The Rheumatism Society of the District of Columbia

Presents...

The 13\textsuperscript{th} Annual Rheumatology Fellows Forum

Saturday, May 16\textsuperscript{th}, 2015

MedStar Washington Hospital Center
True Auditorium
Washington, DC
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10:00-11:00 AM  Podium Presentations
11:00-noon  Keynote Speaker – Brian Walitt MD, MPH, Director of Clinical Pain Research, National Center for Complementary and Alternative Medicine at the NIH

"Lost In Translation: The Science of Fibromyalgia"
Award Winners

Podium Presentations

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- Hanna Kim / CNMC / Validation of a Novel Interferon (IFN)-Regulated Gene (IRG) Score As Biomarker in Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature (CANDLE) Patients on Baricitinib, a Janus Kinase Inhibitor, a Proof of Concept (page 21)

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- Shawn Abraham / GUH / Autologous Fat Grafting for Refractory Digital Ulcerations (page 6)

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- Payam Noroozi Farhadi / NEIHS/ Predictors of Myositis Treatments Received and Associated Treatment Responses in MYOVISION, a National Myositis Patient Registry (page 18)

- Lindsay Holtz / VCU / Can we call it DISH? (page 19)
Title: Autologous Fat Grafting for Refractory Digital Ulcerations

Presenter: Shawn Abraham, MD - Georgetown University Medical Center

Background and Purpose: Autologous fat grafting is a relatively novel procedure used to treat refractory digital ulcers. It has been shown to be effective in scleroderma patients who have failed more traditional measures. We present the case of a patient with digital ulcers refractory to several pharmacologic and surgical interventions who sustained significant improvements in pain and hand function after autologous fat grafting.

Case Description: A 52 year old female with centromere Ab positive limited scleroderma with features including sclerodactyly, esophageal dysmotility, gastroesophageal reflux and severe Raynaud’s presented for management of her digital ulcerations.

Left upper extremity arteriogram in 2005 showed fixed occlusive changes involving the digital vessels of the left hand and distal occlusion of the left ulnar artery. She underwent bilateral digital sympathectomies with distal vascular bypass in 2005 followed by partial amputation of left index finger in 2006. Despite this she continued to have recurrent digital ulcers. Treatment modalities used in her care included calcium channel blockers, phosphodiesterase inhibitors and IV epoprostenol; all with limited efficacy. Underwent palmar botulinum toxin A injections which were ineffective in 2013. In 2014, she underwent a successful sympathectomy of the left common digital vessels for her left 2nd digit ulceration. This was followed by autologous fat grafting into her bilateral hands. During the procedure, an autologous fat harvest was procured from the abdomen via liposuction. The fat was then separated from lipoaspirate via a mesh/Telfa technique. The purified fat that remained was transferred into syringes for insertion into the hands. Small incisions in the interdigital web spaces were created followed by injection of fat in 3 mL aliquots into the interdigital web space superficial to the extensor tendons on the dorsal aspect and superficial to the superficial palmar arch on the volar aspect of the palm. In total, 30 ml of fat was injected into both the right and left hand. Following this, sterile dressings were applied to both hands.

Case Discussion: The proposed mechanism of action of Autologous fat grafting is that the fat graft includes adipose-derived stem cells, which secrete a favorable cytokine profile that promotes neovascularization. These cytokines include upregulation of antifibrotic factors such as interferon gamma and matrix metalloproteinases while downregulating pro-fibrotic factors such as transforming growth factor beta; providing a milieu in which these ulcers can potentially heal. In 3 month follow-up, the patient’s ulcer had healed. She was noted to have significant improvements in hand function, noting less tightness in the palms and improved ROM in the MCPs and PIPs bilaterally.

Conclusions/Significance: Digital ulcers are painful and lead to significant morbidity and altered hand function in scleroderma patients. Autologous fat grafting is a new technique being employed in patients with refractory ulcers when pharmacologic modalities alone are ineffective. The relative ease in procurement of these samples and early reports of improved wound healing make this modality one that is gaining more interest.
TITLE: Clinically Amyopathic Dermatomyositis with Rapidly Progressive Interstitial Lung Disease

Presenter: Asha Mariam Alex, MD – Georgetown University Medical Center

Background: Clinically amyopathic dermatomyositis (CADM) is a subset of dermatomyositis (DM) that manifests as skin limited disease and extra-muscular manifestations such as malignancy or rapidly progressive interstitial lung disease (ILD)

Case Description: We describe two cases of CADM and outline their clinical course.

The first is a 63 year old woman who presented with an erythematous rash on her forehead and elbows, painful palmar rash, joint pains and progressive dyspnea of 6 weeks duration. Examination revealed erythema over her forehead, Gottron's sign, tachypnea and bibasilar crackles. No proximal muscle weakness was noted. Laboratory evaluation revealed a normal CK but elevated aldolase, negative ANA and myositis panel. CT chest and lung biopsy were consistent with interstitial lung disease. She was treated with 3 days of IV steroids, unfortunately her condition deteriorated rapidly and she passed away on day 7 of hospitalization. Autopsy conducted revealed no malignancy and the examined muscle was normal.

The 2nd patient is a 47 year-old lady with 6 months of polyarthritis and 3 months of cough and dyspnea on exertion. On exam she had synovitis, tender palmar papules, skin ulceration and no muscle weakness. Labs revealed normal CK, elevated aldolase, negative ANA and myositis panel. Malignancy workup was negative. CT chest revealed ILD that had progressed on subsequent imaging and she also developed spontaneous pneumomediastinum. Biopsy of her palmar rash was consistent with dermatomyositis. She is currently being treated with methylprednisolone and mycophenolate.

Both patients were strongly positive for anti-MDA5 antibody. TIF-1 gamma testing was negative.

Discussion: We describe two patients with a characteristic phenotype of skin rash with progressive ILD. Both patients had biochemical signals of myositis without weakness. CADM is a diagnostic challenge because of the lack of traditional muscle findings. Laboratory data are significant for normal or mildly elevated CK but a typically elevated aldolase level. There is a strong association with a positive MDA5 (Melanoma differentiation-associated gene 5) antibody, as noted in our patients. CT of the chest reveals interstitial fibrosis and/or alveolitis which is the main cause of morbidity and mortality in the described cohorts of patients with CADM. Treatment for these patients is largely based on case reports with poor response to traditional immunosuppression including aggressive combination therapies.

Conclusion: CADM is a distinct subtype of dermatomyositis that presents with a characteristic skin rash in the absence of significant muscle weakness and is often associated with progressive ILD and MDA-5 antibody positivity.
**Fig. 1 (A-E):**
(A) Erythematous forehead rash, (B) Erythematous scaly rash on bilateral elbows, (C) Painful palmar papules, (D) CT chest with ILD, (E) Lung biopsy with patchy interstitial fibrosis

**Fig. 2 (F-I):**
(F) Palmar papules with ulceration, (G) CT chest with ILD and pneumonic infiltrate, (H) Skin biopsy with lymphocytic infiltrate and (I) mucin deposition
TITLE: An Unusual Hemorrhagic Basal Ganglia Stroke: Bringing Genomics to the Bedside

Presenter: Dareen Almanabri, MD – George Washington University

Background: Polyarteritis nodosa (PAN) is a multisystem condition characterized by necrotizing inflammation of small and medium-sized arteries with predilection for cutaneous, mesenteric and vasoneuronal arteries. PAN does not commonly involve the brain vasculature.

Case Description: A 39-year-old man of Middle Eastern descent presented with loss of consciousness and right-sided hemiplegia. Initial brain CT revealed a massive left sided basal ganglia hemorrhage. He had previously been diagnosed with PAN based on visceral angiogram and was on maintenance immunosuppression with low dose prednisone and mycophenolate mofetil. His brother had died from an intracranial hemorrhage aged 14.

