The Rheumatism Society of the District of Columbia

Presents...

The 16th Annual Rheumatology Fellows Forum

Saturday, May 19th, 2018

MedStar Washington Hospital Center
True Auditorium
Washington, DC
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Award Winners

Podium Presentations

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Title: An Uncommon Presentation of Neuropsychiatric Lupus

Authors: Michael Belsky, Paloma Alejandro

MedStar Washington Hospital Center

Case Presentation: A 46-year-old AAM with a six-month history of progressive headaches, cognitive decline and weight loss was brought to the emergency department by EMS after a witnessed fall in public. On presentation, patient was alert and oriented, in no acute distress, and vital signs were stable. Physical examination revealed multiple facial lacerations resulting from the fall. Strength was intact bilaterally, with no focal neurologic deficits. A non-contrasted CT head was unremarkable. Urine toxicology screen was negative. Initial lab work was notable only for mild thrombocytopenia. Routine EEG showed no evidence of underlying seizure activity. He was subsequently admitted for observation. The patient did not report a significant past medical history, though a thorough review of his outside records revealed that he had been evaluated for cervical lymphadenopathy in 2016. The pathology report from the cervical lymph node biopsy was felt to be suggestive of IgG4-related disease. No treatment was initiated at that time, and follow-up imaging in 2017 showed complete resolution of lymphadenopathy.

Shortly after admission, the patient’s mental status quickly declined, progressing to obtundation. Lumbar puncture initially revealed elevated protein. Additional CSF studies were unremarkable, including flow cytometry, cytology and paraneoplastic antibody panel. Infectious work-up was negative, including gram stain, culture and viral PCR of the CSF. Contrast MRI of the brain revealed diffuse dural thickening consistent with hypertrophic pachymeningitis. Given the cervical lymph node pathology noted in 2016, the diagnosis of hypertrophic pachymeningitis secondary to IgG4-related disease was initially favored. Progressive thrombocytopenia and leukopenia were later noted. Additional lab work revealed hypocomplementemia and high titer antinuclear antibodies, as well as positive anti-Sm, anti-U1 RNP, anti-Ro/SSA and anticardiolipin IgG antibodies. At this point, the diagnosis of neuropsychiatric lupus (NPSLE) was favored. The cervical lymph node biopsy from 2016 was reviewed with pathology, and deemed to be inconsistent with IgG4-related disease, further supporting the diagnosis of NPSLE. The patient received pulse-dose methylprednisolone, followed by high dose prednisone, with resolution of hypocomplementemia and cytopenias. The patient also received a single infusion of cyclophosphamide 1,000mg (500 mg/m2). Altered mentation completely resolved prior to hospital discharge.

Discussion: Hypertrophic pachymeningitis is an inflammatory hypertrophy of the dura mater, which can be a primary process or secondary to infection, autoimmune disease, or malignancy. Hypertrophic pachymeningitis is an uncommon manifestation of systemic lupus erythematosus (SLE). However, there are multiple case reports in the literature of hypertrophic pachymeningitis associated with SLE, which have been very responsive to glucocorticoids and cyclophosphamide. As such, SLE should be considered in the differential diagnosis of hypertrophic pachymeningitis.
Title: Behcet’s disease-like conditions as an example of a diagnostic and therapeutic challenge: Using cytokine biomarkers to apply personalized medicine

Authors: Blas Betancourt¹, Alexandra Drakaki², Amanda Ombrello³, Massimo Gadina¹, Wanxia Li Tsai¹, Ananta Subedi¹, Daniel Kastner³

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Case Description: A 34-year-old woman, originally from Greece, presented with a 22-year-history of recurrent episodes of constitutional symptoms (fever and fatigue), mouth and nose ulcers, gastrointestinal manifestations (nausea, left upper quadrant pain, and constipation or diarrhea), polyarthralgia, and sacroiliitis. The course of her disease was complicated by an episode of isolated ACTH insufficiency that resolved after treatment with hydrocortisone and fludrocortisone for 3 years. At the onset, she had monthly recurrent flares lasting up 2 weeks but was also symptomatic with fatigue and joint pain between the flares. Later during her disease, the symptoms became more chronic with variable improvement. A previous colonoscopy showed terminal ileitis but was negative for inflammatory bowel disease. Multiple conditions were entertained in the differential including systemic lupus erythematosus, spondyloarthritis, Behcet’s disease (BD), and inflammatory bowel disease but not conclusive diagnosed was established. She had a good response to steroids but failed treatment with NSAIDs, colchicine, hydroxychloroquine, mercaptopurine, azathioprine, and adalimumab due to either lack of response or safety concern.

In a second opinion evaluation, she was found symptomatic with multiple joint pain, prolonged stiffness, and fatigue. Physical examination revealed a superficial gingival ulcer and a nasal ulcer but was otherwise unremarkable. Investigations showed elevated CRP up to 67.90 mg/L (normal 0-4.99 mg/L) with normal erythrocyte sedimentation rate. Rheumatoid factor, antinuclear antibodies (ANA), anti-extractable nuclear antigens (ENA), anti-double-stranded DNA antibody, lupus anticoagulant, anti-cardiolipin antibodies (IgM and IgG), aldolase, anti-myeloperoxidase antibody, and anti-proteinase 3 antibody were all negative. Complements (C3 and C4) and urinalysis were normal. Screening for hepatitis B and C, and tuberculosis was negative as well. HLA B51 was positive. The main diagnosis was an incomplete form of BD. Anakinra at a dose of 100 mg daily was unable to control her symptoms but a partial response was obtained with 300 mg daily. Cytokine profile was performed and results showed an increased level of IL-12p40 subunit (see Figure) which indicates that the IL-23/17 pathway could be playing a role in the pathogenesis of her disease. Sample from colonoscopy biopsies also revealed intense staining for IL-17. The patient was subsequently started on ustekinumab in combination with anakinra.

