THE RHEUMATISM SOCIETY OF THE DISTRICT OF COLUMBIA

PRESENTS...

THE 10TH ANNUAL RHEUMATOLOGY FELLOWS FORUM

SATURDAY, MAY 19TH 2012

Washington Hospital Center
True Auditorium
Washington, DC
Rheumatology Fellows Forum
May 19th 2012

Program Schedule

8:30-9:00 AM  Poster Placement
9:00-10:00 AM  Poster Viewing/Breakfast
10:00-11:00 AM  Podium Presentations (4)
11:00-Noon  Keynote Speaker:
Bevra Hahn, MD, MACR
Professor of Medicine
Chief, Division of Rheumatology
David Geffen School of Medicine,
UCLA

Topic: “Update on Systemic Lupus Erythematosus: Pathogenesis and Treatment in 2012”
Rheumatology Fellows Forum
May 19, 2012
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- Sharon Frattalone, DO Rheumatology Fellow/Walter Reed NMC p. 13
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A SPECIAL THANKS TO:

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ABSTRACTS
ABSTRACT

HLA-B*5801 and Allopurinol Induced DRESS (Drug Reaction Eosinophilia and Systemic Symptoms) Syndrome

PRESENTER: Primaljyot Bhatia, Washington Hospital Center
OTHER AUTHORS: Elena Lumezanu, Tazeen Rehman, Christopher Collins, Arthur Weinstein

Background and Purpose: One of the more serious and rare adverse effects of Allopurinol is DRESS syndrome. It is seen in approximately 0.4% of cases. If not recognized early, it can result in multi-organ failure, with a mortality rate of 10-20%. HLA-B*5801 heterozygotes, especially Asians, have an increased susceptibility to developing DRESS syndrome.

Methods or Case Description: We present a 69 yo Indian male, with a past medical history of chronic kidney disease (CKD), gout, hypertension, and type 2 diabetes, who initially went to an outside hospital with a one day history of a pruritic, morbiliform rash, and fever of 102°. Four weeks prior to admission, he was started on Allopurinol 100mg daily. At the time of his initial presentation, his labs revealed leukocytosis with eosinophilia, mild transaminitis, and increased creatinine. Over the next few hours, he developed facial swelling and laryngeal edema requiring high dose IV Solumedrol. This resulted in improvement of the anaphylaxis and rash, but lead to steroid psychosis prompting abrupt withdrawal of the steroids. He subsequently developed multi-organ failure and was transferred to Washington Hospital Center. He was restarted on oral prednisone, and his liver function tests and creatinine improved. Further testing revealed that he was heterozygous for HLA-B*5801.

Results or Case Discussion: The RegiSCAR criteria for DRESS syndrome are hospitalization with suspected drug reaction, and the presence of at least 3 of the following 5 criteria: 1) Fever > 38°C, 2) Acute skin rash, 3) Involvement of at least one internal organ, 4) Blood count abnormalities, and 5) Enlarged lymph nodes of at least two sites. The known risk factors for DRESS syndrome are Asian descent, baseline kidney derangement, simultaneous use of diuretics, initial higher dose of Allopurinol used, and genetic predisposition: HLA-B* 5801. The pathogenesis is thought to be related to an abnormality in the HLA genes located on the major histocompatibility complex region of chromosome 6p21.3, which play a central role in the immune reaction by presenting an antigen to the T cell receptor. The treatment involves the withdrawal of the culprit drug, supportive therapy, steroids, IVIG, Cyclosporine, and Mycophenolate mofetil.
Conclusion/Significance: Allopurinol induced DRESS syndrome should be recognized early in order to improve patient outcome. In Asian patients, especially with CKD, consideration should be given for testing to determine the HLA-B*5801 haplotype, as they represent a cohort much more susceptible to DRESS. Allopurinol should be started at lower dose in CKD patients.
Discrepant assessments exist between parents and their children with regard to physical capability and self-advocacy

PRESENTER: Binoy Bhatt, George Washington University
OTHER AUTHORS: Gulnara Mamyrova, Olcay Jones, Lisa Rider, Adam Huber, Patience White, James D. Katz

Background and Purpose: The American Academy of Pediatrics recently highlighted the importance of addressing transition of care tasks for children with chronic disease by publishing a policy statement in July, 2011 (1). The AAP highlights the importance of addressing barriers to the active participation of children in the management of their own medical problems. To this end, we conducted a study to assess knowledge, self-advocacy, and readiness for myositis patients to transition from pediatric to adult care.

Methods or Case Description: We employed “survey monkey,” an online website for the anonymous collection of data in order to compare the experiences of children and their parents, separately and individually, with regard to issues relating to transition readiness. Patients and their families were solicited from the US and Canada through established clinics for children with idiopathic inflammatory muscle diseases, as well as with the aid of a nonprofit organization for the benefit of such individuals (http://www.curejm.com/). The unique ability to compare, in aggregate, parents’ and patients’ answers enabled us to uncover deficiencies as well as discrepancies revealed by patient and parent reporting.

Results or Case Discussion: We analyzed the responses of children, aged 15 years or less, along with their parents’ (Table 1). 221 different parents’ responses were compared with the responses from 54 children. Not unexpectedly, children tended to attribute greater competency in self-advocacy and self-knowledge as compared to their parents. For example, children overstate their ability to make their own doctor’s appointments. In contrast, children understate their self-assessment of physical capabilities. Specifically, parents were statistically more likely to assert that their children were able to climb stairs without help or support (p < .03).

Conclusion/Significance: Our results are particularly striking because physical development is objective. While patients and their parents agree on the ability to arise from a seated position, they do not agree on stair climbing capability. Therefore, either, 1) patients with myositis may evidence regressive behavior or, 2) parents may be experiencing anxiety concerning their children’s limitations. Further study on the psychosocial interaction between parents and children with myositis should emphasize the child’s involvement in playing the “sick role” either as a reaction to stress or a way to seek positive encouragement from their parents and peers. In addition, research should address the
possibility of parents overestimating their child’s physical functioning owing to an unconscious desire to push unacceptable emotions aside.

Table or Figure

Table 1. Parents vs. Patients ≤ 15.0 years of age.

<table>
<thead>
<tr>
<th>Survey Item</th>
<th>Parents (N=221)</th>
<th>Patients (N=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does your child know where to get her/his doctor’s phone number?</td>
<td>64 (31.2%)</td>
<td>25 (52.1%)</td>
</tr>
<tr>
<td>Right now, can your child climb the stairs without help or using support?</td>
<td>177 (83.1%)</td>
<td>37 (68.5%)</td>
</tr>
<tr>
<td>Right now, can your child stand from a seated position without assistance or support?</td>
<td>190 (93.1%)</td>
<td>49 (90.7%)</td>
</tr>
</tbody>
</table>
ABSTRACT

Case of polymyositis presenting with misleading elevations in Troponin T

PRESENTER: Teena Dhir, Prince George's Hospital Center
OTHER AUTHORS: Ning Jiang

Background: Elevations of cardiac enzymes like CK-MB and Troponin T are commonly used to indicate myocardial ischemia, but they can be falsely elevated in other conditions. Different forms of Troponin, like cardiac Troponin T (cTnT), skeletal Troponin T (sTnT), or cardiac Troponin I (cTnI), can also cause cross-reactivity in the Troponin T assay, leading to false positives. This case report describes a patient with polymyositis with elevated Troponin T, but no cardiac abnormalities. The purpose of this case is to show that elevations in Troponin T can be seen in inflammatory muscle disease, so to look for signs of myocardial ischemia, Troponin I should be used instead.

Case Description: Patient is a 70-year-old woman with history of diabetes, hypertension, gout and polymyositis, presenting with one-day history of lightheadedness, along with upper right quadrant abdominal pain. To rule out silent myocardial ischemia, cardiac enzymes were ordered which showed elevated CK, CK-MB, and Troponin T of 0.148ng/mL (times three). A full cardiac workup was performed, including 2D echo and nuclear stress test, which showed no signs of ischemia or cardiomyopathy. Troponin I was <0.05ng/mL, which was normal.

Discussion: In inflammatory myositis, there is a significant correlation between elevations in CK and CK-MB secondary to repeated skeletal muscle regeneration. Also there is a correlation between elevations in CK and cTnT, CK-MB and cTnT, and CK-MB and sTnT, but no correlation seen between CK-MB and cTnI indicating that cTnI was not re-expressed in the regenerated muscles. In the past, CK-MB to total CK ratio of greater than 3% was used as an indicator of myocardial damage, but false positives in active myositis can be seen, so cTnI should be used to differentiate between enzyme elevations secondary to skeletal muscle regeneration or cardiac muscle damage.

Conclusion/Significance: In patients with history of diabetes and other comorbidities, silent myocardial ischemias must always be ruled out. Following the usual cardiac enzymes may lead to false positives and unnecessary investigations, as in our case. Instead, Troponin I should be ordered to get a more accurate picture and determine if the elevated enzymes are because of damage to the heart or muscle. In patients with inflammatory myopathies, keep in mind they have elevations in CK, CK-MB, and Troponin T, but not Troponin I.
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Table or Figure

![Comparison of CK, CK-MB, Troponin T and CK-MB/CK](image-url)
ABSTRACT

The Use of Hydroxychloroquine in Patients with Rheumatoid Arthritis and Systemic Lupus Erythematosus: To Check or Not to Check Glucose-6-Phosphate Dehydrogenase Levels

PRESENTER: Sharon Dowell, University of Maryland
OTHER AUTHORS: Mercedes Quinones, Archana Sharma, Raymond Flores, Marc Hochberg, Jamal Mikdashi, Violeta Rus

Background and Purpose: There are no recommendations regarding routinely checking serum Glucose-6-Phosphate-Dehydrogenase (G6PD) levels prior to starting hydroxychloroquine (HCQ) therapy. G6PD deficiency is the most common enzymatic disorder of red blood cells in humans and HCQ has been implicated as a potential inducer of hemolytic anemia in individuals with G6PD deficiency. We aimed to identify the frequency with which serum G6PD levels are checked prior to starting HCQ therapy, the frequency of G6PD deficiency within our clinic population, and whether individuals with low G6PD levels had adverse clinical events after exposure to HCQ.

