/105 MAHA, (undetectable haptoglobin, bilirubin of 2, LDH of 856) Cr peaked at 2.6 Kidney biopsy performed</td>
<td>Immediate, aggressive treatment with Captopril with resolution of MAHA, Creatinine 2 months later is 1.4mm/dl</td>
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<tr>
<td></td>
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<td><strong>Subsequent serology:</strong> ANA: 1:1280 nucleolar and speckled pattern Anti-RNA-polymerase III strongly positive</td>
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<td>Case 4</td>
<td>88 year old Caucasian female</td>
<td><strong>Initial serology:</strong> ANA 1:640 homogenous speckled</td>
<td><strong>08/2016 hospitalization:</strong> BP=190/88 No MAHA Cr 3.2 No kidney biopsy performed</td>
<td>Dialysis dependant, but after starting on ACE – BP and CHF are much better controlled and she is doing well on dialysis</td>
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<td></td>
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<td><strong>Subsequent serology:</strong> ANA &gt; 1:2560 RNA-Polymerase III strongly positive</td>
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<tr>
<td>Case 5</td>
<td>63 year Caucasian female</td>
<td><strong>Initial serology:</strong> ANA by IFA 1:160 speckled</td>
<td><strong>12/2016 hospitalization:</strong> BP=200/105 MAHA, (undetectable haptoglobin, bilirubin of 2, LDH of 856) Cr peaked at 2.6 Kidney biopsy performed</td>
<td>Immediate, aggressive treatment with Captopril with resolution of MAHA, Creatinine 2 months later is 1.4mm/dl</td>
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<tr>
<td></td>
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<td><strong>Strongly positive RNA polymerase III</strong></td>
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</table>
Title: Methimazole Induced Diffuse Alveolar Hemorrhage

Authors: Ravi T Pilla¹, Deborah Kim², Konstantinos Loupasakis²

¹Department of Medicine, MedStar Washington Hospital Center, ²Division of Rheumatology, MedStar Washington Hospital Center, Washington, DC

Introduction: Diffuse alveolar hemorrhage due to methimazole is infrequent which makes it a diagnostic challenge. It is usually associated with positive anti-neutrophil cytoplasmic antibodies (ANCA) and clinico-laboratory evidence of vasculitis with a presentation identical to primary ANCA-associated vasculitis.

Case description: Our patient is a 44 year old female with a history of hyperthyroidism (on methimazole which was started 6 months prior to her admission) and diastolic heart failure who presented to the hospital with cough, hemoptysis and shortness of breath for 6 months. On admission, she was febrile, heart rate 128, BP 116/58 and hypoxic (91% on room air). Rapid flu test was positive, therefore she was treated with oseltamivir for 5 days. However, she continued to have hemoptysis, hypoxemia and tachycardia which prompted a chest CT which identified bilateral ground glass opacities. Bronchoscopy was consistent with diffuse alveolar hemorrhage (DAH). ANA, SSA, SSB, Rheumatoid Factor, P-ANCA, C-ANCA, anti-DNA, anti-myeloperoxidase, anti-GMB antibodies were all negative. As the workup was otherwise unrevealing for a primary rheumatologic disorder, methimazole was discontinued as a possible culprit. Patient’s hemoptysis improved (frequency and amount of sputum) and she remained stable weeks after her discharge when she was seen as an outpatient.

Discussion: An antineutrophil cytoplasmic antibody (ANCA)-positive vasculitis has been reported in association with both PTU and methimazole (albeit with much less frequency); therefore the use of methimazole or carbimazole is gaining ground compared to PTU. In a review of studies of patients with thionamide-induced ANCA-positive vasculitis, ANCA were present in 4 to 64 percent of patients taking PTU and 0 to 16 percent of patients taking methimazole. Methimazole induced DAH is a rare disease with a mechanism of action. In the majority of reported cases, ANCA testing was positive and pulmonary capillaritis was the suggested pathogenetic mechanism, as evidenced on lung pathology in some of these patients where biopsy was obtained.

