THE RHEUMATISM SOCIETY OF THE
DISTRICT OF COLUMBIA

PRESENTS…

THE 12TH ANNUAL RHEUMATOLOGY
FELLOWS FORUM

SATURDAY, May 10TH 2014

Washington Hospital Center
True Auditorium
Washington, DC
Rheumatology Fellows Forum
May 10th, 2014

Program Schedule

9:00-10:00 AM  
Poster Viewing/Breakfast

10:00-11:00 AM  
Podium Presentations (4)

11:00-Noon  
Keynote Speaker:  
Brian Mandell, MD PhD

Topic:  “A Historic Perspective of Gout”
Rheumatology Fellows Forum Awardees

Podium Presenters

- Sarthak Gupta, MD
- Brian Stout, MD MHA
- Angeliki Giannelou, MD
- Hanna Kim, MD

Poster Awards

- Shaun Abraham, MD
- Melissa Butts, MD
- Deborah Kim, DO
ABSTRACTS

(**- AWARD)
NAME: Shawn Abraham  DEGREE: MD **

INSTITUTION: MedStar Georgetown University Hospital

Fellowship/Resident/Student/Post Doc/PhD Year: PGY4

TITLE: A rare case of IgG4 related disease presenting as pleural based mass

EMAIL: shawn.g.abraham@gmail.com

Background and Purpose: We present the case of a patient who was incidentally found to have a pleural-based mass on chest X-ray, with a final diagnosis of IgG4-related disease being made after surgical excision.

Methods/Case Description:

A 48-year-old female with a two-year history of hidradenitis suppuritiva involving the groin and axilla was admitted with one-week history of weakness, intermittent cough and generalized malaise. CT chest without contrast during the admission showed evidence of a broad spaced pleural mass located laterally in the right mid hemithorax measuring 4cm by 0.8cm. She was seen by the thoracic surgery department who performed a video-assisted thoracoscopic surgery with wedge resection of the pleural based mass given concern for underlying malignancy.

Results/Case Discussion:

The biopsy showed evidence of a dense fibrous pleural nodule with calcification and chronic inflammation consisting mostly of plasma cells. There was no evidence of neoplasm or malignancy noted. Immunohistochemical investigation using antibodies against IgG4 was performed. Many of the plasma cells showed strong intracytoplasmic IgG4 positivity, coinciding with the diagnosis of an autoimmune sclerosing inflammatory process. Interestingly, her palm lesions were biopsied which showed evidence of nummular eczema.

There are four reported patterns of lung involvement associated with IgG4-PD, including a) solid nodular b) bronchovascular c) alveolar interstitial d) round-shaped ground-glass opacities. Evidence of visceral or parietal pleural thickening can also be seen. Inflammatory pseudotumors presenting as nodular lesions often have surrounding reticular shadows. These lesions have marked infiltration of plasma cells and lymphocytes, evidence of fibrosis, pneumonitis at periphery of nodule, obliterating phlebitis and arteritis and eosinophilic infiltration.
Interestingly, there has also been an association between IgG4 RD and allergic conditions. Patients with IgG4 RD often have allergic features such as atopy, eczema, asthma, and peripheral eosinophilia, as seen in our patient.

**Conclusion/Significance:** In conclusion, we report a case of IgG4-related disease presented as a pleural-based mass. IgG4-related pulmonary disease is a contemporary disease with a plethora of various presentations. Pulmonary involvement in patients with IgG4-RD can prove to be a diagnostic challenge in terms of differentiation from other conditions such as sarcoidosis or carcinoma. Therefore, the diagnosis of IgG4 related disease must be predicated upon specific histopathologic findings and then confirmed by tissue immunostaining, all in the appropriate clinical context. The diagnosis should be suspected in patients with extrapulmonary organ involvement such as autoimmune pancreatitis, sialadenitis, cholangitis, or retroperitoneal fibrosis; and although rare, remain as a differential in the evaluation of a newly identified pulmonary lesion.
Background and Purpose: Takayasu’s arteritis (TAK) is an uncommon vasculitis with a predilection for the aorta and its primary branches. Usually affecting women in the age range of 10 to 40 years; its greatest prevalence is in those of Asian descent. Labs are nonspecific, but indicators of systemic inflammation such as elevated C-reactive protein (CRP) or prolonged erythrocyte sedimentation rate (ESR) may be present. Diagnosis is seldom made histologically, but rather is based on clinical characteristics and on imaging of the arterial tree. TAK is a heterogeneous classification and arteritis in the TAK spectrum may assume several patterns. While carotid arteritis is common in TAK, isolated carotid involvement is rare.

Case Description/Results: A previously healthy 38 year-old Caucasian woman initially presented with symptoms of blurry vision with extension of the neck. An MRI of the brain showed subtle narrowing of the left internal carotid artery. She was symptom free until four months later when blurred vision with neck movement recurred and a new vague headache developed. With this presentation she was admitted and further work-up was pursued. A CTA of the head and neck showed a left common carotid artery thrombosis and thickening of the wall of the right common carotid artery with subtle asymmetric enhancement of the posterior right globe compared to the left. Repeat MRI of the brain showed an interval increase in left common carotid artery narrowing. MRA of the thoracic aorta was unremarkable. Labs were notable for unremarkable CBC, CMP, normal ESR, CRP, negative ANCA, cryoglobulins, RF, CCP, ANA, complement, lupus anticoagulant, B2 glycoprotein, cardioplinps and RPR. She was begun on high dose prednisone during this admission due to concern for a large vessel vasculitis. Her symptoms improved on prednisone which was slowly tapered off after three months, once a PET-CT showed no increased fluorodeoxyglucose (FDG) uptake. One year later, she had a follow-up PET-CT which was again initially read as negative for any increased FDG uptake. She remained asymptomatic off corticosteroids until a year later when the patient reported symptoms of headache, left facial droop and LUE weakness. Her exam included stable vitals, a right carotid bruit (previously present) and a nonfocal neurological exam. A further work-up including MRA of the head and neck, revealed a new high grade short segment stenosis of the right common carotid artery, stenosis of the right external carotid artery and continued long segment stenosis of the left common carotid artery. Her former PET-CT was reviewed again and was remarkable for subtle FDG uptake in the right common carotid artery. She was taken for right common carotid endarterectomy. Tissue pathology was significant for a necrotizing granulomatous arteritis with giant cells and lymphocytes and an organizing occlusive thrombus. Her pathology was most consistent with TAK.
Conclusion/Significance: This is a unique case of TAK. A Caucasian patient presented initially with transient visual complaints ultimately followed by more pronounced neurologic symptoms in the setting of progressive stenotic carotid lesions. She lacked any symptoms of extremity claudication. Tissue obtained at the time of endarterectomy demonstrated granulomatous vasculitis consistent with TAK. The presence of only two ACR classification criteria, an atypical ethnic background and vasculitis limited to the carotids confounded the diagnosis, but the uncommon ability to review a pathologic specimen confirmed that this patient had TAK.