Methods: We conducted a retrospective chart review of patients with RA and/or SLE. A total of 718 patient charts were reviewed and 436 patients met inclusion criteria. We identified the frequency with which serum G6PD levels were checked prior to starting HCQ and the frequency of G6PD deficiency amongst those who were screened. Descriptive statistics were used for data analysis.

Results: Of the 436 charts, serum G6PD levels were documented in 168 patients, and 10 patients were found to have low values. The frequency of G6PD deficiency was 5.65%. All 10 patients were of African American descent, and consisted of 5 women and 5 men. Two patients with G6PD deficiency had concurrent exposure to hydroxychloroquine without adverse clinical events. The frequency of G6PD deficiency was estimated as 11.1% in African American men and 8.9% in African American women.

Conclusion: In our clinic population, routine screening for G6PD deficiency was done in 38% of patients. Two patients, both of African American descent were noted to have G6PD deficiency and were treated with HCQ with no adverse clinical events. Hydroxychloroquine at the recommended standard dose was safe and well-tolerated with in our clinic population, and routine screening for G6PD deficiency does not appear to be warranted. Targeted screening of populations with a higher frequency of G6PD deficiency should probably be performed. A low G6PD level would not preclude treatment with HCQ, but would indicate a need for more vigilant monitoring in these patients.
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Figure
FTY720 Inhibits T-Cell Mediated Tissue Injury in Autoimmune Prone Mice

PRESENTER: Sharon Frattalone, Walter Reed National Military Medical Center
OTHER AUTHORS: Chantal Moratz, Jess Edison, Suzette Peng

Background and Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by complex immune dysfunction, including aberrant T-cell responses. Sphingosine-1-phosphate (S1P) is a bioactive lipid mediator and key regulator of lymphocyte circulation. Fingolimod (FTY720), an FDA approved therapy for multiple sclerosis (MS), is a compound with the ability to modulate T-cell proliferation through retention of central memory T-cells and helper T-cells in lymph nodes. This suggests it may be effective in the treatment of other autoimmune diseases that demonstrate abnormal T-cell function, such as lupus. The effect of FTY720 regulation is thought to occur via inhibition of the S1P-1 receptor, which utilizes the G-alpha-i mediated signaling pathway. We have previously determined that FTY720 inhibits inflammatory T-cell responses in the B6.MRL/lpr murine lupus model but not control animals. In this current study, downstream signaling of the S1P-1 receptor is evaluated by inhibition of the G-alpha-i signaling pathway. Our central hypothesis is that abnormal S1P: S1P1 receptor interactions are a key regulator of T-cell mediated tissue injury in SLE.

Methods: FTY720 and pertussis toxin, a G-alpha-i signaling inhibitor, were evaluated in the mesenteric ischemia reperfusion injury (IRI) model of tissue injury and inflammation. We compared the extent of intestinal IRI in immune competent (C57BL/6) and autoimmune prone (B6.MRL/lpr) mice with and without treatment with inhibitors. Histological analysis of tissue samples was performed to assess tissue injury and the extent of inflammatory cell infiltration into injured tissues. Multiplex array based cytokine analysis of isolated tissue lysates was carried out to determine the extent of induction of inflammatory cytokine production. Immunohistochemistry analysis of tissue section was then performed to confirm the Multiplex array analysis.

Results: FTY720 treatment decreased inflammatory tissue damage in the B6.MRL/lpr autoimmune strain but not the non-autoimmune controls. This was associated with reduced T cell infiltration in the autoimmune strain, and subsequent decreased production of IL-6. Treatment with a G-alpha-i inhibitor (pertussis toxin) decreased inflammatory responses in the normal controls but not in the B6.MRL/lpr autoimmune strain.
**Conclusion/Significance:** These results suggest that S1P:S1P-1 receptor signaling is abnormal in the B6.MRL/lpr autoimmune strain and that the anti-inflammatory action of FTY720 in autoimmune prone mice is through a pathway other than the G-alpha-1 coupled signaling pathway. Further studies are being carried out to explore the role of each individual isoform of S1P receptors, and to determine if a non G-alpha-i signaling pathway is preferentially expressed in autoimmune prone mice and is targeted by FTY720.
ABSTRACT

A Case of Severe Calcinosis in Anti-Synthetase syndrome with anti-Jo-1 and PM/Scl autoantibodies.

PRESENTER: Sarthak Gupta, NIAMS
OTHER AUTHORS: Mark Gourley

Background and Purpose: Antisynthetase syndrome is characterized by myositis, interstitial lung disease, arthralgia/arthritis, mechanic’s hands, fever and Raynaud’s phenomenon. It is associated with autoantibodies against aminoacyl-tRNA synthetases, the most common one being anti-histidyl (anti-Jo-1) antibody.

Methods or Case Description: A 55 year old female presented for evaluation of muscle weakness, debilitating hand deformity and severe calcinosis. She has dermatomyositis for six years and initial manifestations were muscle weakness, skin manifestations, arthritis, elevated inflammatory and muscle enzymes and interstitial lung disease. She has been treated with high dose steroid, rituximab, methotrexate, azathioprine, intravenous immunoglobulin (IVIg) and Mycophenolate mofetil. These improved muscle weakness but her calcinosis progressed to involve the fingers, hands, elbows and feet. Examination revealed severe subcutaneous calcinosis in bilateral fingers, wrists and elbow joints with severe restriction in range of motion. Muscle strength testing showed good strength in all muscle groups. Radiographic examination showed extensive calcinosis in the hands (Panel A), elbows, shoulders and feet. Imaging of the thighs with MRI revealed perifascicular inflammation as shown by hyperintense lesions on Short Tau Inversion Recovery images. Creatinine kinase was 453 U/L. Serologic testing showed a positive Anti Nuclear Antibody, anti-Jo-1 antibody, anti PM-Scl antibody. She continues to be treated with physical therapy, palidronic acid, IVIg and Mycophenolate mofetil.

Results or Case Discussion: Calcinosis has been reported to be more common in juvenile versus adult dermatomyositis. Periarticular calcinosis and hydroxyapatite deposition in or around the joints have been described on rare occasions in patients with anti-synthetase syndrome. Patients with anti-Jo-1 antibodies appear to be a high risk group for this finding. Anti-PM-Scl antibody shows a strong association with scleromyositis (scleroderma/polymyositis) which is an overlapping syndrome clinically characterized by scleroderma, Raynaud’s disease, arthralgia/arthritis, myositis or myalgia, interstitial lung disease, calcinosis and hyperkeratotic rhagadiform eczema of the fingers (‘mechanic’s hands’).

Calcinois cutis is the formation of calcium salt deposits in the skin or subcutaneous tissue. It has been classified into four types: metastatic, dystrophic, idiopathic and iatrogenic. Different therapeutic strategies have been used for calcinosis, such as the use of bisphosphonates (alendronate), aluminum hydroxide, probenecid, warfarin, colchicine,
Conclusion/Significance: This patient presents with a severe form of calcinosis in anti-synthetase syndrome with positive anti-Jo-1 and anti-PM-Scl antibodies with progression of disease even on multiple therapies.

Legend:
Panel A: X-Rays of bilateral hands with extensive calcinosis
ABSTRACT

Severe Hepatitis Associated with Tocilizumab in a Patient with Rheumatoid Arthritis.

PRESENTER: Mohammadali Habibi, MedStar Union Memorial Hospital
OTHER AUTHORS: Majd Alfreijat, Primaljyot Bhatia, Abhijit Bhatia

Background: Tocilizumab (TCZ) is a humanized IL-6 receptor monoclonal antibody that has shown benefit in adults with moderate-severe rheumatoid arthritis (RA), who have an inadequate response to anti-TNF therapy. Mild elevation in serum transaminases has been reported with TCZ use. We describe a patient with refractory RA who developed severe hepatitis after starting TCZ.

Case Description: Patient is a 62-year-old African-American male with diabetes, hypercholesterolemia, and sero-positive RA for twelve years, who presented with progressive jaundice. Patient had history of inadequate response to DMARD’s, methotrexate, infliximab, and adalimumab. He had received three doses of TCZ 8mg/kg, with the last dose one week prior to presentation. He was on metformin, methylprednisolone, esomeprazole, pregabalin, and rosuvastatin. He denied any history of alcohol use. On examination, he was icteric but without any stigmata of chronic liver disease. His lab work showed an AST 1455 IU/L, ALT 2296 IU/L, and total bilirubin 10.5 mg/dL. Work up for the hepatitis, including iron profile, viral serologies, and markers of autoimmune hepatitis were negative. Ultrasound of right upper quadrant, CT scan of abdomen, and MRCP were unremarkable. Percutaneous liver biopsy was consistent with drug induced hepatitis. He was discharged on a prednisone taper. At time of discharge, his ALT was 2203 IU/L, AST 1203 IU/L, and total bilirubin was 16.7 mg/dL. He was also noted to have a mildly elevated lipase with concern for mild pancreatitis. His transaminases normalized after ten weeks, and his lipase level normalized after fifty weeks.