Hemorrhagic strokes are not a common feature of vasculitides. In North American and European populations, 15% of strokes are due to intracerebral hemorrhage and basal ganglia hemorrhagic strokes are often associated with hypertension. After excluding hypertension, vascular malformations, and bleeding disorders, we elected to test this patient for mutations impacting adenosine deaminase-2 pathways.

Loss-of-function mutations in CECR1 (cat eye syndrome chromosome region, candidate 1), which encodes adenosine deaminase 2 (ADA2) have recently been shown to be associated with familial cases of PAN. ADA2 is the major extracellular adenosine deaminase and an adenosine deaminase-related growth factor. ADA2 deficiency results in chronic vascular inflammation without immune deficiency and clinical manifestations of ADA2 deficiency reflect impairment of both catalytic and growth-factor activities.

Results: The patient was enrolled in NIH protocol 94-HG-0105. Using Sanger sequencing a homozygous mutation p.Gly383Ser was identified in exon 8 in CECR1. Analysis using Polymorphism Phenotyping v2 software demonstrates that this mutation alters a highly conserved amino acid adjacent to the active ADA2 protein proton acceptor site at amino acid His384. It is believed that this mutation disrupts the active site impacting function of ADA2.

Conclusion: There is growing evidence that mutations in the CECR1 gene result in ADA2 deficiency, thus contributing to familial cases of PAN. This case is a bedside-to-bench example of genomics not only enlightening disease pathogenesis but also impacting treatment. Identification of the ADA2 mutation dramatically altered management since TNF-α blockade, rather than traditional DMARDs, is the recommend treatment for CECR1 mutation associated vasculitis.
REFERENCES:
**TITLE:** Critical Mass - A Severe Presentation of Crowned-Dens Syndrome

**Presenter:** Melissa S. Butts, D.O. - Walter Reed National Military Medical Center

**Introduction:** Crowned dens syndrome is a rare manifestation of calcium pyrophosphate dihydrate (CPPD) crystal deposition at the cervical spine. Radiographically, this deposition appears as a radiopaque density on the superior or lateral aspects of the odontoid (a.k.a. the dens), hence forming a crown or halo. When crystal deposition occurs at the cervicoaxial joint, often accompanied by calcification of nearby cervical ligaments, severe neck pain and limitation of range of motion can occur. In severe cases, where crystal deposition occurs in the ligamentum flavum or compresses on the spinal cord, cervical myelopathy can result.

**Case Description:** We present the case of a 70 year-old woman who presented to the emergency department after sudden onset of generalized weakness resulting in a fall. She reported no associated head trauma. Prior to her presentation she was fully functional, performing all her own activities of daily living (ADLs). She had significant motor weakness in her bilateral upper and lower extremities, most severe in the left upper extremity. Cranial nerves 2-12 and sensation were intact. She had up going Babinski’s bilaterally. Initial CT of the head revealed an infarct in the left occipital lobe. MRI of the head and neck again showed posterior infarcts, as well as a large mass located in the C1-C2 region with associated cervicomedullary and vertebral artery mass effect. Dedicated CT of the cervical spine, revealed a calcified mass about the C1-C2 articulation with erosion, as well as fracture of the odontoid process base.

Labs consisted of an elevated C-reactive protein and erythrocyte sedimentation rate, as well as a leukocytosis and normal creatinine, LFTs, rheumatoid factor and cyclic citrullated peptide antibody. Bilateral knee and hand/wrist radiographs showed no chondrocalcinosis. During the patient’s hospital course her neurologic exam continued to worsen resulting in quadriplegia. Additional neuroimaging revealed several new infarcts in the distribution of the posterior circulation as well as mild hemorrhagic conversion of her left occipital lobe lesion. All anticoagulant agents were held and high dose steroid therapy was begun with no improvement in the patient’s motor weakness. CT guided trans-oral biopsy of the C1-C2 mass was performed by interventional radiology and tissue pathology showed reactive tissue pathologically without CPPD, hydroxyapatite or monosodium urate crystals, but there were features consistent with a healing fracture of the odontoid, which can commonly be associated with CPPD. Tissue cultures for bacterial and fungal organisms were negative. There was no evidence of a neoplastic process by radiograph or tissue pathology. Due to the high risk associated with spinal decompression, and lack of improvement with high dose corticosteroid therapy, the patient opted for comfort care measures and was discharged to home hospice.

**Discussion/Conclusions:** Crowned dens syndrome is a rare phenomenon associated with CPPD and can often be misdiagnosed as an epidural abscess, meningitis, a rheumatoid pannus, or a spinal tumor. The gold standard for diagnostic imaging is CT of the cervical spine at C1-C2. This patient’s cervical CT showed
erosion through the base of the odontoid process, which can be precipitated by calcification at C1-C2 in CPPD arthropathy, as was seen in this patient. This case demonstrates the importance of suspicion for CPPD arthropathy, even in patients such as this with no history of pseudogout or no radiographic evidence of chondrocalcinosis at alternative sites. Once patients develop neurological sequela, therapy is limited to surgical decompression, or as in this case may be catastrophic.
Title: Characterization of Epitopes Identified With Cerebral Vasculature Injury

Presenter: Melissa S. Butts, D.O. - Walter Reed National Military Medical Center

Objectives: Neuropsychiatric Systemic Lupus Erythematous (NPSLE) may be present in up to 70% of SLE patients and the proportion of these patients with cerebral vascular injury nears 30%. Cerebral vascular involvement may be an indicator of progressive systemic disease. Although there is a correlation of NPSLE with some antibodies, a well-delineated mechanism of how antibody induced cerebral damage occurs has not been defined. Current literature has associated pathogenic natural antibodies with ischemic stroke vascular injury. These natural antibodies are also associated with systemic ischemic vascular injury in murine models of SLE. The objective of this study is to determine if the chronic hyper-inflammatory microenvironment within the BBB established by repeated high intensity focused ultrasound (HIFU) induced vascular injury increases the risk of complement/antibody mediated vascular damage. Specifically, we delineated the exposure of neoepitopes associated with ischemic/reperfusion type vascular injury in a time course study.

Methods: Multiple HIFU exposure was used to induce cerebral vascular injury within the BBB in a longitudinal study. Briefly, the animals were anesthetized with 5% Isoflurane and the scalp region was cleared of fur using Nair. Animals assigned to the HIFU-exposure (3 exposures 24 hours apart) experienced a one-millisecond pulse while sham animals did not, animals were harvested at a series of time points 2 hours to 30 days post injury. Immunocytochemistry and Immunofluorescence analysis and of brain slices were performed to assess vascular integrity and injury, as well as complement deposition, and modulation/activation of the endothelium. RESULTS: In the immune competent (C57Bl/6) strain HIFU injury resulted in the activation of the endothelium of the blood brain barrier (BBB), increased permeability of the BBB to low molecular weight molecules, and deposition of complement C3b, all of which support disruption of endothelial integrity. In longitudinal studies with multiple vascular injuries over time, a sustained neuro-inflammation was evident 30 days after injury and correlated with neuro-cognitive deficits. Initial data has demonstrated increased Ig deposition on the luminal surface of the BBB endothelium immediately after injury and at 30 days post injury. At the 30 day post injury time point there is an increased susceptibility to vascular injury as evidenced by Ferritin deposits within the Virchow-Robin space within the BBB structural unit, specifically in the hippocampus. Anti-phospholipid antibodies bound vascular endothelium at the 30 day time point more efficiently than other pathogenic natural antibodies detecting epitopes such as annexin IV. Work is ongoing to delineate if there is a correlation between the increased vascular weakness at the 30 day time point and increased binding of the pathogenic antibodies.