Conclusion: Methimazole has been infrequently reported to cause ANCA-positive vasculitis which can manifest with DAH. Here we report one of the very few cases where methimazole use was associated with ANCA-negative DAH, without other clinical findings of vasculitis and no laboratory evidence of a systemic vasculitic process. This potentially suggests a non-inflammatory mechanism of DAH in some of these patients, which can be treated by discontinuation of methimazole without the use of corticosteroids and immunosuppressive medications.
Title: An Unexpected Cause of Recurrent Ascites

Authors: Anjani Pillarisetty¹, Anastasia Markopoulou², Christopher Collins²

¹Department of Medicine, MedStar Washington Hospital Center, ²Division of Rheumatology, MedStar Washington Hospital Center, Washington, DC

Case Description: 55 yo AAM with PMHx of hypothyroidism and hypertension presents with recurrent ascites. Patient noticed bilateral lower extremity edema one year ago, which progressed to scrotal swelling and abdominal distension. Since then, he had multiple hospital admissions and an extensive workup with no diagnosis. He was noted to have anemia, renal insufficiency, elevated inflammatory markers and hypergammaglobulinemia. CT scan revealed diffuse axillary, mediastinal and retroperitoneal lymphadenopathy, and hepatosplenomegaly. Paracentesis revealed SAAG 0.6 and negative cytology. Liver biopsy was benign, and renal biopsy showed diffuse chronic tubulointerstitial disease. An axillary lymph node biopsy was performed showing reactive follicular hyperplasia with plasmacytosis and increased IgG4-positive cells. Of note, T-spot, HIV, SPEP/UPEP, and ANA were negative. Given concern for IgG4 related disease, he received pulse dose steroids with no clinical improvement. An extensive review of his clinical findings, lab and imaging abnormalities sparked high suspicion for multicentric Castleman’s disease. HHV-8 serology and immunohistochemical staining were negative, and serum IL-6 levels were low. The axillary lymph node biopsy was reviewed at NIH with the conclusion that the histological (increased vascularity) and clinical features suggest TAFRO syndrome.

Case Discussion: Castleman’s disease was first described by Dr. Benjamin Castleman in the 1950s, and can be subdivided into unicentric (localized) or multicentric (systemic) disease. MCD is driven by hypercytokinemia, particularly interleukin-6, resulting in systemic inflammatory symptoms, angiofollicular lymph node hyperplasia, polyclonal lymphocyte and plasma cell proliferation, and organ dysfunction. It is often associated with HIV and HHV-8, however those individuals who are HIV and HHV-8 negative but display clinical and histological features of MCD are diagnosed with idiopathic MCD. iMCD typically presents in the fourth or fifth decades of life and affects more men than women. Patients may present with a constellation of symptoms including: diffuse lymphadenopathy, B-symptoms, hepatosplenomegaly, anasarca, and organ failure. Common laboratory findings include anemia, elevated inflammatory markers, elevated IL-6, proteinuria, hypoalbuminemia, hypergammaglobulinemia, and thrombocytosis or thrombocytopenia. Kawabata et al recently described a unique clinicopathologic variant of iMCD known as TAFRO syndrome, which involves Thrombocytopenia, Anasarca, Fevers, Reticulin myelofibrosis, and Organomegaly. This entity is characterized by an aggressive clinical course, corticosteroid refractoriness, and hyaline vascular histology. Potential treatments include anti-IL-6 therapies, rituximab, and cyclosporine.