Case Discussion: Given the temporal relationship to starting TCZ with his severe hepatitis, resolution with discontinuing of TCZ, negative other work up for the hepatitis, and liver biopsy showing drug induced hepatitis, this is most likely related to the TCZ.

Conclusion: Mild elevation of transaminases is a known side effect of TCZ. However, the possibility of severe hepatitis should be kept in mind when initiating therapy with TCZ, and the liver function tests should be closely monitored.
Table 1. Biochemical data upon admission and at subsequent intervals.

<table>
<thead>
<tr>
<th></th>
<th>Admission n</th>
<th>Time (weeks) after admission</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline phosphatase (U/I)</td>
<td>89</td>
<td>Two 106, Four 106, Six 82, Ten 68, Fifty 112</td>
<td>38-128</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/I)</td>
<td>1455</td>
<td>Two 423, Four 134, Six 46, Ten 34, Fifty 16</td>
<td>17-59</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/I)</td>
<td>2296</td>
<td>Two 761, Four 436, Six 97, Ten 39, Fifty 32</td>
<td>21-72</td>
</tr>
<tr>
<td>Conjugated bilirubin</td>
<td>8.9</td>
<td>Two 13.7, Four 3.9, -</td>
<td>0.0-0.3</td>
</tr>
<tr>
<td>Total Bilirubin (mg/dl)</td>
<td>10.5</td>
<td>Two 16.1, Four 5.4, Six 2.8, Ten 0.9, Fifty 0.3</td>
<td>0.2-1.3</td>
</tr>
<tr>
<td>Lipase (U/I)</td>
<td>513</td>
<td>Two 592, Four 982, Six 611, Ten 446, Fifty 258</td>
<td>23-300</td>
</tr>
<tr>
<td>Amylase (U/I)</td>
<td>149</td>
<td>Two 225, Four 255, Six 194, Ten 152, Fifty 120</td>
<td>30-110</td>
</tr>
</tbody>
</table>
ABSTRACT

Mixed Connective Tissue Disorder in a 58 year old Female.

PRESENTER: Omar P. Hussain, Prince George's Hospital Center
OTHER AUTHORS: Ning Jiang

Background: Mixed connective tissue disease (MCTD) was originally defined in 1972 as a connective tissue disorder characterized by the presence of high titers of a distinctive autoantibody, anti-U1-RNP (previously termed anti-ENA). MCTD is an overlap syndrome associated with anti-U1-RNP antibodies that comprises of features of systemic lupus erythematosus (SLE), systemic sclerosis (scleroderma), and polymyositis. The definitive diagnosis of MCTD is often complicated by the fact that the overlapping features occur sequentially.

Case Description: A 56y/o female with PMH of chronic back pain, fibromyalgia, arthritis, carpal tunnel syndrome, vitamin D deficiency and a history of smoking presented to her primary care clinic with hair loss for the past three weeks which is patchy and worsening pain all over body especially in her lower back and all her joints. She also notes that her fingers turn blue with the slightest exposure to cold. She has noticed fever that occurs every 2-3 days with a T-max of 101 for the past 4 weeks. She also complains of heartburn. She also complained of a chronic left ear discharge. She has also developed increasing shortness of breath over the past few months with exertion. Home medications include alendronate, cyclobenzeprine, duloxetine, pregabalin, calcium carbonate-vitamin D3, fentanyl patch, and diclofenac. Physical exam showed an overweight female with patchy hair loss, a perforated left tympanic membrane and significant tenderness over the fingers, wrists, elbows and ankles. Cardiovascular and lung exam were normal.

Case Discussion: With the symptoms and signs of esophageal reflux, Reynaud’s phenomenon, joint pain, and alopecia we favored a diagnosis of CREST syndrome. ANA, Anti-scl70 and anti centromere antibody were sent. To work up the fever CBC, CMP, TSH, ESR and CRP were ordered. The results showed a mildly elevated CRP at 5.1, WBC of 11.1. ESR was normal at 11.0. Anti-centromere antibody and Anti-scl70 antibody were negative. ANA was positive with a reflex panel which showed Anti RNP to be elevated at 3.1. Anti DS-DNA was negative.

Conclusion: Mixed connective tissue disorder is one of the rarer connective tissue disorders with an incidence of 0.3 to 2.8 per million. In this case the new appearance of alopecia made us consider a new diagnosis even though many symptoms had been present for years and pain management had been a frustrating issue. Reinvestigating the case revealed laboratory support for a diagnosis of mixed connective tissue disease. She has been referred to rheumatology for further management.
Increased risk of malignancy in RNAP III Scleroderma Patient

PRESENTER: Tahereh Jamshidi, Georgetown University
OTHER AUTHORS: Virginia Steen

Background and Purpose: To show the close temporal relationship between the onset of RNP III positive scleroderma and of Malignancy.

Methods or Case Description: Between Feb. 2011 and Feb. 2012, 250 patients were seen in scleroderma clinic at Georgetown University Hospital. Four patients were found to been diagnosed with malignancy all of which had positive RNA polymerase III:

Case I: 57 y/o female with a history of Hepatitis C, HTN, depression, GERD, and Hashimoto's thyroiditis who was diagnosed with limited SSc in 2009. In 2010 a surveillance CT-scan of her lungs showed a “mass in the spleen. This resulted in surgical removal for evaluation of malignancy and she was found to have aggressive diffuse B cell lymphoma.

Case II: 57 y/o male was diagnosed with scleroderma in Jan. 2012. He developed concurrent symptoms of abd pain and constipation. Colonoscopy and biopsy revealed rectal adenocarcinoma.

Case III: 54 y/o female diagnosed with invasive ductal carcinoma of the left breast in January 2011. She developed diffuse edema and skin changes with her initial chemotherapy and continued to have skin changes throughout, but diagnosis of scleroderma was not made until later that year.

Case IV: 49 y/o female diagnosed with breast cancer in July 2010. However, in May 2010 prior to the breast cancer diagnosis, patient noticed puffiness of hands and fingers and skin thickening of her hands and face. After subsequent evaluation by rheumatology she was diagnosed with diffuse scleroderma.

Results or Case Discussion: We described four cases of malignancy seen at Georgetown University Hospital in patients within a 24 month history of onset of RNA polymerase III positive Scleroderma. We observed three females and one male all with RNA polymerase III antibodies. Two cases were diagnosed with breast cancer, one with diffuse B-cell lymphoma and one with rectal adenocarcinoma. Two recent studies have found a close temporal relationship between the onset of cancer and of scleroderma among patients with autoantibodies to RNA polymerase III, suggesting that tumor antigen expression may initiate a scleroderma-like immune response and drive disease. In this case series we also demonstrated a close temporal relationship between the onset of malignancy and the onset of RNA polymerase III positive scleroderma patient.
Conclusion/Significance: The presence of autoantibodies in systemic sclerosis is associated with specific clinical manifestations. Based on previous studies and our observation we think there is an association between the onset of malignancy and RNA polymerase III positive scleroderma. The presence of this autoantibody should raise the suspicion of a possible malignancy. At the least in this setting clinician should encourage age-appropriate cancer screening.

Table or Figure

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Gender</th>
<th>SSc duration at cancer diagnosis</th>
<th>RNA P III (&lt;20)</th>
<th>Scl-70</th>
<th>Centromere</th>
<th>ANA/Pattern</th>
<th>Type of malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case I</td>
<td>57</td>
<td>F</td>
<td>24 months</td>
<td>123</td>
<td>neg</td>
<td>neg</td>
<td>1:640/Speckled</td>
<td>Diffuse B cell lymphoma</td>
</tr>
<tr>
<td>Case II</td>
<td>57</td>
<td>M</td>
<td>Simultaneous</td>
<td>48.3</td>
<td>neg</td>
<td>neg</td>
<td>1:160/Nucleolar</td>
<td>Rectal adenocarcinoma</td>
</tr>
<tr>
<td>Case III</td>
<td>54</td>
<td>F</td>
<td>- 3 months</td>
<td>191</td>
<td>neg</td>
<td>neg</td>
<td>1:80/n/a</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>Case IV</td>
<td>49</td>
<td>F</td>
<td>2 months</td>
<td>90</td>
<td>neg</td>
<td>neg</td>
<td>1:640/Speckled</td>
<td>Breast cancer</td>
</tr>
</tbody>
</table>
ABSTRACT

Silica and Sjogren’s: A Pathway to Lymphoma?

PRESENTER: Harpreet Singh Kohli, Prince George's Hospital Center
OTHER AUTHORS: Madubindu Musunuru, Linda Green

Background and Purpose: Epidemiologic studies have identified an increased risk of developing clinical connective tissue disease (CTD) including Sjogren’s syndrome among individuals exposed to silica. Studies have also shown an increased risk of malignant lymphoma in patients with Sjogren's syndrome.