Figure 1: Right common carotid artery: necrotizing granulomatous arteritis with giant cells and lymphocytes.
TITLE: Minimal Change Disease (MCD): Is This a Renal Manifestation of Systemic Lupus Erythematosus (SLE)?

PRESENTER: Melissa S. Butts

EMAIL: melissa.s.butts.mil@health.mil

Background: Minimal change disease (MCD) is unusual in adults but accounts for 10-15% of nephrotic syndrome cases. It is mostly idiopathic; however secondary forms do exist from drugs, malignancy, infection, allergy, and other glomerular diseases. MCD has been rarely reported in systemic lupus erythematosus (SLE) patients, but can occur during a flare or after several years of disease activity. Currently, debate is ongoing as to whether MCD in SLE is epiphenomenal, is associated with the disease, or, even perhaps is a histological sub-class of lupus nephritis.

Case Description/Results: A 40-year-old African American female, with a history of SLE that manifested as arthritis with a photosensitive papular rash, mild anemia, slightly prolonged ESR, and low complements, initially presented with unexplained fever, nausea, vomiting, and abdominal pain. She was found to be in acute renal failure of unclear etiology associated with proteinuria. Spot protein/creatinine ratio predicted a urinary loss of 2.2 g/day. A comprehensive evaluation for infection was negative, except for a urine culture growing Klebsiella pneumoniae. She was asymptomatic, but nevertheless, she was treated with a 10-day course of ciprofloxacin. A contrast CT of the abdomen and pelvis showed small bowel wall thickening and mesenteric lymphadenopathy of unclear significance. Regarding her SLE, her serologic profile was notable for a positive ANA, anti-double-stranded (ds) DNA, anti-Smith, RNP and Ro/La antibodies, and elevated beta-2 glycoprotein I IgG. She had negative lupus anticoagulant and cardiolipin antibodies. The new-onset proteinuria and lack of clear infectious source for fevers prompted concern for lupus nephritis. Her oral prednisone was increased from 15mg to 30mg daily, and mycophenolate mofetil was initiated at 500mg daily. She clinically improved but was still febrile when she was discharged home. After a week, the patient was readmitted for continued fevers to 102.8F, nausea, vomiting with decreased oral intake, and loose stools. Her proteinuria had progressed to an estimated 12.6 g/day. She was started on pulse dose glucocorticoids and treated with empiric broad-spectrum antibiotics, and she defervesced. The source of the fever was ultimately thought to be from an infected gall bladder. A renal biopsy was performed. Light microscopy and direct immunofluorescence showed 4/30 glomeruli with segmental endocapillary proliferation (WHO Class III lupus nephritis). Vacuolization was prevalent. No crescents or necrosis were noted. Electron microscopy showed diffuse foot process effacement consistent with MCD. These findings supported the argument that the patient’s acute renal failure with worsening proteinuria was due to the combination of contrast-induced nephropathy (CIN) and MCD of unclear etiology, and less due to focal lupus nephritis.
Conclusions: MCD has been reported in association with SLE patients however whether MCD represents a true manifestation of SLE remains controversial. There is current debate as to whether lupus is a cause for MCD or whether MCD is a histological subclass of lupus nephritis. This case illustrates that not all instances of renal failure in SLE should be attributed to disease specific glomerulonephritis. Additionally, while fever may be seen as a manifestation of active SLE, infection, sometimes occult, must always be considered and ruled out.

Figure 1: Electron microscopy from renal biopsy displaying diffuse foot process effacement seen in MCD (blue arrows).

TITLE: A New Target for Anti-inflammatory Effect of Methotrexate - AMP activated protein kinase

PRESENTER: Cornelia D Cudrici

EMAIL: cudricicd@mail.nih.gov

Background and Purpose: Methotrexate (MTX) remains a first line therapy for treatment for rheumatoid arthritis and other rheumatic diseases. Although MTX has been used for a many years, the molecular mechanisms of its anti-inflammatory action are not completely understood. Through inhibiting AICAR transformylase, MTX increases the levels of AICAR (aminoimidazole-4-carboxamide ribonucleotide). AICAR is through to mediate its anti-inflammatory effects through elevating the concentration of adenosine, which can act through G-protein coupled receptors to reduce inflammatory responses. However, AICAR, also known as ZMP, can mimic AMP to activate AMP-activated protein kinase (AMPK), an important cellular energy sensor that is responsible for maintaining systemic and cellular energy balance. AMPK plays a pivotal role in metabolism, growth, inflammation and immunity. We hypothesize that AMPK activation may mediates a major portion of the anti-inflammatory effects of MTX, and that this may account for some of the the efficacy of MTX in rheumatic diseases.

Methods/Case Description: Human monocytes derived macrophages (MDM) and murine immortalized bone marrow-derived macrophages (iBMDM) were treated with MTX, AICAR and also with A769662 (a small-molecule which activates AMPK independently of AMP3) and AMPK phosphorylation and total AMPK was detected by Western blotting. We have also used compound C, a selective ATP-competitive inhibitor of AMPK in order to determine whether MTX exhibits anti-inflammatory through AMPK. We treated MDM and iBMDM with LPS for six hours following treatment with various concentration of MTX, AICAR and Compound C and detected production of pro-inflammatory cytokines in vitro.