Conclusion: Our patient’s presentation was strongly suggestive of a systemic inflammatory process. It is crucial to consider a broad differential diagnoses such as lymphoma, IgG4 related disease, MCD, multicentric reticulohistiocytosis, Erdheim-Chester syndrome, adult onset Still’s disease, HIV, TB, SLE, RA, and APLS. This patient was started on tocilizumab and prednisone therapy, pending assessment for response.
Title: An Unusual Case of Human Parvovirus B19 Associated Arthritis

Authors: Nancy Sein and Jess Edison

Walter Reed National Military Medical Center, Bethesda, MD

Case Description: Human Parvovirus B19 is a small nonenveloped DNA virus that commonly causes erythema infectiosum primarily in children. B19 associated arthritis is the most common viral arthritis in the United States. Acute-onset symmetric polyarticular arthritis of small joints is the typical pattern in adults. The symptoms are often self-limited lasting several weeks or months and respond to non-steroidal anti-inflammatory medications. In this clinical vignette, we described a case of 48 year-old female with B19 associated arthritis of the large joints with detectable B19 DNA in synovial fluid after 18 months of initial infection requiring immunosuppressive therapy.

Case Discussion: 48 year-old Hispanic female with history of left knee ACL reconstruction with allograft presented with fatigue, anemia, sporadic fevers, recurrent left knee effusion, and bilateral shoulders and hips arthralgia. She was diagnosed with acute parvovirus infection 15 months prior manifested by fever, migratory polyarthritis (bilateral ankles, knees, hips, elbows, and shoulders), elevated inflammatory markers, anemia, and positive parvovirus IgM. Initially, she was treated with a prednisone for the acute arthritis and subsequently with sulfasalazine and adalimumab. She had recurrent left knee effusion and underwent left knee arthroscopy for allograft removal. Adalimumab was held pre-operatively. She remained on sulfasalazine and she was taking it daily when she presented with above mentioned symptoms. Extensive work up for the fever was unrevealing. MRI of hips revealed bilateral hip effusions. The synovial fluid from the left hip revealed inflammatory etiology (7889 WBCs/mm3). Interestingly, B19 DNA was still detectable in the left hip synovial fluid (18 months after the initial infection). She later developed bilateral knee effusion with inflammatory synovial fluid (6000 and 16222 WBCs/mm3). Parvovirus B19 DNA was also detectable in the synovial fluid of the bilateral knees. She was treated with prednisone. Methotrexate and infliximab were subsequently added. Her arthralgia, recurrent left knee effusion, and recurrent fever episodes resolved after the second infusion of infliximab. Inflammatory markers have normalized and anemia has improved. At the time of this report, she is in clinical remission on treatment with methotrexate and infliximab.

Conclusion: This patient presented with B19 associated acute arthritis of the large joints persisting as chronic inflammatory arthritis. Her clinical course described the role of B19 in the etiopathogenesis of inflammatory arthritis via molecular mimicry or by cytokine regulation in genetically predisposed host. The clinical significance of the persistence of B19 DNA in the synovial fluid of inflammatory joints is unknown. Its presence may be triggering inflammatory responses within the joints or it may represent an epiphenomenon. Further studies are required to understand the role of B19 in the pathogenesis of chronic inflammatory arthritis.
Title: Hypogammaglobulinemia with Undetectable IgA in Two Patients with Granulomatosis with Polyangiitis

Authors: Jessica Sheingold and Stephen Ray Mitchell

MedStar Georgetown University Hospital, Washington, DC

Case Description: We report two cases of patients with granulomatosis with polyangiitis (GPA) in remission who suffered from recurrent infections despite the tapering of their maintenance immunosuppressive therapy. They were found to be hypogammaglobulinemic, both with undetectable IgA levels. Although hypogammaglobulinemia of varying degrees has been reported with several different immunosuppressive agents, undetectable IgA levels suggest a primary immunodeficiency which potentially may have increased their risk of developing GPA. Both patients were diagnosed with GPA based on symptoms, elevated cANCA titers, positive anti-proteinase 3 antibodies, and renal biopsies. The first patient presented with “atypical pneumonia”, and later developed acute kidney injury. He was treated acutely with pulse dose solu-medrol and started on oral cyclophosphamide, which was continued for six months with prednisone. The second patient had a history of otitis media and sinusitis, but presented acutely in renal failure. He was treated with pulse dose solu-medrol and plasmapheresis, and was transitioned to oral cyclophosphamide and prednisone for six months. At the six month mark, both patients received a single cycle of rituximab, and were started on azathioprine maintenance therapy. Both remained in remission from a GPA perspective, but frequently developed infections which did not remit with the tapering of their maintenance azathioprine. In 2016, the first patient was hospitalized with recurrent pneumonia complicated by an empyema which ultimately required surgical decortication. Quantitative immunoglobulin levels revealed severely reduced IgG with undetectable IgM and IgA. The second patient’s immunoglobulin levels were checked when a chronic case of otitis media threatened his hearing. He was found to have markedly reduced IgG, normal IgM, and undetectable IgA.