Case Description: A 47 year old African-American male, construction worker with history of hypertension and occupational exposure to silica, presented with painless swelling in the left side of the neck of 4 months duration along with dry eyes and dry mouth. He complained of redness in right eye with discharge from the supra-orbital region for the past 2 weeks. He had had a rash consistent with Herpes zoster in the same area a few months prior. He also complained of progressive shortness of breath. A year PTA he underwent exercise stress testing and passed out. Subsequent cardiac catheterization was normal. On physical exam a 3 cm, firm, non-tender mass was present in the region of the parotid. Laboratory studies showed ESR 104, hyper-gammaglobulinemia, and ANA titer of 1:1280 with anti Smith positive (5.0AI). RPR was positive but FTA was negative. SJO A was positive (>8.0AI). HIV and Hepatitis studies were negative. Hgb A1C was 7.6. CXR showed bullous emphysematous changes with scarring and fibrosis of both apices of lung. CT thorax showed a retrosternal homogenous density. CT abdomen and pelvis showed bilateral inguinal lymphadenopathy. Gallium scan showed increased uptake in both parotids and sub-mandibular glands. Biopsy of the parotid mass revealed classical nodular sclerosing Hodgkin’s lymphoma. Bone marrow aspiration was negative. PFTs showed small airway disease and decreased lung volumes. Echocardiogram was normal. The patient has received chemotherapy with good response.

Conclusion: This case illustrates the possible association of silicosis and development of Sjogren’s syndrome. Recent research into mechanism documents silica induced immune system dysregulation that is manifested by the onset of autoimmunity. This association is also supported by an occupational health study in Michigan which showed increased risk of developing connective tissue disease in individuals with silicosis. Sjogren’s syndrome has usually been associated with non-Hodgkin’s lymphoma but only rarely with Hodgkin’s lymphoma. His progressive shortness of breath was attributed to his silicosis exposure but no biopsy was done. His shortness of breath has remained stable.
COMPARATIVE CYTOKINE ANALYSIS ACROSS A SPECTRUM OF GENETICALLY AND/OR CLINICALLY DEFINED AUTO-INFLAMMATORY SYNDROMES

PRESENTER: Apostolos Kontzias, NIAMS
OTHER AUTHORS: Yongqing Chen, Nicole Plass, Damaris Garcia, Elizabeth Joyal, Robert Wesley, Raphaela T. Goldbach-Mansky

Background and Purpose: Auto-inflammatory diseases constitute a group of disorders that manifest systemic inflammation in the absence of infection, auto-antibodies or auto-reactive T cells. The rapid response to targeted cytokine blocking therapies suggests that these disorders are mediated by specific cytokines. Herein we investigate whether each disease studied is characterized by a specific cytokine signature and whether cytokine levels correlate with CRP across diseases.

Methods or Case Description: Fifty nine (59) clinically active patients were studied among which 24 were NOMID (Neonatal Onset Multisystem Inflammatory Disease) mutation positive, 11 NOMID mutation negative, 3 had CANDLE syndrome (Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature), 4 had CRMO (Chronic Recurrent Multifocal Osteomyelitis), 8 had AOSD (Adult onset Still’s Disease) and 9 had atypical CIAS1 mutation not associated with the classical CAPS phenotypes. 43 inflammatory cytokines were searched in sera and assayed by Luminex. Disease groups were compared to normal controls whose assays were run at the same time. Ratios of patient values divided by the average of corresponding set of healthy control values were log transformed and tested for differences among disease groups with ANOVA, and between patients and controls within each disease group by one-sample t-test. To assess an association of a cytokine/chemokine with the CRP, a nonparametric trend test, dividing the CRP values into 4 ordered groups: <0.5 mg/dl as normal, then: 0.5-2.0mg/dl, 2.0-5.0mg/dl, and >5.0mg/dl was used.

Results or Case Discussion: A distinct cytokine profile is found in different auto-inflammatory diseases. AOSD is characterized by markedly increased levels of Interleukin-18 (p= 0.005, mean= 3.068) compared to controls. NOMID mutation positive patients had increased levels of IL-1a (p= 0.00078, mean=1.7819), IL-6 (p=0.001, mean=1.5376) and IL-18 (p= 0.001, mean=1.4924) compared to controls and NOMID mutation negative patients. IL-18 levels in AOSD were significantly higher than in mutation positive and negative NOMID. CANDLE patients have increased IFNg inducing protein 10 (IP-10) levels (p= 0.00053, mean= 3.9872) compared to controls and the other diseases. CRMO patients had low levels of IL-8 (p= 0.005, mean= 0.1697), GM-CSF (p= 0.00684, mean= 0.0969) and MCP-1 (p=0.002, mean= 0.0687) compared to controls and other diseases.
Conclusion/Significance:

1. During active disease specific cytokine profiles may allow us to detect dysregulated cytokine pathways that discriminate between clinically distinct auto-inflammatory syndromes.
2. Specific cytokines across auto-inflammatory syndromes trend along with CRP levels especially at cut off levels higher than 0.5 mg/dl and can therefore only be detected when the CRP is elevated.
ABSTRACT

LIPID PROFILES IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS: PERFORMANCE IMPROVEMENT PROJECT OF RHEUMATOLOGISTS IN MILITARY HEALTHCARE

PRESENTER: Nicholas Kortan, Walter Reed National Military Medical Center
OTHER AUTHORS: George Mount

Background and Purpose: Cardiovascular disease (CVD) is one of the leading causes of death in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). However, despite mounting data about this significant risk, management of cardiovascular risk factors remains poor amongst patients with RA and SLE. We review lipid management practice patterns of rheumatologists at many of the major military medical centers for use in performance improvement.

Methods or Case Description: We sought to evaluate practice patterns and attitudes of rheumatologists within the United States military medical system via optional survey focusing mostly on lipid profile screening and management. Lipid panel screening and documentation was also studied via chart review process (July 2011 to present) at Walter Reed to establish baseline practice patterns for performance improvement.

Results or Case Discussion: Initial data was collected from optional surveys sent to 22 rheumatologists within the military medical system. We received 11 responses. A peer-review chart review process was started July 2011 to present with an educational intervention attempt made Oct. 2011 to our rheumatology department. Over four quarters of chart review, 35-44% of our providers were monitoring lipids in their RA or SLE patients as compared to 73% of survey respondents.

Conclusion/Significance: Initial survey data suggests that while many attitudes are largely similar across the military medical system, there are wide margins in who actually reported routinely checking lipid panels. The European League Against Rheumatism (EULAR) released recommendations in 2010 for CVD risk factor screening and management in RA, ankylosing spondylitis, and psoriatic arthritis. However, SLE data was not included directly in the EULAR study. The American College of Rheumatology has not yet released any similar formal recommendations. In light of the EULAR recommendations and current literature as well as our initial survey and chart review results, it would appear that CVD screening and management remains an area of focus for improvement. We plan to expand the data search to include review of lipid profile laboratory monitoring in patients with RA and SLE from the military electronic database as well as increase the number of rheumatologists surveyed to strengthen our results. The ultimate goal is to review the current literature regarding CVD in RA and SLE, expand our understanding of how this has shaped rheumatologists’ management in our healthcare system, and help search for ways we can improve this aspect of our patient care.
ABSTRACT

Idiopathic Recurrent Acute Pericarditis: An Autoimmune Entity

PRESENTER: Madiha Latif, Washington Hospital Center
OTHER AUTHORS: Arthur Weinstein

Background and Purpose: Idiopathic recurrent acute pericarditis (IRAP) is a common complication of acute idiopathic pericarditis with recurrence occurring in 20-50% of patients. It may present as initial manifestation of an underlying autoimmune disease and should be identified early in the disease course for appropriate management.

Case Description: 63 yr old female was referred for recurrent episodes of chest pain. Her symptoms started with a URI followed by development of sharp pleuritic chest pain 10 days later. She was diagnosed with pericarditis and treated with NSAIDS. Over the next nine months, she had seven recurrent attacks of substernal pleuritic chest discomfort requiring hospitalization and treatment with NSAIDS and steroids. Cardiac workup was unremarkable and CT Chest revealed small pleural and pericardial effusions. Blood work showed positive ANA of 1:640 with elevated inflammatory markers. She was diagnosed with IRAP and started on colchicine along with MTX with good response.

Case Discussion: IRAP is characterized by the reappearance of chest pain either during convalescence or after complete recovery from initial attack. It has a suspected immune mediated pathogenesis and may present as initial manifestation of a systemic autoimmune diseases like SLE, RA, Sarcoidosis and Wegener's. Serum ANA is detected in 60% of patients. NSAIDs are the main cornerstone of treatment with steroids being reserved for severe cases. Colchicine prevents recurrences and immunosuppressants such as azathioprine, MTX, IVIG and Anakinra are beneficial in some cases. Administration of therapy should not be stopped before achievement of complete pain relief, normalization of inflammatory markers and complete resorption of pericardial fluid to prevent further recurrences.