Results/Case Discussion: Human monocytes derived macrophages (MDM) and murine immortalized bone marrow-derived macrophages (iBMDM) were treated with MTX, AICAR and also with A769662 (a small-molecule which activates AMPK independently of AMP3) and AMPK phosphorylation and total AMPK was detected by Western blotting. We have also used compound C, a selective ATP-competitive inhibitor of AMPK in order to determine whether MTX exhibits anti-inflammatory through AMPK. We treated MDM and iBMDM with LPS for six hours following treatment with various concentration of MTX, AICAR and Compound C and detected production of pro-inflammatory cytokines in vitro.

Conclusion/Significance: Our findings raise the possibility that some anti-inflammatory effects of MTX are mediated by AMPK. These results suggest that AMPK may be a target for the action of
current “antimetabolite” anti inflammatory agents and a target for the development of new anti-inflammatory drugs.
NAME: Angeliki Giannelou  DEGREE: MD  **

INSTITUTION: NIH/NIAMS

Fellowship/Resident/Student/Post Doc/PhD Year: PGY5

TITLE: TRNT1 missense mutations define a new periodic fever syndrome

PRESENTER: Angeliki Giannelou, MD

EMAIL: angeliki.giannelou@nih.gov

Background and Purpose:

Two thirds of the 1700 patients seen at our NIH clinic for autoinflammatory diseases do not have a genetic diagnosis. Whole exome sequencing permits analysis of most of the protein coding regions of the human genome.

Methods/Case Description:

Whole exome sequencing was performed in three unrelated families with four affected children with unexplained autoinflammatory disease, two of who died of their illness. When the sequencing was performed there was no clinical evidence that the children had the same disease. Subsequently, a fifth child was identified through candidate-gene sequencing. One family was from Saudi Arabia and had two affected daughters. The other children were of mixed European Ancestry.

Results/Case Discussion:

All of the patients had early onset disease with recurrent fever, severe microcytic anemia, gastrointestinal symptoms, and a spectrum of immunologic and neurologic manifestations. Sideroblastic anemia was confirmed by bone marrow biopsy in two of the children. B-cell deficiency was most prominent in the three sporadic European ancestry patients. Neurologic manifestations ranged from mild developmental delay to nystagmus, spasticity, optic nerve atrophy, and sensorineural hearing loss. After filtering for novel and rare variants (allele frequency <1:1000), and for the homozygous recessive inheritance in the Arab family, we observed that all four patients carried missense mutations in the same gene TRNT1 (TRNA Nucleotidyl Transferase, CCA-Adding, 1), on chromosome 3. The two affected Saudi Arabian sisters were homozygous for a p.H215R mutation, while the other two children were compound heterozygous for a missense mutation, p. I223T or p. R99W, and one shared mutation p.D163V. The p.H215R mutation was not found in any public database nor was it found in 1061 Arab control DNA samples. The three Caucasian mutations are either novel, or were found at a very
low allele frequency consistent with recessive inheritance. All mutations affect highly conserved amino acid residues and are predicted to be damaging to the protein function. TRNT1 enzyme catalyzes the addition of the CCA terminus to the 3-prime end of tRNA precursors. This is a critical step in tRNA biogenesis that generates the amino acid attachment site. Deficiency of this enzyme might result in mitochondria dysfunction and sideroblastic anemia. However, the molecular basis of inflammation in those children is unclear.

Conclusion/Significance:

Mutations in TRNT1 define a new autoinflammatory disease. Further studies to characterize the immune and inflammatory phenotypes both in peripheral blood and bone marrow cells are ongoing. Functional studies to demonstrate mitochondria stress and possible inflammasome activation are also in progress
TITLE: Spectrum and Activity of Anticytokine Autoantibodies in Rheumatologic Diseases

PRESENTER: Sarthak Gupta, MD **

EMAIL: sarthak.gupta@nih.gov

Background: Anticytokine autoantibodies are gaining increasing recognition as direct actors in disease pathogenesis. Despite the proclivity for autoantibody formation in rheumatologic diseases, including Rheumatoid Arthritis (RA), Sjogren’s Syndrome (SS) and Systemic Lupus Erythematosus (SLE), the prevalence and impact of anticytokine autoantibodies remain largely unknown.

Methods: Magnetic beads (Bio-Rad Laboratories) were amide coupled to recombinant human cytokines. Sera from patients with RA (n=100), SS (n=100), and SLE (n=199) were compared to healthy controls (n=179) for autoantibodies against 24 cytokines. Data were acquired on a Bio-Plex 100 instrument and analyzed using Prism (Treestar, v6.0). Values two standard deviations above the healthy controls were considered positive. To evaluate the biological activity of anticytokine autoantibodies, normal PBMC or cell lines were incubated in control or autoantibody-containing plasma (10%) and then stimulated with a cytokine of interest. The ability of the autoantibodies to block normal cytokine-induced signal transduction and protein expression was measured by assays using flow cytometric and luminex-based techniques.

Results: Fifty patients with RA, 36 with SS and 85 with SLE had anticytokine autoantibodies (Table 1). Those with RA had mostly anti-TNFα and anti-TNFβ antibodies, while SS patients had autoantibodies against GM-CSF, TNFβ, IFNγ, Interleukin (IL)-1α, and IL-12. SLE patients had antibodies against GM-CSF, M-CSF, interferons (IFNs) types I, II and III, IL-4, IL-12, IL-18 and IFNγ-induced Protein 10 (IP-10). Some antibodies against type I IFNs, IL-12 and IL-22 were blocking in a manner that appeared related to titer. Other anticytokine autoantibodies, such as those to IFNγ, were not neutralizing regardless of titer.