Case Discussion: The finding of severe hypogammaglobulinemia in the two reported patients, particularly IgA deficiency, suggests that their immune deficiencies were not likely secondary to immunosuppressive treatment, but may have in fact been primary processes that predisposed them to develop GPA. IgA deficiency is common, and patients with this condition suffer from increased rates of sinopulmonary infection, similar to our patients. Whether IgA deficiency specifically puts patients at risk for GPA has not yet been studied, but is an avenue of potential exploration which could have implications for the pathogenesis of this rare disease.
Title: Rheumatic Manifestations of WHIM Syndrome

Authors: Ananta Subedi\textsuperscript{1}, Shubhasree Banerjee\textsuperscript{1}, Blas Betancourt\textsuperscript{1}, Peter Grayson\textsuperscript{1}, James D. Katz\textsuperscript{1}, Elena Cho\textsuperscript{2}, Daniel Velez\textsuperscript{2}, Philip M. Murphy\textsuperscript{2}, David H. McDermott\textsuperscript{2}

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Background: WHIMS (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis Syndrome) is a rare autosomal dominant primary immunodeficiency due to gain of function mutations of the CXC chemokine receptor 4 (CXCR4). CXCR4 signaling is crucial in hematopoietic stem cell homeostasis, and plays an important role in innate and adaptive immune responses. The disease often manifests with recurrent bacterial infections and Human papillomavirus (HPV)-induced warts of the hand, feet and genitals. The focus of our study is to characterize the rheumatological manifestations in WHIMS patients.

Methods: Nine patients out of 36 diagnosed with WHIM syndrome at the NIH who had rheumatological complaints were reviewed. Demographics, clinical presentation, laboratory data and the imaging studies were tabulated to look for patterns of presentation.

Results: The majority of the patients had rheumatological complaints as children or young adults and 67% were female. The initial presentation spectrum ranged from arthralgia to overt arthritis. The pattern of joint involvement included asymmetric or symmetric oligo- or polyarthritis involving small and large joints. Three patients (W-31, W-35, W-02) seemed to exhibit a spondyloarthropathy resembling reactive arthritis and one of these had a positive urethral Chlamydia PCR close to symptom onset. Three patients had a presentation like juvenile idiopathic arthritis (W-32, W-23, W-02). One patient had septic arthritis (W-03) and one had idiopathic avascular necrosis of the hip in childhood (W-23). Four of the patients had worsening of joint symptoms temporally related to the use of medications for the treatment of the primary disease. Two of the eight patients had tenosynovitis involving the fingers leading to deformity. Auto-antibodies were negative in all eight patients and none of the tested patients has the HLA B27 allele. Arthrocentesis was performed in two patients and revealed inflammatory synovial fluid. One of the patients underwent synovial biopsy revealing chronic synovitis involving T and B lymphocytes. The response to NSAIDs was poor. Sulfasalazine was used in two of the five patients for purposes of steroid sparing with partial response and a biologic was used in another with resolution of symptoms.