Conclusion: IRAP may represent an autoimmune disease in evolution and patients should be screened for underlying autoimmune and auto inflammatory conditions for timely diagnosis and appropriate management.
Rheumatism Society of the District of Columbia
10th ANNUAL
RHEUMATOLOGY FELLOWS FORUM
May 19, 2012

Table or Figure

**IDIOPATHIC RECURRENT PERICARDITIS**

**TREATMENT PROTOCOL**

**STEP 1**
NSAID at full dose for ~10 days, then taper over next 3-4 wks + Colchicine x 6 months → GOOD RESPONSE

RECURRENCE

**STEP 2**
Steroids (prednisone 0.2-0.5 mg/kg daily) x 1 month, then taper over next 3 months + Colchicine x 12-24 months → GOOD RESPONSE

RECURRENCE

**STEP 3**
Continuation of prednisone + Colchicine x 12-24 months + Addition of NSAID as in STEP 1 for control of symptoms → GOOD RESPONSE

RECURRENCE

**STEP 4**
Return to minimum effective dose of prednisone x 1 month then taper over next 3 months + Colchicine x 12-24 months + Continuation of NSAID → GOOD RESPONSE

RECURRENCE

**STEP 5**
Addition of immunosuppressant → GOOD RESPONSE

RECURRENCE

Complete pericardiectomy
ABSTRACT

Rhomboencephalitis with Cerebral Salt Wasting as initial manifestation of primary Sjögren's Disease

PRESENTER: Madiha Latif, Washington Hospital Center
OTHER AUTHORS: Jose Lucar, Christopher Collins

Background and Purpose: Central nervous system involvement in primary Sjögren's is rare and its prevalence is a matter of controversy. We present a case of rhomboencephalitis with cerebral salt wasting as initial manifestation of primary Sjögren's syndrome.

Case Description: 49 year-old female with history of asthma and hepatitis C presented to an outside hospital with generalized weakness, progressive ataxia and cramps in lower extremities with diarrhea. Labs revealed hyponatremia (116 mmol/L), hypokalemia and microscopic hematuria. She was hospitalized for IV hydration with improvement in symptoms. 4 weeks later, she presented to our hospital with complaints of progressive dyspnea. Workup revealed non ischemic cardiomyopathy with pulmonary edema (EF 30%) and she was managed medically with some clinical improvement. However, she presented again 10 days later with diplopia, dysphagia and gag reflex. Labs showed hypotonic hyponatremia and brain MRI showed patchy enhancement of ventral medulla and bilateral cerebellum. CSF studies were unremarkable and an extensive infectious and paraneoplastic workup was unyielding. Rheumatologic workup revealed high titer SS-A (Ro) and SS-B (La) autoantibodies. Schirmers test was positive and a lip biopsy revealed lymphocytic infiltration consistent with primary Sjögren’s. Patient received pulse steroids and was started on monthly IV cyclophosphamide with improvement in symptoms.

Case Discussion: Sjögren's Syndrome is an autoimmune disorder characterized by hypofunctioning of the salivary and lacrimal glands. It affects 2-3% of the population and 50% of these cases are secondary to other autoimmune disorders like SLE and RA. CNS involvement in primary Sjögren's is very rare and its true prevalence is unknown. Spectrum of symptoms may range from focal central lesions to dementia and conditions that mimic multiple sclerosis. Transverse myelitis and aseptic meningoencephalitis are common reported CNS manifestations. However rhomboencephalitis as initial manifestation of primary Sjögren's is extremely rare and there are just 2 other cases reported in literature. Treatment of CNS Sjögren's remains largely empirical based on anecdotal reports and experience drawn from treatment of CNS lupus since no randomized controlled trials is available to date. Mild cases are treated symptomatically while severe cases warrant treatment with IV steroids and cyclophosphamide. There are some case reports of success of chlorambucil and azathioprine as well.
**Conclusion:** CNS involvement in primary Sjogren's may precede onset of classic sicca symptoms and can present a diagnostic dilemma due to the spectrum of manifestations ranging from focal central lesions to dementia and conditions that mimic multiple sclerosis. Hence primary Sjogren’s syndrome should be part of the differential for patients presenting with rhomboencephalitis.
ABSTRACT

Rituximab as adjunct therapy in isolated retinal vasculitis in systemic lupus erythematosus

PRESENTER: David Michel, NIH

Background and Purpose: Systemic lupus erythematosus is an autoimmune disease that affects many organs and is characterized by the production of autoantibodies. The eye is affected in up to one third of patients and can involve virtually all sites. Although SLE-related retinal vasculitis is considered a rare event, it carries significant morbidity and complications. Specific therapeutic guidelines do not exist, although most approaches parallel that of CNS vasculitis. Here we present a patient with severe isolated bilateral retinal vasculitis in the setting of SLE, and we offer the combination of cyclophosphamide and rituximab as a viable therapeutic regimen.

Methods or Case Description: The patient is a 45 year-old black female with a history of systemic lupus erythematosus manifested by arthritis, oral ulcerations, rash, cutaneous vasculitis, and class II nephritis maintained on azathioprine and low dose prednisone. The patient developed sudden onset of visual loss first in the left but that quickly evolved to the right eye—over the course of 2 days. She was evaluated by ophthalmology and was diagnosed with acute retinal vasculitis. She did not have any extra-ocular symptoms, aside from mild arthralgias 2 weeks prior, and denied any constitutional symptoms. She was admitted to the Clinical Center at the National Institutes of Health. Her general exam was grossly unremarkable; her ophthalmology evaluation showed severe bilateral retinal vasculitis, left greater than right. Her laboratory workup included stable blood counts, renal function, liver function tests, negative double stranded DNA and normal complements. Her urinary studies were unremarkable. Her radiographic evaluation included a normal brain MRI and MRA. Vitreous sample of eyes were negative for HSV and CMV, and gram stain and culture were negative. The patient was treated with pulsed solumedrol for 3 days and was continued on prednisone at 1mg/kg. She received a course of Rituximab (1g x 2 doses, 2 weeks apart) and underwent 6 monthly pulses of cyclophosphamide.

Results or Case Discussion: The patient responded well to induction therapy and had remarkable improvement in her vision, able to work, drive without issues. She was converted to cellcept for maintenance therapy and continues to do well—free from any major flare—1 year from her initial presentation. There is very scant literature on the treatment of retinal vasculitis in SLE. Here we present a patient who has undergone successful treatment of a severe case of retinal vasculitis with rituximab as adjunct therapy to cyclophosphamide.

Conclusion/Significance: Rituximab is a viable option as adjunct therapy in severe cases of retinal vasculitis in SLE.
Psoriasis and Psoriatic Arthritis in a Diverse Ethnic Cohort

PRESENTER: Seema Qaiyumi, VA Medical Center & Georgetown University
OTHER AUTHORS: Gail Kerr, John Steuart Richards, Sean Whelton, Florina Constantinescu, Chesahna Kindred

Background: Few clinical studies describe psoriasis (PSO) and psoriatic arthritis (PsA) in ethnic minority groups. Previous patient reported data show PSO/PsA to be less frequent in African Americans but with equal severity compared to Caucasians. We describe the clinical characteristics of a diverse ethnic cohort of patients with PSO and PsA in an urban outpatient setting.

Methods: IRB consented patients with PSO diagnosed by a dermatologist or PsA satisfying CASPAR criteria, were enrolled from four academic outpatient clinics. Socio-demographic data, disease duration, time to diagnosis, disease phenotype and status, quality of life measurements, disease modifying anti-rheumatic drugs (DMARD) and biologic therapies and comorbidities were recorded.

Results: Of 160 enrolled PSO patients, 93 (58%) were Caucasian and 67 (42%) were Non-Caucasian [62 African American, 5 Other]. The majority were male (78%) and average BMI was 30.0 ± 5.8. PsA occurred in 83 (52%) and oligoarthritis (<4 peripheral joints) was the most common phenotype (33%). The cohort had longstanding disease (PSO = 17.9 ± 14.1 years, PsA = 12.8 ± 10.8) and the average delay in diagnosis was 3 years. Of the cohort, 41% had nail changes and 53% received either DMARD or biologic agents. Compared to Caucasians, African Americans had a lower frequency of PsA (34% versus 65%, p<0.001), higher PASI scores (8.6 ± 10.4 versus 5.5 ± 6.4, p=0.04), fewer tender and swollen joints (1.7 versus 3.4, p=0.04; 0.5 versus 1.3, p=0.01, respectively), worse psoriasis quality of life scores (9.3 ± 6.6 versus 6.1 ± 6.6, p<0.01), less psychological impact of psoriatic disease (43.5 ± 12.2 versus 47.7 ± 11.7, p=0.04), lower Vitamin D levels (21.6 ± 10.8 versus 31.3 ± 13.9, p<0.01) and more frequent hypertension (65.5% versus 36.3%, p<0.001). African Americans were also less frequent recipients of DMARD and biologic therapies (10.5% versus 28%, p<0.01, 13.4% versus 46.2%, p<0.0001, respectively) and private insurance (11.9% versus 28%, p=0.02). Though not statistically significant, there was a trend towards higher inflammatory markers (ESR/CRP), less dactylitis and higher rates of Hyperlipidemia and CVA in African Americans.

Conclusions: In African Americans, PsA occurred less frequently than in Caucasians. Despite worse skin disease, African Americans received less DMARD and biologic therapies. While African Americans appeared to experience less psychological impact from their disease, their psoriasis related quality of life was reduced compared to Caucasians. Our cohort is unique in describing ethnic differences in psoriatic disease and further study to examine these differences is ongoing.
ABSTRACT

Potential disease specific role for a de-ubiquitinating enzyme, ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCHL1) in myositis.