Conclusions: Preliminary data suggest that anti-phospholipid type natural antibodies have a stronger association with vascular damage at the 30 day time point than other pathogenic type antibodies. We are currently assessing if the anti-phospholipid antibodies are co-localized with C3b and ferritin breaches at specific location along the endothelium. Elucidation of these pathophysiologic mechanisms may prove useful in guiding development of future targeted therapies for NPSLE.
Figure 1: Increased Antibody binding to Phospholipid Epitopes in Hippocampus 30 days post multiple exposure High Frequency Focused Ultrasound (mHIFU) animals. (A&B) At 2 hr. and 30 days post exposure in sham treated animals minimal IgG (white) is detected at the vascular endothelium surface (CD31: green), while phospholipid epitopes (anti-phospholipid: Red) are associated with the blood brain barrier vascular unit it is not associated with antibody binding. (C&D) In animals exposed to multiple HIFU injuries, at the early time point (C), IgG (white) is detected at the luminal surface of the endothelium (CD31: green) with limited association with phospholipid epitopes (Red). By 30 days post mHIFU exposure (D) IgG (white) is strongly associated with Phospholipid epitopes (Red) within the blood brain barrier vascular unit.
TITLE: Identifying the Investment Needed to Generate a Durable Prednisone Dose Decrement

Presenter: Martha Delgado, MD – NIAMS

Background and Purpose: Assessment of the total cost of care requires a model that is based upon clinical, epidemiological, patient-centered, and economic data. Barriers to a value-driven outcome assessment such as this include the resource-intensive nature of activity-based costing. One aspect of the total cost of care is direct (drug) costs. Government-based outpatient, nonprocedural health care delivery enables an analysis that controls for all direct costs apart from medication costs. We aim to understand one aspect of the direct cost of care upon a given index decision (steroid decrement).

Methods: We reversed the Branching Decision Tree for identification of expenses attributable to clinical care by restricting our assessment to a given successful outcome of care (steroid reduction) and then looking back. This requires analyzing direct costs over the preceding 10 weeks to the incident date as the basis for allocating identified direct care costs to given encounters. The ten-week look back timeframe is chosen because it is the average time between outpatient clinic appointments where the majority of medical decision-making occurs. Captured data included diagnosis, current and new prednisone dose, other rheumatology medications prescribed over the preceding ten weeks and outcome of each prednisone taper. All consecutive patients seen over a 6-month period at the CHC who are tapering their prednisone dose were included in this study.

Results: Direct costs invested over a ten-week period for all patients undertaking a prednisone taper were $1659 (Table 1), which normalizes to $421/4mg decrement (Table 1). A greater normalized cost was invested per patient for rheumatoid arthritis as compared to systemic lupus erythematosus and as compared to other autoimmune diseases. We are in the process of collecting outcome data for each prednisone taper.

Conclusion: This study asks the question, what are the direct (drug) costs leading up to the outcome of care for patients? The disadvantage of this study is that indirect costs, and social costs are not analyzed. Moreover, direct costs alone underestimate the total cost of an illness. The advantage of this study is that reimbursement, coverage levels, and access to care are controlled for because our protocol-based health care delivery model renders this a unique opportunity to assess relatively pure direct costs. Our analysis demonstrates that outpatient drug costs for rheumatoid arthritis are those costs most fruitful to target when looking to contain direct health care costs.

<table>
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<th>Category</th>
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TITLE: Methotrexate-Associated Epstein Barr Virus “Hodgkins-Like” Lymphoma in a Patient with Dermatomyositis

Presenter: Ayyappa Duba – HUH

Background: Methotrexate (MTX) is an effective immunosuppressive agent commonly used in treatment of many rheumatic disorders. Recently, it has been implicated with various forms of iatrogenic Lymphoproliferative disorders (LPDs), and in most instances, in association with Rheumatoid arthritis. Although MTX is associated with many histological forms of LPDs, a subset, Hodgkins “like” lymphoma is rarely described. The present case, to our knowledge, is the first report of MTX-associated Epstein Barr Virus (EBV) positive LPD with Hodgkins “like” lesions in an African American male treated for Dermatomyosistis (DM).

Case Report: A 66 year old male presented with proximal muscle weakness, periorbital violaceous rash and extensive macular rash on the upper back. An elevated creatinine phosphokinase of 6000 md/dl and a muscle biopsy were consistent with idiopathic inflammatory myositis. A definitive diagnosis of DM was made after age appropriate screening excluded any malignancy. Following an initial response to oral prednisone with tapering to discontinuation, and weekly MTX he presented several months later with generalized fatigue, malaise, significant weight loss and was found to have supraclavicular, submandibular and axillary lymphadenopathy with an Erythocyte sedimentation rate of 104 mm/hr and a normal lactate dehydrogenase. MTX was discontinued and a mediastinal lymph node biopsy was obtained. Histopathology showed atypical lymphoid proliferation with Reed-Sternberg (HRS) cells. On immunohistochemistry, the HRS cells were CD 30 and EBV-positive, but lacked expression of CD 15, with a background of CD 20 and CD 3 positivity. These findings were consistent with a very rarely described form of Hodgkin “like” LPD associated with MTX. Chemotherapy and radiation were initiated, with tumor regression and resolution of symptoms.

Discussion: The diagnosis of this rare iatrogenic LPD can be challenging, particularly when treatment for the rheumatologic disorder itself poses an increased risk for malignancy. Phenotyping with immunohistochemistry plays a key role in identifying the subsets of MTX-LPDs and help differentiate classical Hodgkin lymphoma (CHL) from Hodgkin “like” LPD. Unlike patients with CHL who are CD30 (+), CD20 (-), CD15 (+) and EBV (-) on immunophenotyping, Hodgkin “like” LPDs although also CD30 (+), are CD20 (+), CD15 (-) and EBV (+) as in our patient.

Conclusion: In MTX-associated EBV positive LPDs, the lack of expression of CD15 in CD 30 positive HRS “like” cells is considered a feature that is not diagnostic of Hodgkins lymphoma. The distinction is important as MTX withdrawal alone may be definitive therapy, and survival ratios differ from CHL and other LPD.
Figure 1

Mediastinal Lymph node pathology
Mediastinal Lymph node pathology

Title: Predictors of Myositis Treatments Received and Associated Treatment Responses in MYOVISION, a National Myositis Patient Registry

Presenter: Payam Noroozi Farhadi, MD - NEIHS

Background and Purpose: Little is known about medications received for myositis and patients’ responses. We present information on self-reported myositis therapy use and responses from a national patient registry.

Methods: MYOVISION consists of 1796 patients who met probable or definite Bohan and Peter criteria for myositis (708 DM, 483 PM, 466 IBM, 139 JDM) with a median diagnosis date of March 2002. Enrolled patients were queried about myositis treatments received and effectiveness. Logistic regression modeling, using backwards elimination, was used to determine demographic and clinical covariates; a significance level of <0.1 was required to retain variables.

Results: Most DM, PM and JDM patients reported receiving Prednisone (96-98%) and Methotrexate (70-84%); these treatments were reported less commonly in IBM patients (54%, and 28%, p< 0.0001). Use of Azathioprine (41%, 47%) and Rituximab (14%, 16%) were reported more frequently in DM and PM, in contrast to IBM and JDM (11%, 15%, P <0.012 and 9%, 10% P<0.007). JDM patients reported receiving Hydroxychloroquine (60%), IV-Methylprednisolone (54%), IVIG (48%), and cyclosporine (19%) more frequently than other subgroups (2-10% p<0.021 for all). Overall, Rituximab was the most common biologic therapy (13%), and anti-TNFs were received by 10% of patients. Factors associated with Methotrexate treatment among DM, PM and IBM patients included younger age, geographic region, absence of lung disease, and rheumatologist as treating physician (p = 0.022 - < 0.0001). Younger age, SES, and being treated by a neurologist were factors associated with receiving IVIG in DM and PM, and presence of dysphagia, fever, and lung disease were additional factors for DM.