Conclusion: RA, SS and SLE had distinct spectra of anticytokine autoantibodies. Those in RA were mostly against TNFα and TNFβ and likely due to monoclonal biologics; SS patients had few autoantibodies to TNFs or type I IFNs; SLE were diffusely reactive. We confirmed autoantibodies against types I and II IFNs, GM-CSF, TNFα, TNFβ, IL-1α, IL-6, IL-10, IL-12 as previously described. However, antibodies to M-CSF, IL-7, IL-17 and IL-22 have not been previously identified in rheumatologic conditions. Anti-type III IFNs (IL-28A, IL-28B), anti-IL-4 and anti-IP-10 autoantibodies are newly recognized. Autoantibodies to Type I interferons have varying degrees of biologic activity, while autoantibodies to IFNγ were not blocking. These data confirm that functionally active anticytokine autoantibodies are an important presence in autoimmune diseases and extend
to more cytokines than previously appreciated. Further investigation of their significance may enhance our clinical and pathophysiologic understanding of rheumatologic disease.

Table 1

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* Blocking autoantibodies detected
Background and Purpose:

Cervical spine involvement is common in rheumatoid arthritis (RA) affecting up to 70% of patients, but is considered a feature of long-standing disease, usually occurring at least 10 years after diagnosis. Early recognition of RA is critical as potential neurologic complications may result if untreated. We report on two patients who presented with cervical symptoms as early manifestations of RA.

Methods/Case Description:

We first describe a 68 year-old woman with a reported history of cervical spondylosis who presented with persistent, non-radicular neck pain and stiffness. After a full evaluation, it was found that her rheumatoid factor (RF) was highly positive, and magnetic resonance imaging (MRI) demonstrated abnormalities consistent with RA including bone marrow edema, erosions, and pannus formation involving C1-C2. Ten months later, the patient developed peripheral synovitis. Our second case is an 82 year-old man with history of crystal-proven gout and cervical spondylosis who presented with symptoms of cervical radiculopathy. RF was highly positive with MRI synovitis in C1-C2, strongly suggesting a diagnosis of RA. These patients both reported significant improvement after the initiation of anti-TNF alpha therapy.

Results/Case Discussion:

We describe two patients with cervical arthritis presenting with unresolving neck pain without peripheral joint involvement who were found to have positive RF and classic MRI C1-C2 findings of RA. Based on the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for RA, our patients did not meet the criteria for a diagnosis of RA. However, given potential neurologic complications from atlanto-axial involvement, treatment for RA was initiated promptly with dramatic improvement in symptoms.
Conclusion/Significance:

Our cases demonstrate that it is critical for clinicians to recognize that RA could masquerade as cervical arthritis and unusual presentations of neck pain should trigger further radiographic and potentially serologic evaluation.

**Table or Figure**

Short T1 Interversion Recovery (STIR) saggital MR image. There is marrow edema in the anterior arch of C1 and at the base of the dens (arrow).
TITLE: Proof of Concept Study on Pharmacodynamics of Baricitinib (JAK 1/2 inhibitor) in CANDLE Patients

PRESENTER: Hanna Kim, MD (Pediatric Rheumatology Fellow) **

EMAIL: hkim@nih.gov

Background and Purpose: Inflammatory disease manifestations in chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome are hypothesized to be mediated through upregulation of interferon-regulated genes (IRGs). IRGs signal through Janus kinases (JAKs). Baricitinib, a JAK 1/2 inhibitor, blocks such signaling. Clinical improvement has been seen in CANDLE patients on baricitinib with significantly decreased steroid requirement and symptom diary scores. We assess IRG expression in CANDLE patients on baricitinib as a proof of concept.

Methods/Case Description: Ten CANDLE patients (1.8–24.7yo, 7 males) enrolled in the NIH compassionate use protocol for JAK 1/2 inhibition had pharmacokinetic (pK) and pharmacodynamic (PAX gene tubes) evaluation at baseline and scheduled timepoints (predose, 1 hour after dose, etc.) after reaching steady state at 2-11 mg/day of baricitinib. 89 interferon-regulated genes (IRGs), including previously highly upregulated genes in CANDLE, and 4 housekeeping genes, were analyzed from RNA extracted from PAX gene tubes using NanoString nCounter gene expression system (Seattle, WA). 3 pediatric and 1 adult healthy controls (HCs) were used for comparison. Z-score was calculated for each gene per patient-timepoint, further selecting against low variability genes to narrow to 31 genes. Box plots and trellis plots were created using Partek, version 6.6.

Results/Case Discussion: At baseline, 7 patients had higher IRG Z-scores (mean of medians 35.3, 22.6-58.7) and 3 patients had lower elevation of IRG Z-score (mean of medians 6.4, 3.0-10.7). After treatment in “higher IRGs group,” 3 had clinical response and showed decreased Z-score values and variability approaching that of HCs (ex:Figure 1A). 4 had continued clinical activity with increased variability with mild or no decrease in Z-score values. After treatment in “lower IRGs group,” 1 had lower values and variability of IRG Z score in dose-dependent fashion, correlating with clinical response (Figure 1B-C). 1 had close to normal values and variability without clear clinical response at 2 dose levels.* Another had unchanged Z-score and variability versus baseline and continues to be clinically active. IRG expression does not directly correlate with pK drug levels at specified timepoints.
Conclusion/Significance: In general, CANDLE patients with clinical response have decreased IRG expression Z scores values in a dose-dependent manner with less variability, and those without clinical response continue with elevated Z-scores and variability, regardless of baseline level. Further analysis is needed on specific relationship between pK drug level and IRG expression.