PRESENTER: Sree Rayavarapu, Children's National Medical Center & George Washington University
OTHER AUTHORS: William Coley, Erdinc Cakir, Kristy Brown, Yetrib Hathout, Kanneboyina Nagaraju

Background: Idiopathic inflammatory muscle diseases (polymyositis, dermatomyositis and inclusion body myositis) are characterized by severe muscle weakness, elevated levels of serum muscle enzymes and muscle inflammation. Others and we have shown that endoplasmic reticulum (ER) stress, autophagy and hypoxia have pathogenic role in myositis. However, the interaction between these processes and their specific relationship to myofiber damage in myositis has not been completely elucidated. We hypothesize that the chronic ER stress triggered in myositis muscle due to unusual overexpression of major histocompatibility complex class I (MHC) activates ubiquitin proteosome pathway (UPP) and contribute to degradation of proteins and loss of muscle mass in myositis. Here we utilized conditional transgenic mouse model that over expresses MHC class I in skeletal muscle to test the hypothesis.

Objective: To understand the role of UPP in myopathic muscle using mass spectrometry based novel quantitative in vivo stable isotope ($^{13}$C)–labeled’ mouse proteomic strategy.

Methods or Case Description: Muscle lysate from ‘unlabeled’ conditional MHC class-I transgenic mice and the age matched ‘labeled’- C57BL6 mice were obtained. Lysates were mixed (1:1), electrophoresed and individual bands were tryptic digested and global protein alterations were identified using LC-MS/MS. Disease specific proteomic modulations were identified and validated using specific antibody based biochemical assays [n=4 mice/group]. Tissue interstitial fluid was obtained by micro-dialysis of muscle and analyzed for the presence of UPP member proteins.

Results: A total of 829 proteins were accurately quantified in the muscle of which ~53% proteins were differentially modulated between control vs diseased muscle. We used dystrophin deficient skeletal muscle as a myopathic control. Out of differentially modulated proteins, 24 belong to UPP and these proteins showed >2 fold up-regulation compared to controls. We have identified ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCHL1), a de-ubiquitinating enzyme to be specific to myositis muscle. Further analysis of differentially modulated proteins supported the activation of other members of ER stress response and UPP in myositis muscle. The specificity and the increased expression of UCHL1 was validated using independent set of samples. Interstitial fluid
from myopathic muscle demonstrated disease specific increase of UCHL1 suggesting its role as a potential biomarker for myositis. The specific involvement of UCHL1 and other members of UPP in muscle damage in myositis are currently being investigated.

**Conclusion:** Enhanced expression of UCHL-1 and the activation of UPP might be the connecting link between chronic ER stress and muscle fiber degeneration in myositis. UCHL-1 might be a potential biomarker for disease progression in myositis.

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**Table or Figure**

![Figure 1](image.png)

*Figure 1. Ubiquitin proteasome pathway (UPP) is enhanced specifically in myositis muscle. A) Muscle lysates from unlabeled conditional MHC class-1 transgenic mice (myositis) and the age matched labeled C57BL6 mice were mixed (1:1) and electrophoresed. Individual bands were tryply digested and protein alterations were identified using mass spectrometry (LC-MSMS). Relative abundance of some UPP proteins were expressed as (disease/control) ratio. These ratios indicate that UPP is upregulated in myositis muscle. B) UCHL1 is specifically expressed in myositis but not in controls, dysferlin deficient (SjL), and dystrophin deficient (mdx) muscles. Immunoblotting for quadriceps muscle lysates (n=3/group) was performed using anti-UCHL1 antibody. β-actin was used a loading control. C) The immunoblots were scanned and the data quantified by normalizing the levels of UCHL1 relative to that of β-actin in the same lysate. Data were represented as mean ±SEM (**p<0.001 vs controls, by student's t-test).*
ABSTRACT

A Case of Cutaneous Vasculitis: Levamisole versus Lupus Vasculitis

PRESENTER: Tazeen Rehman, Washington Hospital Center
OTHER AUTHORS: Sarah Shao, Christopher Collins

Background and Purpose: Levamisole induced cutaneous vasculitis is a newly recognized and increasingly reported entity that is associated with levamisole adulterated cocaine use. It can often result in diagnostic confusion with several rheumatologic conditions due to positive serologies for p-ANCA.

Methods or Case Description: 39 year old female with a history of SLE and cocaine abuse presented to the ER with a 1 week history of bilateral ear pain with progressive darkening of bilateral pinna. On exam, patient had bilateral marked necrosis of her pinna with multiple small vasculitic type ulcers on the buttocks, upper and lower extremities. Her laboratory data was consistent with lupus (high titer ANA and positive serologies for anti dsDNA, anti-SSA, anti-RNP and anti-cardiolipin but with normal complement levels). The patient was thought to likely have levamisole induced cutaneous vasculitis given the time course of her clinical presentation in relationship to cocaine exposure, the classical manifestation of aural necrosis and little evidence for active SLE.

Results or Case Discussion: With initial moderate dose steroid treatment, her purpuric lesions progressed with rapid enlargement on multiple body sites including the thighs and arms. She was then initiated on pulse solumedrol as well as IV cyclophosphamide with dramatic improvement.

Conclusion/Significance: Levamisole induced cutaneous vasculitis responds to withdrawal of the offending agent however may on occasion necessitate more robust anti-inflammatory and immunosuppressive therapy. Concomitant medical conditions which can individually cause vasculitis can cause a diagnostic and treatment dilemma highlighting the importance of a careful history, physical exam and clinical and laboratory evaluation of the underlying disease processes.
Before Treatment
After Treatment
Behçet's Disease with Valvulitis

PRESENTER: Nicole Saddic, Georgetown University
OTHER AUTHORS: Thomas Cupps

Methods or Case Description: A 46 year old man of South Asian descent noted acute onset dyspnea on exertion. Past medical history was significant for acne and a scrotal ulcer 10 years prior to presentation. Scrotum shave biopsy showed “neutrophilic dermatitis with pseudoepitheliomatous hyperplasia without clear evidence of vasculitis.” Echocardiography revealed redundant aortic leaflets causing severe aortic regurgitation with myxomatous mitral valve leaflets with moderate mitral regurgitation necessitating a mechanical aortic valve replacement and mitral valve repair. The operative report noted inflammation of the aortic wall. His pre-operative ESR was 71 mm/hr with negative blood cultures. The aortic valve biopsy had a focal neutrophilic infiltrate associated with degenerative changes and fibrin deposition. The aorta biopsy showed an elastic artery with laminar medial necrosis. An extensive rheumatologic and infectious disease workup was unrevealing. Four months post-operatively he developed fevers and dypsnea associated with ruptured mitral valve chordae, tricuspid valve dilatation, and dehiscence of the aortic prosthesis. The aortic and the mitral valve were both replaced by bioprostheses and tricuspid annuloplasty was performed. Both the first and second surgeries were accompanied by poor wound healing. Intercurrent fevers persisted. Four months after the second surgery, he shared his history of scrotal ulcer (this information was initially withheld) and prednisone, azathioprine and adalimumab were initiated sequentially. Echocardiograms have remained stable since initiation of immunosuppression.

Results or Case Discussion: Cardiac abnormalities in patients with Behçet's disease (BD) are rare and have been reported in 1-6% of BD patients. Geri et al. reviewed 807 patients with BD and found that 9 patients had aortic valve insufficiency, and 3 had both mitral and tricuspid regurgitation respectively. Valvulitis is a rare finding in BD. Surgical treatment for BD valvulitis has a high risk of post-operative morbidity secondary to fragile, inflamed tissues. There have been several studies showing that pre- and post-operative steroid treatment in patients with BD undergoing valve surgery improve surgical outcomes and mortality. Characteristic echocardiographic findings, and histology can help diagnose BD valvulitis early to allow for prompt initiation of immunosuppression. Han et al. identified that 80% of patients with BD valvulitis had aneurysmal changes with redundant coronary cusps motion. Han considers this finding pathognomonic for BD aortic valvulitis.
The microscopic features of the aortic valve in BD are most commonly diffuse myxoid degenerative change. The aorta wall most often shows characteristic vasculitis with medial narrowing and thickened adventitia with myxoid degenerative change.

**Conclusion/Significance:** Valvulitis in Behçet's disease is rare but associated with significant morbidity and mortality. Prompt diagnosis and initiation of immunosuppressive therapy improves outcomes. Echocardiographic findings of aneurysmal changes with redundant coronary cusps motion and histologic findings of myxoid degenerative change in the valve and can aid in early diagnosis.

ABSTRACT

A New Diagnosis of Myositis Ossificans in a Young Female

PRESENTER: Adam Schiffenbauer, NIAMS
OTHER AUTHORS: Apostolos Kontzias

Background and Purpose: Myositis Ossificans is a rare disorder of non-neoplastic heterotopic proliferation of bone and cartilage in the muscle and soft tissue. It is one of the pseudosarcomas and can present a diagnostic dilemma. Here we present an atypical complicated case to focus on the difficulty of making this important diagnosis.

Case Description: The patient was in good general health until August 2003 when at the age of 35 the patient had a traumatic tear of the right plantaris with hematoma and a meniscal tear of the knee. Her plantaris necrotized and was resected in February 2004. She underwent knee arthroscopy in May of 2004 for medial meniscal repair. She then developed an equinas contracture of the right ankle and had surgical lengthening of the gastrocnemius in June 2005. She underwent a second knee arthroscopy in June 2005.

In early 2005 the patient developed erythema nodosum isolated to the lower extremities. She was started on supersaturated potassium iodine for this in January 2007. Since then the lesions have significantly improved, but do recur on the right lower extremity.

March 2007 the patient had right patellar release surgery. Following this surgery she developed swelling of the leg thought to be lymphedema. In October 2007 she noticed a hard lump in the thigh. She underwent a MRI which revealed myositis. A muscle biopsy in May of 2008 showed a single focus of lymphocytic vasculitis and excessive fibrovascular tissue. Throughout 2009 imaging showed enlarging heterotopic ossification of the mid thigh and proximal tibia-fibula region. This was treated unsuccessfully with methotrexate and plaquenil.