Overall, prednisone was reported to be the most helpful medication (39%, p<0.007), followed by IVIG (35%, p<0.005). Mycophenolate mofetil (31%) and Rituximab (24%, p<0.029). 17% of patients did not find any treatments helpful, and 46% of these had IBM. Absence of dysphagia in DM, presence of fever in IBM, and fewer myositis therapies were factors associated with a response to prednisone in DM, PM and JDM. Absence of an overlapping autoimmune disease in PM (OR 0.35) and fewer myositis therapies in DM (OR 0.67) were factors associated with response to IVIG. IBM patients reported physical therapy as the most effective treatment (38%). Older age (OR 1.03), overlapping autoimmune diseases (OR 2.58), absence of fever (OR 0.13), presence of lung disease (OR 2.06) and receipt of fewer myositis therapies (OR 0.48) predicted a positive response to physical therapy in IBM.

Conclusion: Prednisone and MTX are the most frequently prescribed medications in DM, PM, IBM and JDM. Patients vary in their assessment of the effectiveness of these medicines. Demographic, clinical factors and the specialty of the treating physician appear to influence which myositis therapies are received by patients and the perception of their effectiveness. Prospective registries of inception cohorts may aid in identifying effective therapies in rare disorders.
Title: Can We Call It DISH?

Presenter: Lindsay Holtz, MD – Virginia Commonwealth University

Background: We report on a 51 year-old male presenting with severe back and shoulder pain and stiffness that have progressed significantly over three years.

Case Description: The patient previously worked as an electric company technician and first noted back and shoulder pain about ten years ago. He attributed these symptoms to the physical demands of his job and also had a left shoulder arthroplasty to treat osteoarthritis. He felt a slight improvement in his range of motion (ROM) immediately after the surgery, but then quickly developed worsening stiffness and lost nearly all ROM of that shoulder. Over the past three years, he has developed a significant decrease in spinal and bilateral shoulder ROM and back, hip, and shoulder pain. Activity does not improve his pain or stiffness. He has not noticed synovitis or rashes and denies ocular symptoms. He has been taking Acitretin for the past twenty years to treat Ichthyosis and has not been able to taper this medication.

His exam is notable for extremely limited right shoulder ROM, mildly limited left shoulder ROM, hip internal external rotation of five degrees in each plane, and his spine is flexed forward at five degrees and lacks any ROM. His cervical ROM is limited to five degrees of flexion and extension and ten degrees of rotation. He has normal ROM and no tenderness or synovitis of his other joints. His skin is smooth and erythematous which is related to Ichthyosis. His X rays are shown in Figure 1:

Results/Case Discussion: If we just look at the AP view of his spine, we see a “Bamboo Spine” characterized by the ossification of the outer fibers of the intervertebral discs resulting in syndesmophytes, which is suggestive of a spondyloarthropathy. However, if we look at the other X-rays, another diagnosis becomes much more likely. Looking at the SI joints and pelvis, we see ossification of the Rectus Femoris entheses and lack of true joint fusions. We also see sclerosis at the proximal portion of SI joints, which is the ligamentous portion, and the distal portion, which is the synovial portion, is spared. The enthesophytes and lack of joint fusions are much more suggestive of Diffuse Idiopathic Hyperostosis (DISH).

Conclusion/Significance: DISH is characterized by ossification of ligaments and entheses which most often affect the axial skeleton, but can also affect the peripheral skeleton. The important distinguishing features in this case are the lack of distal SI joint fusions where synovium is located(1) and ossification of the ends of joints but not true fusion of the entire joint.

The pathogenesis of DISH is not well understood. There is a definite association between insulin resistance and use of Isoretinoin with development of DISH. It has been discovered that insulin stimulates osteoblast activity by binding directly to osteoblasts and stimulating differentiation through the MAP Kinase pathway which results in increased bone formation; however, further details of this pathway still need to be elucidated(2). The pathogenesis by which hypervitaminosis A causes hyperostosis is not known. Our patient in this case had tried several times to taper off of Acitretin, but was not able to maintain control of
Ichthyosis, so he remains on the medication. We have referred the patient to physical therapy, working on pain control, and are considering a trial of bisphosphonates. Bisphosphonates have not been well studied in DISH or known to help prevent progression of DISH; however, they are relatively low risk and could potentially help slow progression of this patient’s disease.

**Figure 1:**

- **AP view of lumbar spine** - This shows a “Bamboo Spine” characterized by ossification of the outer disc fibers which cause the vertebra to fuse. Arrow pointing to ossification.

- **Sacroiliac Film showing ossification of the Iliolumbar ligaments.**

- **CT Abdomen** - The SI joints are fused by bridging calcifications at the end of the joint (which is characteristic of DISH), not across the entire joint (which is characteristic of a spondyloarthropathy.)
Title: Validation of a Novel Interferon (IFN)-Regulated Gene (IRG) Score As Biomarker in Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature (CANDLE) Patients on Baricitinib, a Janus Kinase Inhibitor, a Proof of Concept

Presenter: Hanna Kim, MD – Children’s National Medical Center

Background and Purpose: CANDLE syndrome is a novel autoinflammatory disease with strong IFN signature. We hypothesize that IFN dysregulation may drive CANDLE clinical manifestations. Treatment with baricitinib, a janus kinase (JAK) inhibitor reduces the IRG signature. Clinical improvement has been seen in CANDLE patients on baricitinib with significantly decreased steroid requirement and symptom scores.

Objective: Assess IRG expression in CANDLE patients on increasing doses of baricitinib to validate an IRG score as a potential biomarker.

Methods: 12 CANDLE patients (1.8-24.7yo, 9 male) enrolled in a NIH compassionate use protocol for baricitinib were assessed at baseline and on increasing doses of baricitinib (2-11mg/day). Initial IRG list included all genes at least 2x upregulated in a chronic hepatitis patient and healthy peripheral blood mononuclear cells (PBMCs) exposed to IFN alpha was selected for IFN pathway genes in Ingenuity Pathway Analysis (IPA, Ingenuity Systems). IFN alpha, beta, and gamma and IFN receptor genes were added. IRGs with lowest Z-scores from initial studies on 10 CANDLE patients were cut to reduce list to 31 IRGs. These and 4 housekeeping genes, were analyzed through RNA extracted from PAX gene tubes by the NanoString nCounter gene expression system (Seattle, WA). 3 healthy pediatric and 1 healthy adult were used as controls (HCs). IRG scores were calculated by a) summing Z-score IRGs (summary score) and b) summing normalized value for IRGs on 0-1 scale (normalized score) for the a) 31 genes selected above. Paired t-test of IRG scores in patients from baseline versus highest dose of treatment, and then also comparing lowest and highest dose of treatment, excluding flaring patients.

Results: Summary score (p=.008) and normalized score (p=.005) were significantly lower on treatment versus baseline (Figure 1, top row). Summary score (p=.029) and normalized score (p=.003) significantly decreased with lowest dose (0.12 mg/kg/day, 0.05-0.29) versus highest dose (0.26mg/kg/day, 0.10-0.56) (Figure 1, bottom row).

Conclusion: In CANDLE patients, the 31 gene IRG scores significantly decrease on baricitinib or JAK inhibitor therapy in a dose-dependent manner. The normalized score may be more sensitive in showing significant changes in IRG expression. IRG scores may be a useful biomarker for disease activity and response to treatment in CANDLE and other autoinflammatory conditions with IFN-driven pathology. Further validation of the score is needed.
**Figure 1**

Figure 1: In the top row, baseline 31-gene interferon-regulated gene (IRG) scores are compared to highest dose via summary score and normalized scores. In the bottom row, the IRG scores are similarly compared at lowest versus highest baricitinib dose.
Title: Non-Systemic Vasculitic Neuropathy (NSVN)

Presenter: Richard HC Lai, MD - MedStar Washington Hospital Center

Background and Purpose: This case describes a rare form of vasculitis limited only to the peripheral nervous system known as Non-Systemic Vasculitic Neuropathy (NSVN). It is poorly understood and under-recognized. The clinical and pathologic features are indistinguishable between the systemic vasculitis and NSVN except for the presence of multi-organ involvement.