References
(1): Liu Y et al, Mutations in proteasome subunit beta type 8 cause chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature with evidence of genetic and phenotypic heterogeneity. *Arthritis and Rheumatism* 2012; 64(3):895-907

* Patient with multiple co-morbidities including IgA nephropathy and esophageal varices.
Figure 1: Each graph shows a patient baseline Z score on the left in blue, pK timepoints in the middle, and the healthy controls (HC) in green on the right, with increased Z score indicating increased IRG expression. Serum baricitinib levels at pK timepoints. A shows a patient with higher baseline Z score (higher IRG group) with suppression of IRG Z-score to HC range. B and C show a patient with lower baseline Z score (lower IRG group) at increasing baricitinib doses, with Z-scores decreased to HC range in C.
Demographics and Clinical Features of Patients with Adult and Juvenile Dermatomyositis, Polymyositis and Inclusion Body Myositis Participating in a National Myositis Patient Registry.

Abdullah Faiq MPH¹; Payam Noroozi Farhadi MD¹; Nastran Bayat MD¹; Lukasz Iert⁵; Mikaela Chase¹; Karen Malley²; Jesse Wilkerson³; Anne Johnson⁵; Kathryn M. Rose PhD³; Richard Morris PhD¹; Christine Parks PhD⁴; Edward Giannini DrPH⁵; Hermine Brunner MD⁵; Bob Goldberg⁶ Frederick Miller, MD PhD¹; Lisa G. Rider, MD¹

¹EAG, NIEHS, NIH; ²Malley Research Programming, Inc, Bethesda, MD; ³SRA International; ⁴Epidemiology Branch, NIEHS, NIH; ⁵Division of Pediatric Rheumatology, Children’s Hospital, Cincinnati; ⁶The Myositis Association

Abstract

Background: Myositis syndromes are rare systemic autoimmune diseases. Little is known about their epidemiology. We present the demographic and illness features of a newly established national myositis patient registry.

Methods: Between December 2010 and July 2012, 9211 questionnaires were mailed to patients with adult and juvenile dermatomyositis (DM, JDM), polymyositis (PM, JPM), inclusion body myositis (IBM) and other forms of myositis in the US and Canada. The questionnaire queried demographics, clinical features, environmental exposures, and quality of life.

Results: 2209 patients returned a questionnaire and consented to participate; 1806 patients meeting probable or definite Bohan and Peter criteria for myositis were included in analysis (708 DM, 483 PM, 466 IBM, 139 JDM, 10 JPM). IBM patients also met possible Griggs criteria. Patients had a median date of diagnosis of March 2002, and median disease duration of 9.2 yrs. IBM patients were older at diagnosis (median 62.3 yrs) than PM and DM (47.8 and 46.4 yrs); Most were female (84% DM, 75% PM, 78% JDM), except for IBM (41%, p<0.0001). The majority was non-Hispanic Caucasian (86% DM, 82% PM, 94% IBM, and 88% JDM); Blacks were more frequent among PM patients (12%) than DM (5%), IBM (3%), or JDM (0.7%). Patients were well-educated, with 22% completing a graduate degree and 28% a college degree. The majority of DM and PM patients were diagnosed by an adult rheumatologist (59% and 52%), whereas IBM patients were more often diagnosed by a neurologist (76%) and JDM patients by a pediatric rheumatologist (48%). DM and JDM frequently had skin rashes as a major clinical manifestation (85% vs. 14% PM, 6% IBM); DM most often had arthritis (49% vs. 34% PM, 21% IBM; p< 0.0001); DM and PM were more likely to have lung disease (31% each vs. 15% IBM, p < 0.0001), and DM most often had fever (23% vs. 17% PM, 5% IBM; p<0.008). An associated autoimmune disease was present in 25% of patients (30% DM, 32% PM, 11% IBM and 18% JDM, p<0.01). Most patients with DM, PM and JDM received prednisone therapy (96-98%), compared to 54% of IBM patients. Methotrexate was the most common steroid-sparing agent (63%), followed by
azathioprine (34%), IVIG (32%), hydroxychloroquine (29%), rituximab (13%), and anti-TNFα (10%).

**Significance:** A nationwide myositis patient registry has been established. This large myositis population appears to be representative of published reports and should be useful for understanding associated environmental factors and functional outcomes.
TITLE: Disseminated Coccidioidmycosis Presenting as Sarcoidosis

PRESENTER: Carol Deane Benedict Mitnick

EMAIL: deebenedict@gmail.com

Background and Purpose:
Extrapulmonary disseminated coccidioidomycosis including osseous and joint involvement is uncommon, as is bone involvement in sarcoidosis. The infrequency of these disorders and the fact that they are both great imitators can make the diagnosis very challenging.

Case Description:
33-year-old healthy female with history of Valley Fever three years prior to admission treated with oral fluconazole, presented with fatigue, shortness of breath, anemia, and right ankle pain. Six months previously she developed acute left lacrimal gland swelling that resolved with an empiric three-week course of prednisone 60 mg followed by taper. While on prednisone, she developed left ankle pain. She was referred to a rheumatologist, where she was found to have hilar predominance concerning for possible sarcoidosis on chest x-ray. CT of the chest revealed diffuse mediastinal and hilar lymph node enlargement and reticular interstitial marking in upper lobe. An endobronchial ultrasound biopsy (EBUS) of the hilar lymph node was recommended. In the interim, the patient’s left ankle pain improved. However, she then developed right ankle pain and swelling and two weeks later also had left knee pain with no swelling. She underwent a bronchoscopy and had a biopsy of the right hilar lymph node. Pathology of lymph node showed non-caseating granulomas consistent with sarcoidosis. Ten days after bronchoscopy, patient developed acute shortness of breath and was admitted to our hospital. The CT of chest revealed a moderate right plural effusion with near complete atelectasis of right lung and demineralization and possible periosteal reaction of right seventh rib. Prominent mediastinal and hilar lymph nodes and retroperitoneal lymph nodes in upper abdomen were also noted. She underwent a VATS procedure for lung biopsy and biopsy of the rib lesion. Fluid and tissue were sent for cytology, chemistries, and microbiology. Further evaluation of right ankle revealed a lytic lesion over the right medial malleolus on x-ray, and multifocal uptake was seen on bone scan throughout the axial and appendicular skeleton. Cultures from biopsy sites of right seventh rib, lytic lesion of the right ankle, and from fluid taken during VATS revealed *Coccidioides immitis*. Cultures of the hilar lymph nodes eventually also grew *Coccidioides immitis*. Treatment was initiated with fluconazole.