The patient then underwent open bone biopsy that showed well organized tissue with trabeculated bone without malignant appearing cells.

Case Discussion: Based on this data the patient was diagnosed with myositis ossificans.

Significance: It is often difficult to differentiate myositis ossificans from other disorders. The location of this calcification being separated from the underlying bone, not occurring in the digits, and not having an outer ring of osteoblasts made it unlikely to be a reactive lesion of the periostium, such as florid reactive periostitis, subungual exostosis, or bizarre parosteal osteochondromatous proliferation. Fibro-osseous pseudotumor (ossifying fasciitis) unlike the lesions in this patient originates from the soft tissue and has a random organization unlike the zonation seen in our patient. The lack of malignant cells on large open biopsy made the lesions unlikely to be osteosarcoma.
IS IT A RHEUM RASH?

PRESENTER: CPT Jison Sim, Walter Reed National Military Medical Center
OTHER AUTHORS: Sharon Frattalone, Patricia Papadopoulos

Case Description: A 29-year old female presented with arthralgias and tender palpable purpura in the lower extremities. Laboratory work up for vasculitides including complete blood count, metabolic panel, urinalysis, coagulation studies, and complement levels were normal and antinuclear antibody, extractable nuclear antibody panel, anti neutrophil cytoplasmic antibody panel, hepatitis panel, complement levels, and throat cultures were negative. Punch biopsy demonstrated leukocytoclastic vasculitis histologically. Direct immunofluorescence testing of the skin biopsy was negative. Further inquiry of the patient’s history revealed Crohn’s disease treated with sulfasalazine and an anti-tumor necrosis factor alpha agent.

Case Discussion: Patients with palpable purpura are commonly referred to the rheumatologist. There are many rheumatologic causes of palpable purpura as well as medications and other systemic processes in the differential. The most common dermatologic manifestation of Crohn’s Disease is erythema nodosum while leukocytoclastic vasculitis is a rare manifestation with limited literature available to guide the clinician. There are only a handful of case reports of this extragastrointestinal manifestation in Crohn’s disease. Additionally, leukocytoclastic vasculitis is the most common manifestation of anti-tumor necrosis factor alpha agent induced autoimmune disease. This case represents development of leukocytoclastic vasculitis in a patient under treatment of Crohn’s disease with an anti-tumor necrosis factor alpha agent.

Conclusion: Leukocytoclastic vasculitis it is a rare extragastrointestinal manifestation of Crohn’s disease. Meanwhile, many patients with Crohn’s disease are treated with anti-tumor necrosis factor alpha agent and leukocytoclastic vasculitis is the most common manifestation of anti-tumor necrosis factor alpha agent induced autoimmune diseases. These causes should be considered in patients under treatment of Crohn’s disease with anti-tumor necrosis factor alpha agents. Obtaining autoantibody titer prior to initiating the anti-tumor necrosis factor alpha agents may be helpful in discerning the cause.
ABSTRACT

Early disease manifestations of Enthesitis related arthritis reveals elevated TGF-beta

PRESENTER: Hemalatha Srinivasalu, NIAMS & Nemours/Alfred I Dupont Hospital for Children
OTHER AUTHORS: Michael G. Barnes, Gerlinde Layh-Schmitt, Michael M. Ward, Robert A. Colbert

Background and Purpose: Enthesitis-related arthritis (ERA) is a subtype of Juvenile idiopathic arthritis (JIA) as defined by ILAR. Most ERA cohorts have been established retrospectively, and consequently there is a paucity of data on early disease characteristics of ERA. The purpose of this study was to examine an inception cohort of ERA and determine correlation between serum cytokine levels and disease manifestations.

Methods: Thirty-seven patients who satisfied ILAR criteria for ERA were included in the study. At their baseline visit, information about demographics, active joint & enthesis count, presence of eye disease, family history of HLA-B27-associated disease, physician global, lab analyses including CBC, ESR, CRP, HLA-B27, ANA, RF and imaging studies when indicated, were collected. Serum collected at the baseline visit from patients and healthy controls were analyzed by ELISA for IL-22, IL-23, GM-CSF, IFN-gamma, IL-6, IL-10, IL-12p70, MCP-1, TNF-alpha, G-CSF, IL-17, IP-10, MIP-1alpha and TGF-beta1. Mann-Whitney U tests, one-way ANOVA, and Tukey’s multiple comparison tests were performed for statistical analyses.

Results: The median interval from disease onset to enrollment was 5.4 months (IQR 2.05-9.8). Most of the disease characteristics were comparable to other historic cohorts with the exception of lower percentage of sacroiliitis (clinical and radiographic 8 and 2.7 % respectively compared to 19-66% in other cohorts), and percentage of enthesitis was higher in our cohort (78% compared to 37-66% in other cohorts). TGF-beta1 was elevated in ERA patients compared to controls (p=0.0075). Further, levels of TGF-beta1 were significantly elevated in patients with a history of GI complaints when compared to healthy controls (p=0.0082) and when compared to patients without GI complaints (p<0.05). Levels of TGF-beta1 were elevated in patients without arthritis when compared to controls (p<0.05). There was no difference in TGF-beta1 levels on comparing patients by presence of enthesitis, HLA-B27 status and inflammatory markers.
**Conclusion/Significance:** This study informs us on the early disease characteristics of ERA. TGF-beta1 has been reported to be elevated in the serum of patients with ankylosing spondylitis. To our knowledge, this is the first study reporting elevation of serum TGF-beta1 in patients with ERA. This finding correlates with earlier studies we have published on evidence for a TGF-beta1 peripheral blood gene expression signature in ERA patients. Additionally, TGF-beta is known to be elevated in chronic gut inflammation; its elevation in patients with GI complaints seen in our cohort suggests a role of gut inflammation in early ERA.

### Table or Figure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>12 (10.2-13.6)</td>
</tr>
<tr>
<td>Interval from disease onset to enrollment in months</td>
<td>5.4 (2.1-9.8)</td>
</tr>
<tr>
<td>Active joint count</td>
<td>1 (0-4)</td>
</tr>
<tr>
<td>Enthesitis count</td>
<td>4 (2-6)</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>8 (4-17)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>0.3 (0.3-0.7)</td>
</tr>
<tr>
<td>Male</td>
<td>29 (78)</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>19 (59)</td>
</tr>
<tr>
<td>ANA</td>
<td>4 (25)</td>
</tr>
<tr>
<td>RF</td>
<td>0</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>31 (89)</td>
</tr>
<tr>
<td>African American</td>
<td>3 (3.4)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (3.4)</td>
</tr>
<tr>
<td>Other (Asian)</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Eye disease</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Family history of HLA-B27 associated disease</td>
<td>6 (16)</td>
</tr>
<tr>
<td>NSAID use</td>
<td>27 (93)</td>
</tr>
<tr>
<td>GI symptoms</td>
<td>9 (33)</td>
</tr>
<tr>
<td>Radiological evidence of joint damage (n=20)</td>
<td>8 (40)</td>
</tr>
</tbody>
</table>
ABSTRACT

REFRACTORY LYME ARTHRITIS IN A PREGNANT FEMALE

PRESENTER: Christopher L Tracy, Walter Reed National Military Medical Center
OTHER AUTHORS: Jefferson Roberts

Case Description: Lyme disease was first described in 1977 as ‘Lyme Arthritis’ among patients initially thought to have arthritis or juvenile rheumatoid arthritis. Lyme arthritis, caused by the tick-borne spirochete Borrelia burgdorferi typically causes intermittent or persistent arthritis in a few large joints, especially the knee, and can last for several years.

Case Discussion: Our patient is a 24 year old female, 16 weeks pregnant who initially presented with an acute presentation of left monoarticular arthritis of the knee with accompanying hydrarthrosis that worsened over the course of 24 hours. She reported no prodromal symptoms or systemic symptoms preceding this event. She has a medical history that includes latent Tuberculosis infection with negative chest xray and no history of treatment. She lives in Montgomery County, Maryland and immigrated to the US from Nepal in 2006. She reports mostly indoor activities but had recently gone on a rafting trip in West Virginia 2 weeks prior to this presentation. Physical exam was remarkable for an afebrile gravid female with normal vital signs and normal HEENT, Cardiac, Pulmonary and Abdominal exam. No rashes, petechiae or lesions were noted on examination of the skin. Exam of the left knee revealed warmth, tenderness to passive and active range of motion and a large effusion. Serum studies were notable for a sedimentation rate 63, white blood cell count 9.3 and IgM/ IgG Antibody Positive to Borrelia burgdorferi. Synovial Fluid analysis was culture negative and inflammatory in nature with polymerase chain reaction analysis positive for B. burgdorferi. Amoxicillin therapy was begun for treatment of active Lyme infection and the patient has since returned multiple times with complaints of knee pain and re-accumulation of her knee joint effusion for therapeutic knee joint aspirations.