Case Description: This is a 42-year-old previously healthy African American male who presents with one and half months of pain in his ankles and feet bilaterally in addition to right foot weakness. Physical exam reveals pain in both ankles without active synovitis and decreased ability to dorsiflex at his right foot without other systemic findings. Labs including CBC, CMP, UA, lyme disease, HIV, RF, anti-CCP, hepatitis panels, cryoglobulin, SPEP, RPR, ANA, ENAs, paraneoplastic panel and ANCA are all negative. CSF is also unrevealing. ESR is slightly elevated at 23 while CRP is within normal range. Imaging studies including CXR, xray of hands and feet, CT chest, MRI of brain and spine are all insignificant. EMG/ NCS however show evidence of overlapping multiple mononeuropathies in the lower extremities. Sural nerve biopsy shows marked acute axonopathy with small vessel vasculitis consistent with microscopic polyangiitis. Patient is started on high dose of prednisone with taper over the subsequent months. Patient has shown recovery of his strength of his lower extremities.

Case Discussion: This is a rare case of vasculitis limited to only the peripheral nervous system known as NSVN. The incidence, the prevalence and the natural history of such entity remain elusive and variable. Patterns of EMG/ NCS and sural nerve biopsy show typical neuropathic and vasculitic processes. There are no diagnostic or specific investigating laboratories. As this entity may present with various degree of severity, there is no standardized treatment except the use of high dose steroid with slow taper similar to that used in systemic vasculitis. Other immunosuppressants may be used for severe deterioration or failure of monotherapy.

Conclusion/Significance: Features of NSVN are indistinguishable from other systemic vasculitides with exception of no organ involvement. Laboratories are essentially unremarkable with no or mild elevation of inflammatory markers. EMG/ NCS show mononeuritis multiplex while nerve biopsy reveals a vasculitic process.
Title: Inflammatory Arthritis Secondary to Immune Check Point Inhibitors

Presenter: Diman R Lamichhane, MD – MedStar Washington Hospital Center

Background and Purpose: This case describes an inflammatory polyarthritis that developed after use of immune check point inhibitor. Since there is no diagnostic test for this condition, it is a diagnosis of exclusion.

Case Description: A 45-year-old Caucasian female with history of metastatic melanoma under treatment with Ipilimumab (CTLA-4 blocker) followed by Nivolumab (Programmed death-1 blocker) presented with symmetric polyarthritis of the elbows, knees and ankles. Ipilimumab was stopped 11 months prior to her symptom onset due to autoimmune colitis, which resolved after short course of steroid. She also developed autoimmune thyroiditis and she needs thyroid hormone supplementation. Nivolumab was stopped soon after she developed polyarthritis. She had knee arthrocentesis, which was inflammatory with WBC of 32K with neutrophilic predominance. Synovial fluid culture was negative. Serum Uric acid was not elevated; RF, CCP, HLA-B27, ANA and synovial Lyme PCR were negative so were acute viral panel (hepatitis B/C and HIV). Her inflammatory markers were markedly elevated - ESR 75mm/hr and CRP 326.9 mg/L; she had anemia and thrombocytosis. X-rays of the knees showed effusion and X-rays of the hands were normal. Synovitis initially responded to steroid but reoccurred once the dose was tapered.

Case Discussion: Since the patient could not be successfully weaned off steroid, she was treated with infliximab (2 doses). After the first dose her symptoms significantly improved and CRP decreased to 23 mg/L. The effect lasted only 2 weeks and the second dose did not make any difference in symptoms. Subsequently, she was started on methotrexate, which was up titrated to 25mg/week, and steroid was gradually tapered. Arthritis has improved but not resolved. In the mean time, the nature of arthritis has progressed to symmetric polyarthritis with small joints involvement including hand joints. Her CRP is still high (54mg/L) and she continues to remain seronegative.

Diagnosis of “opportunistic autoimmune disease” is one of exclusion. With increasing use of immune checkpoint inhibitors to treat cancer, there is associated risk of inducing autoimmune disease. Association between immune check point inhibitors and autoimmune thyroiditis, colitis, pneumonitis, hypophysitis and vitiligo are well established in phase 3 trial of each of these medications. Most of these adverse effects abate after cessation of treatment/short course of immunosuppressant (depending on the severity of adverse event).

Nivolumab may take up to 9 months to washout. Her last dose was in September of 2014. We are monitor her if the arthritis will resolve after the duration or it will continue; we are considering additional treatment options including tocilizumab.

Conclusion/Significance: Autoimmune diseases are established adverse events after treatment with immune check point inhibitors. One should remain vigilant when encountering patient on these medications as they have opened Pandora’s box. Since the treatment with immune checkpoint inhibitors are new, we may see emergence of new autoimmune diseases.
Title: Anti-NXP2 antibody, an Evolving Biomarker in Dermatomyositis

Presenter: Dr Leeza Nayyar, MD - PGY-2, IM resident PG County Hospital Center

Background and Purpose: Anti MJ/NXP-2, myositis specific antibody has been previously identified in Juvenile Dermatomyositis. In adults, studies have shown its association with calcinosis and malignancy. Although there is limited literature regarding Anti-NXP2 antibody in Adult dermatomyositis and its association with gastrointestinal involvement, it is now being considered as frequent association by experts, though there are only few case reports about it.

Case Description: 21 year old African American male with no past medical history was apparently in good health until January 2014, when he developed unusual periorbital swelling for which he was treated with prednisone. After completing the treatment, he started developing rash, proximal muscle weakness followed by dysphagia. Extensive work up and evaluation of dysphagia done by his primary care physician was inconclusive. He was waiting to be seen by rheumatology, but he had to be sent to John Hopkins Hospital emergency room, as he became extremely weak. His work up, including ANA, serum myoglobin, aldolase, anti-Jo, anti-Ro, Anti-LA, CMV/EBV titer, Anti-RNP, Anti-Smith, Anti-histone antibodies was negative. His MRI chest/abdomen/pelvis revealed intramuscular and subcutaneous edema, but no occult malignancy. He was diagnosed with Dermatomyositis based on biopsy from his right arm. He was noticed to have enteritis/proctitis on imaging studies, also had colonoscopy and biopsy that was normal. He had dysphagia, failed swallow evaluation and got PEG tube. He was treated empirically with high dose pulse steroids as well as IVIg and had improvement in his symptoms. Based on his presentation of proximal muscle weakness, rash associated with bowel involvement, there was concern for the presence of NXP-2 antibodies by experts, which came out to be positive.

Case Discussion: Patient was diagnosed with dermatomyositis after biopsy from his right upper arm. No significant lab abnormality, except elevated creatine kinase and mildly elevated inflammatory markers, and was negative for usual myositis specific antibodies, except anti-NXP-2 antibodies. Anti NXP2 antibodies has been suspected to be related Dermatomyositis with gastrointestinal involvement, based on few cases reported and expert opinion, though it may need further research.

Conclusion/Significance: As per the few case reports, NXP-2 is present in patients of Dermatomyositis with gastrointestinal involvement. Research is going on the same whether NXP-2 will be helpful in predicting the prognoses and also the phenotype.

(not from actual patient, picture from MedScape)
Title: A Rare Case of EGPA (Eosinophilic Granulomatosis with Polyangiitis) Presenting as a Movement Disorder

Presenter: Aaron Pumerantz, D.O. - Walter Reed National Military Medical Center

Background: EGPA is a small-to-medium sized vessel vasculitis that affects multiple organ systems. In addition to severe asthma, pulmonary infiltrates, EGPA frequently presents with cutaneous and peripheral nerve manifestations. Among peripheral nerve manifestations, mononeuritis multiplex predominates. We present a case of EGPA presenting with a movement disorder.