Significance:
This case illustrates how disseminated coccidioidmycosis can present in an immune competent person with physical, radiologic, and even histological features similar to that of sarcoidosis. Thus, the value of complete history and careful differential diagnosis is important when assessing such a patient.
TITLE: Central Retinal Artery Occlusion as an Initial Presentation of Eosinophilic Granulomatosis with Polyangiitis

PRESENTER: Dr. Thu Zar Myint

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Background and Purpose:
Central retinal artery occlusion (CRAO) is a very rare manifestation of Eosinophilic Granulomatous with Polyangiitis (EGPA) with only a few case reports in the literature. Early recognition and aggressive treatment is essential for good visual outcomes.

Methods/Case Description:
A 46 y/o AAF with a PMHx of asthma and allergic dermatitis was admitted for acute painless vision loss in the right eye for 1 day. She also described a right foot drop starting about two months prior. She denied any other symptoms at that time. On exam, she was found to have only minimal light perception with absence of light reflex in right eye with a “cherry red spot” in the center of the macula. Neurologic exam revealed right foot drop with decreased sensation.

Results/Case Discussion: Initial labs demonstrated marked eosinophilia with increased inflammatory markers and IgE levels. CT head/chest and MRA head/neck were unrevealing and hypercoagulability work was negative. Additional serologic studies revealed a positive ANA (1:320) and RF, however she was negative for C-ANCA, P-ANCA, PR3 and MPO. A preliminary diagnosis of EGPA was made and she was treated with IV pulse steroid, followed by daily oral cyclophosphamide and oral prednisone. A right sural nerve biopsy was performed and was consistent with a diagnosis of vasculitis. Her vision improved gradually as well as plantar flexion and sensation in the right foot. Additionally, her eosinophilia resolved.

Conclusion/Significance: While rare, CRAO can be the initial presentation of EGPA. Early recognition and aggressive treatment is essential for good visual outcomes.
### Table or Figure

**Table- Eosinophils level after treatment**

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</table>
TITLE: GPA (granulomatosis with polyangiitis) Presenting with Hemoptysis and Bilateral Deep Vein Thrombosis in Deployed Active Duty Male

PRESENTER: CPT Aaron Pumerantz, DO

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Case Description:

A 32 year-old active duty Caucasian male deployed to Afghanistan, with 9 month history of recurrent rhinitis and sinusitis, presents to an aid station with recurrent epistaxis. Symptoms rapidly progressed to sub-massive hemoptysis and bilateral lower extremity DVT (deep vein thrombosis). His left lower extremity DVT was so extensive, he developed compartment syndrome, and fasciotomies were performed.

Reviews of the patient’s past medical/surgical/family history were unremarkable. No toxin exposure, new medication, or sick contacts.

Eventual transfer to WRNMMC-Bethesda, at which time his exam was significant for macerated nasal mucosa, bilateral nasal crusting, and diffuses wheezing in lungs. Laboratory work-up was significant for positive c-ANCA high titer >1:640 (<1:20), and PR3-ab (proteinase 3 antibody) >8.0 (<1.0).

Pulmonary imaging revealed significant patchy opacities, coin lesions, and cavitations (Figure). Significant sinus disease with septal perforation, destruction was evident on CT sinuses. Left nasal tissue biopsy showed marked lymphoplasmacytic inflammation, occasional multinucleated giant cells, extensive squamous metaplasia with desquamated necrotic debris, and cartilage necrosis highly suggestive of GPA. Bronchoalveolar lavage revealed diffuse alveolar hemorrhage.

Diagnosis of GPA was made based on sinopulmonary disease (granulomatous inflammation, pulmonary cavitations), high titer PR3-ab, and strongly supportive tissue biopsy. Managed initially with pulse methylprednisolone, followed by high dose prednisone taper, along with initial course of 7 plasmapharesis treatments due to pulmonary end organ damage. He responded quickly to treatment, and induction was started with rituximab, followed by azathioprine. He will remain on anticoagulation with rivaroxaban.

Case Discussion:

GPA is an ANCA associated vasculitis, which presents with significant clinical complications. Well known to rheumatologists are the pulmonary, CNS, and renal end organ manifestations. We present a relatively straightforward case diagnostically, but
with a complication of VTE (venous thromboembolism), which caused significant comorbidities.

Increased risk of thrombosis has been well described in Behcets disease, Giant Cell Arteritis, along with other autoimmune disease states. Recently, several cohort and case reports have found significant increase in VTE at disease onset and during states of high disease activity, delineating VTE as an increasingly recognized feature of GPA.

**Case Significance:**

Our case highlights the need for vigilance in assessing GPA patients for VTE, and treating high disease activity as a potential independent risk factor for VTE.

Figure: coin lesions, cavitations, ground glass opacities, broncho-interstitial disease
TITLE: Spinal Fracture in a Patient with Coincident Ankylosing Spondylitis and Diffuse Idiopathic Skeletal Hyperostosis

PRESENTER: Seema Qaiyumi, MD

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Background and Purpose:

Patients with ankylosing spinal disorders including Ankylosing Spondylitis (AS) and Diffuse Idiopathic Skeletal Hyperostosis (DISH) have high rates of complications including non traumatic and traumatic fractures with risks of morbidity and mortality.

Methods/Case Description:

We describe a patient with coincident AS and DISH who presented after a fall with severe pain and was found by CT to have a Type I fracture of the thoracic spine. Successful surgical intervention was performed avoiding untoward neurologic sequelae.