Conclusion: Rheumatological manifestations have not been reported as a major component of the clinical manifestation of WHIM syndrome. These patients may have impaired clearance of infectious organisms associated with arthritis or an increased probability of autoimmune disease. We present the first detailed cataloguing of such manifestations in a cohort of WHIM patients. The rheumatological management of these patients is challenging due to the baseline immunodeficiency and the risk of further immunosuppression with the use of DMARDs and biologics.
<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>W-31</th>
<th>W-35</th>
<th>W-02</th>
<th>W-23</th>
<th>W-03</th>
<th>W-10</th>
<th>W-05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first visit</td>
<td>7</td>
<td>25</td>
<td>15</td>
<td>29</td>
<td>51</td>
<td>30</td>
<td>22</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>F</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>Age of WHIMS Diagnosis</td>
<td>6</td>
<td>25</td>
<td>12</td>
<td>28</td>
<td>4023</td>
<td>30</td>
<td>22</td>
</tr>
<tr>
<td>Age of first joint</td>
<td>2</td>
<td>7</td>
<td>5</td>
<td>29</td>
<td>52</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Initial Presentation</td>
<td>Uveitis, Arthritis</td>
<td>Arthritis, Arthritis</td>
<td>Arthritis, arthritis and finger deformity</td>
<td>Tenosynovitis of fingers, Arthritis</td>
<td>Arthritis (allowing pneumonia and sepsis)</td>
<td>Septic arthritis, Arthritis</td>
<td>AVN of hip</td>
</tr>
<tr>
<td>Pattern of Joint Involvement</td>
<td>Oligoarticular</td>
<td>Polyarticular</td>
<td>Polychondritis, progressive radial head deformity of fingers</td>
<td>Polychondritis, stiffness, swelling, tenosynovitis of the fingers</td>
<td>Polychondritis</td>
<td>Monoarticular</td>
<td>Oligoarticular</td>
</tr>
<tr>
<td>Type of Joint Pain</td>
<td>Inflammatory</td>
<td>Inflammatory</td>
<td>Inflammatory</td>
<td>Inflammatory</td>
<td>Infectious</td>
<td>Inflammatory</td>
<td>Non-infectious</td>
</tr>
<tr>
<td>Type of involved joints</td>
<td>Large</td>
<td>Small, large</td>
<td>Small and large</td>
<td>Small, large</td>
<td>Large, large</td>
<td>Large, large</td>
<td>Large, large</td>
</tr>
<tr>
<td>Involved joints</td>
<td>Ankle, wrists, knees, DIP, PIP, wrist, knee, SI (X ray)</td>
<td>Knees, MCP, PIP</td>
<td>Wrist, MCPs, knee</td>
<td>Ankle, knees, wrists, elbows, knees</td>
<td>Knee, knees, shoulder, hip, Hip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symmetrical (TN)</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Additive arthritis</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>YN</td>
<td>N</td>
</tr>
<tr>
<td>ANA</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>ND</td>
</tr>
<tr>
<td>RF</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>ND</td>
</tr>
<tr>
<td>Anti-CCP</td>
<td>ND</td>
<td>ND</td>
<td>WBC: 8570/mm3 L 28%, other cells 72%</td>
<td>WBC: 2389/mm3 L 28%, N 62%</td>
<td>ND</td>
<td>NA</td>
<td>ND</td>
</tr>
<tr>
<td>Arthrocentesis</td>
<td>ND</td>
<td>ND</td>
<td>X ray SI joint: Minimal sclerosis of the bilateral sacroiliac joints with irregularity of the articular surfaces, suspicious for mild sacroiliitis.</td>
<td>X ray SI joint: Minimal sclerosis of the bilateral sacroiliac joints with irregularity of the articular surfaces, suspicious for mild sacroiliitis.</td>
<td>ND</td>
<td>NA</td>
<td>ND</td>
</tr>
<tr>
<td>Radiology Findings</td>
<td>ND</td>
<td>ND</td>
<td>A patchy superficial lymphoido-monocytic infiltrate consistent with chronic inflammation. Predominant CD5+ T cells, few CD20+ B cells, JG30+ dendritic cells within the nodular aggregates. No synovial proliferation.</td>
<td>X ray SI joint: Minimal sclerosis of the bilateral sacroiliac joints with irregularity of the articular surfaces, suspicious for mild sacroiliitis.</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Surgery</td>
<td>Yes: ankle</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Surgery yrs: AVM</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Poor response</td>
<td>Aspirin Unknown</td>
<td>Poor response</td>
<td>Partial Improvement</td>
<td>Good response</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>Poor response</td>
<td>ND</td>
<td>ND</td>
<td>Partial Improvement</td>
<td>Good response</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DMARDs</td>
<td>NA</td>
<td>NA</td>
<td>Plaquett: Failed</td>
<td>Sulfaalexine: Improved</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Biologics</td>
<td>Remicade: complete response</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Other Associated Features</td>
<td>NA</td>
<td>Polyarthrits relieved by teenage</td>
<td>Shoulder pain temporarily related to hlg</td>
<td>NA</td>
<td>Chlamydia urethritis</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