Case Description: A 22 year-old Caucasian male, active duty United States Marine, with a medical history significant for childhood asthma and occasional migraines presented with blurry vision, mild headache, and uncontrolled movements. He reported 1-2 weeks of cough, wheezing, and dyspnea. He also reported numerous episodes of protracted wheeze, cough and dyspnea, at times associated with infiltrates on CXR over the previous 3 years. On presentation, the patient was noted to have myoclonic jerking and choreiform movements in addition to end expiratory wheezes on pulmonary auscultation. A chest CT revealed multilobar ground-glass opacities with areas of tree-in-bud nodularity. Two trials of antibiotics failed to relieve his pulmonary symptoms. Further evaluation revealed peripheral eosinophilia (9.6%), elevated IgE (620.9) and severe left maxillary sinusitis on CT. His ANCA panel was negative. Pulmonary function tests demonstrated severe obstruction. Bronchoalveolar lavage produced negative cultures, but a gram stain did reveal numerous eosinophils. Corticosteroids were started with complete resolution of dyspnea, choreiform movements, myoclonic jerks, and blurry vision. Additionally, PFTs normalized, and the CXR infiltrates and maxillary sinusitis completely resolved. He was given a diagnosis of EGPA based on his multiple supportive clinical features.

Discussion: In this case we discuss an atypical presentation of EGPA, mimicking a movement disorder with myoclonic-appearing jerks and choreiform movements. Neurological involvement is common, reported in up to 75% of patients with EGPA, but typically presents as mononeuritis multiplex or polyneuropathy. Rare manifestations of EGPA include cranial nerve palsies, cerebral and cerebellar infarctions. Chorea has been described in the pediatric populations, but is not well represented in the adult literature. This patient met ACR 1990 diagnostic criteria for EGPA, with 4 out of the 6 criteria. He responded promptly to high dose oral prednisone. This case highlights the variable nature of EGPA, specifically with the neurologic findings.

Significance: To our knowledge, this is the first case of EGPA presenting in an adult as a movement disorder. This case exemplifies the need for further research and investigation into the spectrum of EGPA neurologic manifestations, and considerations for broadening future EGPA neurologic diagnostic criteria. Awareness of atypical cases may lead to earlier diagnosis and initiation of appropriate therapy.
Title: Kikuchi-Fujimoto Disease in a Young Girl with Abdominal Pain

Presenter: Kaitlin Quinn, MD – Georgetown University Medical Center

Background and Purpose: We present the case of a patient with abdominal pain who was found to have mesenteric lymphadenopathy, with pathology consistent with Kikuchi-Fujimoto disease. She was also found to have positive autoantibodies with concern for co-expression of SLE.

Case Description: A 13 y/o female with history of seizure disorder presented with abdominal pain. On initial examination she was febrile to 38.4 C. She had left sided palpable cervical adenopathy and abdominal tenderness. Labs revealed elevated ESR >150, leukopenia, anemia.

Contrast-enhanced CT showed bulky soft tissue nodularity throughout the mesentery. Subsequent whole body PET/CT showed hypermetabolic lymphadenopathy in the abdomen (see figure) and a single cervical lymph node. She underwent laparoscopic biopsy and pathology revealed histiocytic necrotizing lymphadenitis consistent with Kikuchi-Fujimoto disease. She had positive ANA 1:1280 speckled, anti-smith >8.0, and RNP >8.0. Complement and dsDNA testing was normal. Given positive antibody testing, there was concern for concurrent SLE.

Case Discussion: Kikuchi-Fujimoto Disease (KFD; a.k.a. histiocytic necrotizing lymphadenitis) is a rare condition of unknown etiology, classically affecting young women of Asian descent. The most common clinical features are fever, constitutional symptoms, and painful lymphadenopathy, particularly in the posterior cervical region. Mesenteric lymph node involvement is relatively rare. Diagnosis is confirmed by excisional lymph node biopsy, showing cortical and paracortical necrotizing nodules and a histiocytic cellular infiltrate (CD68+). The disease is usually self-limiting with resolution in several months.

The pathogenesis remains unknown and although infectious agents (EBV, HHV-6, HHV-8, HTLV1, Yersinia, Toxoplasma, parvovirus B19) have been implicated, this has not been confirmed. An autoimmune mechanism has also been proposed as autoimmune disorders have also been reported in patients with KFD, with systemic lupus erythematosus (SLE) being the most common. In many reports, KFD preceded the development of SLE, but it may also occur simultaneously or follow SLE diagnosis. Retrospective studies have described a number of cases of SLE associated with diagnosis of KFD, ranging from 4-25%. Due to an increased association between KFD and SLE, periodic follow-up is recommended to assess for development of SLE in this patient population.

Conclusion/Significance: Kikuchi-Fujimoto disease should be considered in the differential of a young patient with fever and painful lymphadenopathy. As KFD may precede or be part of the initial presentation of SLE, the possibility of the co-expression of SLE should be considered in patients diagnosed with KFD.

Figure:
Whole body PET/CT with large conglomerate of hypermetabolic mesenteric lymph nodes
Title: Adrenal Hemorrhage with Resultant Adrenal Insufficiency in Antiphospholipid Syndrome

Presenter: CPT Rachel Robbins, MD - Walter Reed National Military Medical Center

Background and Purpose: Antiphospholipid Syndrome (APS) is a potentially devastating disorder that leads to recurrent thrombosis if not recognized and treated promptly. It can be categorized as either primary or secondary, with the primary subtype commonly occurring in young females whereas secondary APS is frequently encountered as a complication of systemic lupus erythematosus. APS commonly causes deep vein thrombosis (DVT), pulmonary emboli (PE) and miscarriages, but it can also cause many other end organ manifestations.

Case Description: This is a case of a 50 year old male with a past medical history notable for a recent diagnosis of unprovoked PE and lower extremity DVT admitted for abdominal pain and CT findings concerning for possible aortitis. He was well until two months prior to presentation when he developed gradually worsening left lower extremity edema that prompted a visit to the emergency department where he was diagnosed with a DVT and started on rivaroxaban. Over the next two days he was seen twice more in the emergency room and subsequently diagnosed with pneumonia then a PE. He then developed severe abdominal pain, was again evaluated in the emergency room and admitted after a CT abdomen/pelvis revealed streaking around the aorta concerning for aortitis. His anticoagulation was transitioned to heparin shortly after admission. An extensive work up showed no evidence of a systemic vasculitis, though his antiphospholipid antibodies were markedly elevated. Four days into his hospitalization he developed tachycardia. The following day he developed severe back pain and a repeat CT abdomen/pelvis revealed large, bilateral adrenal hemorrhages but no evidence of aortitis. Adrenal insufficiency was subsequently diagnosed.

Case Discussion: Adrenal hemorrhage with resultant adrenal insufficiency is a rare complication of antiphospholipid syndrome that can be potentially life threatening if not recognized quickly. Though this patient was anticoagulated, it is unlikely that the heparin was the source of his hemorrhage particularly since he had only three supertherapeutic values (none higher than 118) that were all appropriately corrected.

It is theorized that patients with APS develop adrenal hemorrhage in one of two ways: 1) micro hemorrhage of the adrenal vasculature with subsequent infarction or 2) thrombosis of the adrenal vein with edema and subsequent obstruction of the arteries, infarction, then bleeding into the infarct. This patient may have had progression of his disease due to his initial treatment with rivaroxaban when the only oral anticoagulation approved for APS is warfarin.
Title: Adenosine-Mediated Inflammation and Neutrophil Extracellular Traps Associated with Mutations in CECR1 Gene

Presenter: Kyawt W. Shwin, MD - NIAMS

Background: Deficiency of adenosine deaminase 2 (DADA2) shares many features with idiopathic polyarteritis nodosa (PAN), including abundant neutrophils in affected tissue. Immune cell response to treatment with TNF inhibitor and the role of neutrophils were studied in a family consisting of children with DADA2 and several family members afflicted by various autoimmune diseases including PAN.