Results/Case Discussion:

Coincident AS and DISH is more common than original thought. Patients with ankylosing spinal disorders have a propensity for more unstable fractures due to spinal rigidity and poor bone quality. There are four major types of fractures which are distinguished based on anatomical location. No difference in fracture characteristics have been reported between AS and DISH patients. However devastating neurologic sequelae are not uncommon in these diseases, particularly in cases of delayed fracture diagnosis. Treatment with posterior fixation alone is typically sufficient for healing and decreased mortality

Conclusion/Significance:

Urgent evaluation, recognition and treatment of spinal fractures in patients with ankylosing spinal disorders including AS and DISH is important to prevent significant morbidity and mortality.
Figure 1.
Title: An Unusual Case of Calciphylaxis, Mimicking Vasculitis

Authors: Leili Parsa MD, Christopher Collins MD

Introduction: Calciphylaxis, also called pseudo-vasculitis, is a rare and serious disorder characterized by systemic medial calcification of arterioles leading to ischemia and subcutaneous necrosis. Histology shows small vessel calcification, extravascular calcification and thrombotic vaso-occlusion. Calciphylaxis is most commonly seen in patients with end stage renal disease (ESRD) on hemodialysis and has a 55% mortality rate in the first year. Chronic inflammatory conditions like connective tissue disorders (CTD) are a potential risk factor for calciphylaxis.

Case: A 29 y/o AAM presented to the ER with progressive dyspnea and bilateral lower extremities (LE) pain with swelling and blister formation starting approximately 3 weeks prior. He was discovered to have acute renal failure (creatinine 18 mg/dL), new onset CHF (EF 35%) and anemia (Hgb 5.2 g/dL). Because of multi-organ involvement and the LE rash/ulcer formation, a work up for vasculitis was initiated. CTD labs were unremarkable including normal/negative ANCA/ANA/RF. Biopsy of ulcers was performed and revealed classic calciphylaxis without evidence of vasculitis.

Conclusion: Calciphylaxis is a rare condition with a very high mortality rate. The most common presentation is skin ulcers in the setting of ESRD. This case describes an unusual presentation of calciphylaxis in a patient with acute renal failure not previously on dialysis. An important differential diagnosis consideration is vasculitis. Physicians should be aware of this phenomenon because administration of steroid or other immunosuppressants is not indicated for this disease and indeed may worsen the patient’s condition.
TITLE: “Not Your Average Clot”

PRESENTER: Pragya Singh, MD

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Background and Purpose: (word count 103)

This is a presentation of a case involving a patient with recurrent clots, abdominal pain, and hydronephrosis with the final diagnosis as retroperitoneal fibrosis (RPF). RPF is a rare condition characterized by the presence of inflammatory and fibrous retroperitoneal tissue that often encases the ureters or abdominal organs. The diagnosis is often missed until there is significant organ, most commonly the kidney, involvement. This particular case raised suspicion of this diagnosis on the basis of recurrent clots.

Methods/Case Description: (word count 118)

61 year old African American female with history of diabetes, obesity, hypertension, hepatitis C, deep vein thrombosis on anticoagulation who presented with complaints of right flank pain. CT scan of the pelvis revealed bilateral hydronephrosis. A subsequent cystoscopy showed tortuosity of the ureter with dilation diffusely and right renal pelvis dilation but no obvious signs of obstruction or extravasation of contrast. Further review of the CT scan revealed a concern for a retroperitoneal mass and a mantle of soft tissue involving the iliac vessels extending into the pelvis anterior to the sacrum. The abdominal survey during the biopsy displayed a diffuse inflammatory desmoplastic reaction from the liver down to the pelvis, the biopsy unfortunately only revealed adipose tissue.

Results/Case Discussion: (52)

While there are no standardized diagnostic criteria for RPF, most diagnoses are based on clinical manifestations, imaging, and elevated inflammatory markers. The patient was treated with prednisone, 40 mg/d, tapered over 6 months, and mycophenolate mofetil, 1000 mg twice daily for 7 months. Within three months there was radiological evidence of improvement.

Conclusion/Significance: (45)

This case illustrates the potential of a rare disease to masquerade as a common process, thus delaying adequate treatment. RPF is a rare condition characterized by the presence of inflammatory and fibrous retroperitoneal tissue that often encases the ureters or abdominal organs, with obstructive uropathy.
Figure 1

Imaging
Rheumatism Society of the District of Columbia  
12th ANNUAL  
RHEUMATOLOGY FELLOWS FORUM  
May 10th, 2014

**TITLE:** Investigating Mechanisms of Neurovascular Injury in Systemic Lupus Erythematosus  

**PRESENTER:** CPT Brian J Stout, MD, MHA **  

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**Background and Purpose:**

The term Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) refers to Systemic Lupus Erythematosus (SLE) disease activity occurring within neurologic tissue. NPSLE is common in patients with SLE and may result in significant psychiatric and neurocognitive dysfunction. Pathophysiologic mechanisms of injury in NPSLE and their correlation with neurologic symptoms remain poorly defined. Specifically, more information is needed regarding autoantibody activity, complement activation patterns, S1P2 receptor utilization, and vascular barrier integrity alteration in neurologic tissue subject to inflammatory stress. The objective of this ongoing study is to further define and compare the pathophysiologic response to induced cerebral vascular injury in control and autoimmune SLE murine models.

**Methods/Case Description:**

Utilizing high intensity focused ultrasound (HIFU) in immune competent (C57Bl/6) murine strains (background for SLE/autoimmune (B6.MRL/lpr and MRL/lpr) murine strains) we investigate whether vascular damage results in inflammatory changes to the vascular barriers of the brain and alterations in neurocognitive function. We assess for complement activation, expression of auto-antibody reactive antigens, endothelium utilization of S1P1/2 receptors, and vascular leakage within specific vascular barriers. Histologic analysis of brain sections is performed to assess vascular integrity, as well as complement/IgG deposition and modulation/activation of the endothelium/epithelium at multiple sites of injury. Neurocognitive alterations associated with cerebral vascular damage are assessed by Open Field Analysis, Novel Object Recognition and Novel Location analysis.