Conclusion: Antibiotic-refractory Lyme arthritis may result from persistent infection or from post-infectious immune phenomena. Treatment recommendations have changed over time but it is generally accepted that early use of antibiotics with long durations can prevent persistent, recurrent and refractory Lyme disease. What remains unclear is how to best follow disease progression in patients with refractory disease and when to use alternative treatment modalities to include DMARD’s and intra-articular steroid injections.
Castleman Disease: Three Case Reports

PRESENTERS: Hashem Vahabzadeh-Monshie, Georgetown University
OTHER AUTHORS: Sean Whelton

**Background:** Castleman disease (CD) is a rare atypical lymphoproliferative disorder. The exact etiology of disease is poorly understood. Human Herpes Virus type 8 (HHV-8) especially in HIV patients, and dysregulated overproduction of Interleukin-6(IL-6) are implicated in the pathogenesis of disease.

**Case 1:** A 47 year old African American male presents to GUH with malaise, fever, abdominal pain and anasarca. CT reveals diffuse lymphadenopathy with marked ascites; the fluid is exudative with negative cultures. He has elevated inflammatory markers, negative infectious and autoimmune work up. Patient develops profound anemia, thrombocytopenia and renal failure requiring HD. Excisional cervical LN biopsy reveals vascular proliferation and hyalinization, with interfollicular polyclonal plasmacytosis and atretic follicles with “onion skin” pattern in mantle zones consistent with mixed variant of CD. Immunohistochemistry analysis for HHV-8 and HIV test are negative. The Interleukin-6 is elevated at 44(<17.4 pg/ml). Tocilizumab resulted in marked improvement of symptoms and lab abnormalities. HD was discontinued about one week after initiation of Tocilizumab.

**Case 2:** 57 year old African American male presents with diffuse edema and dyspnea. Few weeks ago he received pericardial window for pericardial effusion. Autoimmune work up is negative. Chest CT reveals large pleural effusion with mass effect on mediastinum and an anterior mediastinal mass. The pleural fluid is exudative. Thymectomy and excisional mediastinal lymph Node biopsy are consistent with mixed variant of CD involving the thymus and lymph nodes. Immunohistochemistry for HHV8, HIV and HHV-8 Ig G are negative. IL6 is elevated. The therapeutic options, rituximab vs. Tuculizumab were discussed with patient.

**Case 3:** 38 year old African American male, with history of HIV and Kaposi Sarcoma, presents with fever and exsional dyspnea. Examination reveals crackles in lungs, splenomegaly and pedal edema with overlying thickened skin with hyperpigmentation. Infectious work up is unremarkable. Pan CT scan reveals diffuse lymphadenopathy. Cervical LN excisional biopsy is consistent with CD. The patient is positive for HHV-8 infection and IL-6 is elevated. He was treated with Rituximab infusion and gancyclovir.

**Discussion:** Castleman's disease could be associated with HHV-8 and HIV; the systemic symptoms are consequence of elevated IL-6 production. CD includes two distinct diseases with different prognoses; unicenteric (UCD) and multicentric (MCD). CD is classified according to the histopathologic findings as hyaline-vascular, plasma-cell type, or mixed type. UCD is usually cured by surgical excision; however MCD is often refractory to
treatment. Steroids, combination chemotherapy and antivirals have been used in treatment of MCD. Rituximab has resulted in durable clinical remission in HIV/HHV-8 positive MCD in multiple studies and Tocilizumab has been shown to be effective in the alleviation of systemic manifestations in HIV/HHV-8 negative patients. Lymphoma and Kaposi sarcoma are common causes of death in MCD.

**Significance:** Clinician should consider MCD in differential diagnosis of lymphadenopathic presentations with symptoms of systemic involvement. Tocilizumab is promising in treatment of HIV/HHV-8 negative MCD, yet the efficacy in HIV/HHV-8+ patients to be determined.
ABSTRACT

Cerebellar Ataxia in primary Sjogren syndrome with positive anti-GWB antibodies in serum and cerebrospinal fluid: a case report

PRESENTER: Runsheng Wang, NIAMS
OTHER AUTHORS: Camilo Toro, Marvin Fritzler, Gabor Illei

**Background and Purpose:** Primary Sjogren syndrome (PSS) is a systemic autoimmune disease characterized by keratoconjunctivitis and xerotomia. Cerebellar ataxia is a rare manifestation of PSS. GW bodies (GWBs) are unique cytoplasmic structures involved in messenger RNA (mRNA) processing and RNA interference (RNAi). Recently, it is reported that anti-GWB autoantibodies in serum are associated with neurological conditions (33%) and Sjogren syndrome (31%). Here we report a case of PSS with immune-mediated cerebellar ataxia and positive anti-GWB autoantibodies in serum and cerebrospinal fluid (CSF).

**Methods or Case Description:** 59 year old lady with a 30 year history of PSS was referred for evaluation of diplopia, nystagmus, dysarthria and imbalance for seven years. Five prior lumbar punctures revealed persistent lymphocytic pleocytosis. Multiple brain MRIs, EMG/NCV studies, paraneoplastic antibodies and genetic tests for spinocerebellar ataxia were negative. During our evaluation, patient fulfills 2002 American-European classification criteria of PSS. A repeat lumbar puncture showed persistent lymphocytic CSF pleocytosis. An extensive infectious disease evaluation was negative. Antibodies to cell surface neuronal antigens were all negative in CSF and serum. Antibodies to LGI1 and Caspr2 were also negative in CSF and serum. Finally, anti-GWB antibody panel, including anti-GW182, anti-EAA1, anti-Ge-1, anti-Jo-1, anti-SRP, anti-Ribosomal-P, anti-GW2n, and anti-Clip170, was measured. Anti-Ribosomal-P was highly positive in both serum and CSF; anti-Clip170 highly positive in serum, moderately positive in CSF; anti-Ge-1 was moderately positive in both; anti-GW 182 moderately positive in serum, mildly positive in CSF. The patient was given a diagnosis of PSS with immune-mediated cerebellar ataxia. Six months of IVIG or a trial of Rituximab was recommended given there is no other etiology or treatment at this moment.

**Results or Case Discussion:** CNS manifestations are uncommon in PSS, with cerebellar ataxia being a very rare occurrence. On the other hand, the presence of anti-GWB autoantibodies has been reported mainly in patients with neurological conditions, PSS, or less often, systemic lupus erythematosus (SLE), rheumatoid arthritis, primary biliary cirrhosis. Our patient with a long history of PSS with a recent onset cerebellar ataxia, was found to have high titers of anti-GWB antibodies both in serum and in CSF, which has not been previously reported. For now, there is no evidence that these autoantibodies are pathogenic. Interestingly, anti-Ribosomal P, which is associated with neuropsychiatric...
lupus, is significantly positive in this patient, although she does not fulfill classification criteria of SLE.

**Conclusion/Significance:** Further investigations are needed to study the prevalence of anti-GWB antibodies in CSF of PSS patients with neurologic symptoms, and their potential pathogenic significance.

**References:**
2. Primary Sjögren syndrome in Spain: clinical and immunologic expression in 1010 patients.
ABSTRACT

An In-Depth Analysis of Responses in the Rituximab in Myositis (RIM) Trial in Patients Enrolled at the NIH

PRESENTER: Adrienne Yip
OTHER AUTHORS: Lisa Rider, Iren Horkayne-Szakaly, Rita Volochayev, Joseph Shrader, Maria Turner, Heidi Kong, Mina Jain, Anna Jansen, Chester Oddis, Thomas Fleisher, and Frederick Miller

Purpose: Treatment-refractory myositis patients were enrolled into a clinical trial to evaluate the efficacy of Rituximab. In addition to the myositis core set measures, supplementary clinical and laboratory data were collected from patients enrolled at the NIH. This report presents an in-depth analysis of the change in different outcome measures in response to rituximab therapy in these patients.

Methods: Eighteen patients (5 dermatomyositis [DM], 8 polymyositis [PM], and 5 juvenile DM) received Rituximab and completed the additional assessments, including detailed muscle and skin assessments, patient reported outcome measures, and additional laboratory tests. Thirteen adult DM/PM patients had muscle biopsies at weeks 0 and 16. The percent change in various measures was examined for all patients from weeks 0-16, 16-44, and 0-44, as well as by disease subgroup and treatment group. The standardized response mean was calculated to examine responsiveness of the different measures, and the percentage change in the DOIs was compared in a pair-wise manner.

Results: All core set measures improved by 18-70% from weeks 0-44. We also found that the core set measures were sensitive to change over the 44 week period, although the CK level was less responsive. Using various preliminary definitions of improvement (DOI), response rates varied from 83-94%. For adult and juvenile DM patients, muscle strength and functional measures improved 17 – 64% over the course of the trial, and the muscle measures were more sensitive to change than the skin assessments tools. The Extra-muscular portion of the MDAAT improved by 70%, with improvements in Constitutional, Gastrointestinal and Pulmonary systems of 44 - 70%. Improvements were also noted in the patient reported outcomes, including SF-36 physical score by 28% and Peds QL fatigue by 25%. There were no differences detected in these measures by treatment group or disease subgroup. CD20 generally depleted following rituximab therapy both in the peripheral blood and muscle tissue; however, 4 patients did not deplete CD20 but still met the DOI.
Conclusion/Significance: Patients enrolled at the NIH had similar responses to Rituximab as the overall Rituximab in Myositis trial. A large proportion of patients improved throughout the trial using the other DOIs developed by the IMACS Group, and that these definitions performed similarly. All measures were very responsive based on the standardized response mean, but muscle measures improved to a greater degree than cutaneous measures. Finally, we found that CD20 depleted in the muscle and blood, but depletion did not correlate with clinical response.

Figure
Figure 1. Absolute counts of CD20 in the peripheral blood and muscle following Rituximab therapy.