Methods: Candidate-gene sequencing of the CECR1 gene was performed in two children who had early-onset lacunar infarcts and biopsy-proven vasculitis. Histopathology characterization was performed on affected tissues. Neutrophils and low-density granulocytes (LDGs) were isolated during active disease, and neutrophil extracellular traps (NETs) were quantified and visualized by fluorescence microscopy. Neutrophils were incubated with adenosine +/- ADA2 enzyme across a range of concentrations under high-stringency conditions; resultant NET formation was quantified. Evaluations were conducted during active disease and four months later during disease remission after treatment with etanercept. Immune cell subsets were quantified by multi-panel flow cytometry in response to treatment.

Results: Both children were compound heterozygotes for the G358R and G47R mutations in the CECR1 gene, which encodes the ADA2 protein. The mother was a carrier for G358R mutation and had a history of unexplained lacunar infarct at age 45. A maternal great grandmother had a history of biopsy-proven PAN onset at age 69, and a maternal great uncle had a history of autoimmune colitis. The father was a carrier for G47R mutation and had a history of Guillain-Barre syndrome. Fibrinoid necrosis of medium-sized blood vessels, intravascular thrombi, and dense perivascular infiltrates of netting neutrophils were visualized in affected skin and small bowel sections (Figure). Immunohistochemistry showed aggregates of MPO, CD163 and CD3 positive cells predominantly in perivascular region. An abundance of LDGs prone to spontaneous NET formation were observed during active disease. Different concentrations of adenosine [0.2, 0.5, 16 μM] stimulated robust NET formation, and adenosine-induced NET formation was inhibited by ADA2 at specific concentrations. Flow cytometry analysis showed significantly reduced CD14+/CD16+ monocytes after treatment with etanercept (8% vs 2%) with minimal changes in T and B cell compartments.

Conclusion: Neutrophils have a pathogenic role in DADA2. LDGs and NETs are observed during active disease. Deficiency of ADA2 may increase risk for adenosine-induced NET formation, which is a novel mechanism of NETosis. The autoimmunity observed in this family suggests that carriers of CECR1 gene mutation may have increased risk for autoimmune diseases and that DADA2 and idiopathic PAN may be genetically related.
**Figure:** Neutrophil Extracellular Traps (NETs) seen as web-like structures in a section of small bowel obtained from a child with Deficiency of Adenosine Deaminase 2 (DADA2) and biopsy-proven vasculitis; white arrows showing NETs in the tissue; Myeloperoxidase (MPO) shown in red and DNA in blue.
Title: Inflammatory Arthritis as an Initial Manifestation of Thromboangiitis Obliterans

Presenter: Pragya Singh, MD – MedStar Washington Hospital Center

Background and Purpose: We present a case of a patient who presented with a two week history of progressive myalgias and symmetric polyarthritis, whom was eventually diagnosed with thromboangiitis obliterans (TAO). TAO is a rare condition characterized by nonatherosclerotic, segmental inflammation that mostly affects the small to medium sized arteries and veins of the extremities. Tobacco is essential for the initiation and progression of TAO. Inflammatory arthritis has been rarely described as an initial manifestation of TAO.

Case Description: Mr. “B” is a 56 year old African American male with history of HIV, previous Kaposi sarcoma, prostate cancer status post prostatectomy, and thirty pack year smoking history. He initially presented to an urgent care facility with progressive myalgias and arthritis in his left wrist and was subsequently given NSAIDs and wrist splints, only providing minimal relief. Two days later, he experienced swelling in bilateral elbows followed one week later by pain in his bilateral knees plus swelling in a few DIPs. Nearly two weeks after the initial presentation, he again presented for evaluation, and on examination was noted to have polyarthritis, dactylitis, subtle subungual lesions, and olcranon bursitis. Olecranon bursal fluid revealed a white blood cell count of 2,425 with 45% neutrophils, but no evidence of organisms or crystals. He was initially treated with high dose oral prednisone for possible seronegative vasculitis, however there was only partial improvement in his inflammatory arthritis. A CT angiogram of chest and abdomen were unrevealing of any vasculitis. Conventional angiogram of both upper extremities however revealed segmental vascular occlusion, and collateralization around areas of occlusion (corkscrew collaterals) (Figure 1) consistent with TAO.

Case Discussion: The Criteria of Olin is used for diagnosis TAO and this patient met three of four of these criteria. Note that while inflammatory arthritis is not part of the criteria, several case reports have described this feature in patients. Our patient was counseled on smoking cessation and started on Sildenafil 20mg three times daily, resulting in rapid and marked improvement in his symptoms.

Conclusion/Significance: While TAO is a rare process, it should be on the differential diagnosis of acute polyarticular inflammatory arthritis, especially in the setting of a strong smoking history.

Figure 1
Conventional angiogram of hand revealed segmental vascular occlusion, and collateralization around areas of occlusion
Title: Neurosarcoidosis as a Rare Presentation of Immune Reconstitution Inflammatory Syndrome (IRIS) in a HIV Positive Patient Treated with Highly Active Antiretroviral Therapy

Presenter: Janki Trivedi, MD – Georgetown University Hospital Center

Background and Purpose: We present a case of an HIV positive man treated with HAART therapy who developed clinical, laboratory and imaging findings consistent with a diagnosis of isolated CNS neurosarcoidosis. We suspect our patient developed neurosarcoidosis as the result of immune reconstitution following HAART therapy. To our knowledge this is the first case documenting neurosarcoidosis as part of immune reconstitution inflammatory syndrome (IRIS).

Case Description: 49 year old Latin American male presents with intermittent headaches, diplopia, disequilibrium, anosmia, and bilateral proximal lower extremity weakness for 9 months. Prior to the onset of his symptoms he developed unilateral Bell’s palsy which resolved within a few weeks. His past medical history is notable for HIV diagnosed one year prior to his presentation, currently on HAART therapy. He also had hypothyroidism treated with a stable dose of levothyroxine. He denied allergies, asthma, cough, dyspnea. No weight loss, fevers/chills, night sweats. He denied tinnitus, decreased hearing. Denied hoarseness, sicca symptoms, oral/nasal ulcers, dysphagia, GERD. The rest of review of systems was unremarkable. During evaluation by various other specialists, he was given oral steroids with rapid taper over 7-10 days. He noted that each time steroids were given, he had complete resolution of his symptoms. And when the steroids were discontinued, he noted return of symptoms.

Case Discussion: Based on the clinical presentation, responsiveness of symptoms with steroid use, and with the available laboratory and neuroimaging studies, we made a diagnosis of probable neurosarcoidosis. Since our patient did not have signs, symptoms, laboratory involvement or imaging studies suggesting systemic sarcoidosis, we established that he likely has isolated CNS. After discussion with his infectious disease physician, he was started on oral hydroxychloroquine and weekly methotrexate as steroid-sparing agents in order to gradually taper his prednisone dose. He has been doing well clinically and we are continuing to taper his prednisone.