**Results/Case Discussion:**

In the Wild-Type strain, HIFU injury results in the activation of the blood brain barrier (BBB) endothelium, increased BBB permeability to low molecular weight molecules, and deposition of complement C3b/IgG. Endothelium within the BBB shows increased expression of complement receptors and cell junction permeability regulators, to include S1P receptors. Time course studies in single-event injury subjects reveal rapid resolution of these markers of vascular injury. With multiple vascular injuries over time, however,
sustained neuro-inflammatory changes were evident 30 days after injury and correlate with neurocognitive deficit.

**Conclusion/Significance:**

These data suggest that, in the immune competent strain, similar pathophysiologic mechanisms are involved in both cerebrovascular and systemic vascular injury. Our findings also support the assertion that recurrent neuro-inflammatory responses from vascular injury correlate with long term neurocognitive dysfunction. Previous investigations have demonstrated an exaggerated inflammatory response to systemic vascular injury in the autoimmune strain. Our ongoing study investigates neuro-inflammatory responses in SLE strains and assesses for a similar exaggerated inflammatory response to injury in the cerebrovascular tissue.

**Table or Figure:**

S1P2 Expression at Neurovascular Branch Points

![Image](image_url)

**Title:** Granulomatosis with Polyangiitis with Valvulitis

Blue DAPI: Cell Nucleus, Red lectin: Vascular Endothelium, Green: S1P2, Yellow: co-staining
PRESENTATION: Janki Trivedi MD

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Background and Purpose:
Granulomatosis with polyangiitis (GPA) is a systemic necrotizing small vessel vasculitis characterized by granulomatous lesions involving the respiratory tract and kidneys. Cardiac manifestations including pericardial effusion, pericarditis and cardiac muscle and vessel involvement have been reported in the literature. Valvulitis is exceedingly rare with few reported cases. Our case outlines the clinical course of a patient with GPA and aortic valve involvement resulting in severe valvular dysfunction and morbidity.

Methods/Case Description:
49 year old Ethiopian male with a history of granulomatosis with polyangiitis (GPA) presented with a 2 week history of hemoptysis. Six months prior he had presented with acute kidney injury, found to have high titer PR3 (>8.0), a pulmonary nodule on CT chest and pauci-immune crescentic glomerulonephritis on renal biopsy. Findings were consistent with the diagnosis of ANCA positive vasculitis. The patient was treated with five days of pulse methylprednisone (1g IV daily) and cyclophosphamide (1000mg IV infusion) followed by oral prednisone and Rituximab 375mg/m2 weekly for total of four weeks. He was also placed on hemodialysis for renal failure. Two months after treatment, renal function improved and the patient was no longer dialysis dependent. Three months after treatment with Rituximab completed, the patient presented with two week history of hemoptysis.

Physical Exam:
Vital Signs:  T 36.3 C BP 147/71 HR 127 R 20 O2 95% on room air
General: African American male, coughing bright red sputum.
Respiratory: Bilateral diffuse rales.
Cardiac: Tachycardic no murmurs on exam. 1+ lower extremity pitting edema.
Skin: No rashes or vasculitic skin lesions.
Rest of the exam unremarkable.

Labs:
Creatinine 2.6 mg/dL (baseline was 2.6 mg/dL) BUN 90 mg/dL (9-20 mg/dL)
Albumin 2.8 g/dL (35.-5.0 g/dL), LFTs unremarkable.
Normal PT/PTT/INR.
UA 5 RBC, small blood, 100 protein, no WBC, 1 granular cast
WBC count 5.1, H&H 7.7/24.6 MCV 94 Platelet count 191
C3 134 mg/dL C4 71.7 mg/dL
ESR 35 MM/hr (0-16 MM/hr), CRP 13.6 mg/L (0-3.0 mg/L)
c-ANCA, p-ANCA both negative
PR3: 1.5 U (normal < 1.0) MPO (previously negative)
CD 19+ cells: 0%

Bronchoscopy confirmed diffuse alveolar hemorrhage. He was also found to have active urinary sediment with acute on chronic kidney injury and volume overload requiring dialysis.

Patient was treated with five days of pulse methylprednisone (1g IV daily) followed by oral prednisone.

Hospital course complicated by findings of severe aortic valve thickening with a moderate sized vegetation or mass on the aortic valve (Fig. 2 & 3) with moderate to severe aortic regurgitation on trans-thoracic echocardiogram. Moderate thickening anterior mitral leaflet, which could not be ruled out as a vegetation. Mild mitral regurgitation
Infectious workup for endocarditis was unrevealing. The source of the vegetations was thought to be related to valvulitis.

Recommendation was made to start low dose daily cyclophosphamide but the patient was concerned about the potential side effects and declined. He was given a second course of Rituximab weekly for four weeks. The patient presented with symptoms of decompensated congestive heart failure. Repeat trans-thoracic echocardiogram revealed persistence of vegetations and severe aortic insufficiency. Cardiology recommended follow up with cardiothoracic surgery. Patient failed to follow up and he declined surgical intervention.

He continues to have severe pedal edema, orthopnea, and dyspnea but refuses medical intervention.

Results/Case Discussion:
- The findings of valvulitis in patients with granulomatosis with polyangiitis are rare.
- Only about half of patients will have valvular involvement when the diagnosis of granulomatosis with polyangiitis is made.
- Many patients develop valvular lesions despite ongoing immunosuppressive therapy, as in our patient’s case.
- Aortic regurgitation is the most commonly encountered valvular disorder.
- Patients with valve involvement tend to be male and younger in age.
- Histopathology varies, from degenerative myxomatous and mucoid changes to mixed inflammatory infiltrate with granulomatous inflammation.
- A study by Oliveria et al. found a mortality rate of 46% (12/26) in patients with echocardiographic lesions attributed to the disease.
No treatment guidelines have been proposed for these cases. Many cases involving the valves require valvular replacement.

**Conclusion/Significance:**
Although no routine screening guidelines are available, it is important to recognize the cardiac manifestations of granulomatosis with polyangiitis and appropriately screen patients for cardiac involvement when necessary.

Fig 2: Arrow pointing to vegetation in the aortic valve in our patient.