AVN: Avascular Necrosis, N: Negative, ND: Not Done, NA: Not available
Title: *Why is my Foot Swollen?*

Authors: CPT Rodger Stitt and CAPT Michael Keith

Walter Reed National Military Medical Center, Department of Medicine, Rheumatology Services, Bethesda, MD

**Introduction:** Neuropathic arthropathy is a rare disorder characterized by rapid joint destruction. The most common cause of neuropathic arthropathy in the United States is diabetes mellitus. Multilevel spondylosis is not a well described cause for neuropathic arthropathy. We describe a case of an elderly male with severe multilevel spondylosis who developed neuropathic arthropathy of his right foot.

**Case Description:** An 80 year old male with long standing insensate right lower leg presented with one month of right foot swelling and overlying erythema. The swelling progressed abruptly and was not accompanied by pain or other joint involvement. He was started on ciprofloxacin for concern of cellulitis and was referred to podiatry. A radiograph of his right foot was obtained and showed erosive changes suspicious for gout. Serum uric acid was 7.1 mg/dL. He was subsequently referred to rheumatology. He had no improvement in symptoms with ciprofloxacin. He denied trauma or penetrating injuries to his right foot. He reported longstanding insensate right leg secondary to spondylosis with severe right neural foraminal stenosis of his lumbar spine (L1-L2, L2-L3, L3-L4, and L4-L5). Past medical history was otherwise non-significant. Physical examination was significant for diffuse pitting edema over mid foot to distal right leg, erythema on dorsum of right foot, complete loss of sensation from distal right leg to toes, and deformity of medial midfoot. His left foot was normal appearing. He had no other significant joint or physical examination findings. Repeat radiograph of his right foot showed interval fragmentation, disorganization, subluxation, effusions, and degeneration of midfoot consistent with neuropathic arthropathy. His rapid plasma regain (RPR) was nonreactive and hemoglobin A1c was 5.2%. He was diagnosed with neuropathic arthropathy secondary to severe neural foraminal stenosis of lumbar spine.

**Discussion:** Neuropathic arthropathy, also known as Charcot joint, is a rare disorder characterized by rapid painless joint degeneration and destruction. The French neurologist Jean-Martin Charcot is recognized for his early description of the disease in a series of French soldiers with tertiary syphilis. Today, the most common cause in the United States is diabetes mellitus. Other causes include syringomyelia, tabes dorsalis, leprosy, and amyloidosis. The underlying pathogenesis is not well established but likely involves loss of protective reflexes, repetitive microtrauma, and/or hyperemia from loss of autonomic control of the microvasculature. Radiographic findings include “the five Ds”: destruction, disorganization, increased density, dislocation, and debris. Our patient was diagnosed with neuropathic arthropathy based on his history of an insensate right foot, the rapid progression of degeneration, and the classic radiographic findings. A literature search found a single reported case of neuropathic arthropathy occurring due to multilevel lumbar spondylosis.
Acknowledgements

Special Thanks to the members of the Rheumatology Fellows Forum Committee

Chris Collins, MD, Committee Chair, Washington Hospital Center
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Thank you also to the following companies whose generous support to the DC Rheumatism Society helped fund this activity