Conclusion/Significance: Isolated CNS neurosarcoioidosis (NS) is a very rare condition, reported to occur in only 1% of all patients with sarcoidosis. Clinical symptoms are not specific and NS mimicks many other diseases. Cranial nerve palsies: facial nerve palsy, optic neuritis and sensorineural hearing loss are common manifestations. Mass lesions, meningeal disease, hydrocephalus, longitudinal transverse myelitis, peripheral neuropathy, mononeuritis multiplex, and a Guillain-Barre phenotype have been reported in the literature. Hypothalamic-pituitary axis dysfunction is also a feature of NS and is radiographically silent in 50% of cases. It should be noted that no correlation has been found between clinical symptoms and radiographic lesions. The diagnosis of NS is one of exclusion. Serum elevated ACE level is non-specific. Elevated CSF ACE level has been reported to have high specificity in some studies. Patient's suspected of NS should undergo lumbar puncture the main purpose of which is to rule out infectious and malignant etiologies. CSF findings include elevated protein level, mild to moderate pleocytosis with lymphocytic predominance and low/normal CSF glucose. Studies have reported that a CD4:CD8 T cell ratio of greater than 5:1 may be present in the CSF fluid in patients with NS.
Immune reconstitution inflammatory syndrome has been previously described in a subset of HIV positive patients who went on to develop clinical signs and symptoms of a pre-existing infection after treatment with highly active antiretroviral therapy and with recovery of immune function. The definition of the same syndrome has been expanded to include the following clinical symptoms not previously explained by a new acquired infection clinical symptoms not previously explained by the expected clinical course of previously recognized infectious agent clinical symptoms not previously explained by the side effect of therapy occurring after withdrawal or reduction of immunosuppressive therapy. Immune reconstitution inflammatory syndrome (IRIS) presenting with pulmonary sarcoidosis has been reported in several case reports and case series. To our knowledge, neurosarcoidosis developing as a result of IRIS has not been reported in the literature.

In our patient, HIV was treated with HAART for 12 months prior to the onset of his symptoms which paralleled increases in his CD4/CD8 ratio and absolute CD4 count (Fig. 2). Given the clinical and laboratory findings, we postulate that our patient’s clinical presentation of isolated CNS neurosarcoidosis is likely the result of immune reconstitution inflammatory syndrome.

Fig. 1(A-D). MRI with contrast: to the left are pre-contrast T1 images and right are post-contrast T1 images. A) Axial view of the brain: yellow arrows show bilateral cranial nerve V enhancement. B) Axial view of the brain: yellow arrow showing cranial Nerve VII enhancement. C) Sagittal view of the lumbosacral spine: yellow arrow shows enhancement of the spinal cord. D) Axial view of the thoracic spine: yellow arrow showing enhancement of the spinal cord.
Title: Dupuytren’s Contractures as an Early Manifestation of Inherited Collagen Diseases

Presenter: Rujuta Trivedi MD – MedStar Washington Hospital Center

Background and purpose: The aim of this clinical case presentation is to illustrate a possible inherited collagen vascular disorder as an unusual cause of early-onset Dupuytren contractures.

Clinical case: A 35 year old Caucasian male was seen by Rheumatology for evaluation of a possible collagen vascular disease. His medical history was significant for early onset Dupuytren contractures of both hands (started at age 18, treated with surgery including right 5th finger amputation), Ledderhose’s disease (plantar nodular fasciitis) in both feet (started in his early 20’s and treated with surgery), and recent onset (May 2014) acute vascular problems such as celiac artery dissection and saccular aneurysm of right subclavian artery.

Case Discussion: This is a case of very early onset Dupuytren contractures (typically benign, slowly progressive fibroproliferative disease) in conjunction with Ledderhose disease (nodular plantar fibromatosis). This patient had a very aggressive form of fibromatosis/ Dupuytren’s requiring amputation of his fingers. It was however the recent development of his multiple vascular aneurysms and dissections which promoted an evaluation for a possible inherited collagen diseases such as vascular type Ehlers-Danlos (Type 4 ED).

While uncommon, early onset palmo-plantar contractures have been reported in vascular type Ehlers-Danlos. In vascular Ehlers-Danlos, a mutation in the COL3A1 gene results in abnormal procollagen III production, the primary collagen found in the walls of hollow organs and blood vessel. Patients usually experience marked vessel aneurysms and spontaneous arterial rupture by the age of 40. Other clinical features include poor wound healing, acrogeria, and a relative lack of skin hyperextensibility, Genetic testing is underway for our patient, but given the clinical presentation, we believe this case likely represents an inherited collagen disorder, likely vascular type Ehlers-Danlos, as the primary reason for his Dupuytren contractures.

Conclusion: When Dupuytren contracture/plantar fibromatosis is seen at early age without usual predisposing factors such as insulin-dependent diabetes, the differential is wide but should include inherited collagen disorders. Clinical examination, family history and high index of suspicion are key to the diagnosis. Clinical suspicion requires confirmation by genetic test. If patient is diagnosed with vascular Ehlers-Danlos type 4, he/she should carry medical attention.
Title: A Case of Granulomatosis with Polyangiitis Associated with Pregnancy in a 19 Year Old Female

Presenter: Vanya D. Wagler, D.O. - Walter Reed National Military Medical Center

Background and Purpose: Granulomatosis with Polyangiitis (GPA) is a rare systemic vasculitis that may affect multiple systems including the upper airways, lungs, and kidneys. It is has a strong association with cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) specific to proteinase 3 antigen (PR3). The incidence in the United States is approximately 3 cases per 100,000 people. Primary systemic vasculitides are uncommon and pregnancy in patients with GPA is relatively rare. Additionally, pregnancy in GPA is associated with a high complication rate, especially among patients actively undergoing treatment. Data on pregnancy outcomes are limited and knowledge about gestational risk is mostly provided by single case reports.

Case Description: A 19 year old female 12 weeks postpartum initially presented with hemoptysis, nasal inflammation, and extensive bilateral pulmonary infiltrates evolving into diffuse alveolar hemorrhage and subsequent respiratory failure. The patient had a positive c-ANCA specific for PR3, and a nasal biopsy demonstrating a small vessel vasculitis. A clinical diagnosis of GPA was made and she was treated with high dose methylprednisolone, seven therapeutic plasma exchanges, and induction therapy with Rituximab. The patient continued to do well while receiving weekly Rituximab therapy every week for a total of four treatments. The patient was found to be pregnant approximately one month after completion of Rituximab therapy despite extensive counseling regarding risks associated with pregnancy. Due to the pregnancy risks associated with the patient’s known disease and medication therapy, a multidisciplinary approach with Maternal-Fetal Medicine was initiated. Patient has had no evidence of recurrent vasculitis and there have been no pregnancy-associated maternal or fetal complications to date.

Discussion: Although uncommon, primary systemic vasculitis can present in women of childbearing age. In addition to side effects associated with treatment of GPA, the manifestations and pathology of GPA itself is associated with an increased risk of fetal complications. A review of the literature focusing on pregnancy in GPA suggests a patient’s condition at conception may be a strong prognostic factor in overall outcomes. This patient presented with severe manifestations of GPA postpartum which responded well initially to early, aggressive therapy.

Conclusion/Significance: Pregnancy in vasculitis is becoming more common as result of improved vasculitis therapies that preserve fertility while prolonging survival; mortality remains very high without treatment. Due to complexity of pregnant patients with vasculitis, management by a multi-disciplinary team including Rheumatology and Maternal Fetal Medicine is essential. Counseling patients with vasculitis prior to pregnancy is mandatory, though somewhat limited by lack of data regarding outcomes and evidence-based guidelines. Vasculitis therapies for pregnant patients are similar to therapies considered in non-pregnant patients, but treatment decisions during pregnancy must be weighed based on risk of fetal harm along with risk of maternal harm.

<table>
<thead>
<tr>
<th>Maternal</th>
<th>Fetal</th>
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</thead>
<tbody>
<tr>
<td>Increase in thrombotic events</td>
<td>Therapeutic abortion</td>
</tr>
<tr>
<td>Preeclampsia, especially with renal involvement</td>
<td>Early spontaneous abortion</td>
</tr>
<tr>
<td>Episcleritis, tracheal crusting, subglottic stenosis</td>
<td>Preterm delivery</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td>Intrauterine growth retardation</td>
</tr>
<tr>
<td>High mortality without treatment</td>
<td>Few reports of neonatal pulmonary renal syndrome</td>
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<tr>
<td>Renal insufficiency</td>
<td></td>
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</tbody>
</table>

Table 1. Maternal and fetal complications of GPA in pregnancy.
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