Case Discussion: BD is a multisystemic and chronic inflammatory vasculitis of unknown etiology. The diagnosis of BD can be sometimes difficult since it is a complex disease with a wide spectrum of presentations and with no specific laboratory tests or histopathology. Our case did not meet the classification criteria of BD but was considered in the spectrum of Behcet’s disease-like syndrome. We were able to identify a pathway that could be playing a significant role in the pathogenesis of her disease and to tailor the treatment accordingly. IL-12 and IL-23 have been identified as important mediators of BD. High levels of IL-23 have been found in sera of BD patients. Studies have identified a correlation of Th1 and Th17 with the disease activity. In patients with BD, peripheral blood Th17/Th1 ratio is significantly
higher compared to control. Moreover, GWAS has also identified an association between single nucleotide polymorphism (SNP) of IL-23R/IL-12RB2 genes and BD.

**Conclusions:** This case highlights the difficulty in diagnosing and treating Behcet’s disease-like conditions. We successfully used cytokine biomarkers as an approach to apply personalized medicine and tailor the treatment in clinical practice. We recommend using this method in patients with complex medical conditions and a history of failing multiple medications.

**Figure:** Results of whole blood stimulation assay for Hu IL-12p40.
Title: Digital Ischemia Exposing Light Chain Myeloma

Authors: Shannon Davis

Georgetown University Hospital

Introduction: Most commonly identified causes of digital ischemia are arterial thrombosis, autoimmune connective tissue diseases (especially systemic sclerosis), vasculitis, and local injuries. Rarely, digital ischemia may present as a paraneoplastic syndrome associated with both solid and hematologic malignancies. This abstract presents a patient with digital ischemia as the presenting symptom of light chain myeloma.

Case Description: Rheumatologic evaluation was requested of a 61 year old AAM with a history of HTN, HLD, and CKD V s/p renal transplant 4/2017, on Tacrolimus and Cellcept due to a 5 week history of painful bluish discoloration in the bilateral toes and fingers with subsequent development of gangrene requiring amputation of multiple digits. The laboratory tests were negative for hepatitis, HIV, ANA, ANCA, cryoglobulins and cryofibrinogen, RF and CCP. Complements were normal. Mild anemia otherwise unremarkable CBC and CMP. No embolic source was identified with TEE, TEE, arterial duplex of UE and LE and CTA of abd/pelvis with run off. He was started on empiric anticoagulation and prednisone. He had negative ACL and B2GP antibodies with a positive lupus AC while on lovenox. Lab work also revealed hypogammaglobulinemia and a monoclonal spike on SPEP and UPEP with free kappa monoclonal protein detected on electrophoresis. A serum free kappa light chain was markedly elevated at 81560 mg/L with K/L of 20912. He underwent bone marrow biopsy which confirmed plasma cell myeloma. Skin biopsy of right thumb revealed mildly thickened blood vessels and focal congo red positive dermal deposit but birefringence was unable to be demonstrated. Skin biopsy from subsequent toe excision showed vasoocclusive/thromboembolic vasculopathy with direct immunofluorescence revealing large intravascular kappa deposition most consistent with light chain deposition disease. He was subsequently started on chemotherapy with carfilizomib, cyclophosphamide and dexamethasone.

Case Discussion: Malignancy is a possible etiology of acral vascular syndrome with a reported prevalence ranging from 2.2%–8% of cases. Paraneoplastic acral vascular syndromes (Raynaud’s phenomenon, acrocyanosis, and acronecrosis) have most commonly been found to be associated with adenocarcinomas (41%) and hematologic malignancies (19%). Occurrence of digital ischemia may precede, coincide or follow the diagnosis of cancer. Proposed mechanisms of this phenomenon are various including: vasospasm due to sympathetic hyperactivity, arteritis induced by tumor antigen-antibody complexes deposition or as consequence of immune deregulation, blood hyperviscosity and/or hypercoagulability.

Conclusion: Although rare, awareness that malignancy can cause digital ischemia is important for early diagnosis and treatment.
**Title:** Neck Swelling and Abdominal Distension in A 4 Year Old Boy

**Authors:** Brian L.P. Dizon, MD PhD and Hemalatha Srinivasalu MD

Department of Pediatric Rheumatology, Children’s National Health System.

**Case Description:** A 4 year-old boy developed acute progressive bilateral neck swelling over a 2-week period. Despite antibiotic treatment for presumed streptococcal pharyngitis, the cervical lymphadenopathy persisted, and later the swelling extended to his jaw with stertorous breathing and orthopnea. Two months later, he developed shortness of breath and difficulty breathing while playing on a playground swing, prompting emergency room evaluation. CT neck revealed no evidence of airway compromise; symmetric bilateral parotid and submandibular gland swelling; and scattered, mildly prominent cervical nodes. The patient was subsequently evaluated by Otolaryngology as an out-patient, who performed biopsy of parotid and salivary glands. One week later, his mother noticed abdominal distension and diffuse pain, and was admitted for evaluation. Bloodwork was notable for elevated sedimentation rate and C-reactive protein, eosinophils, total IgG and IgG4; mild transaminitis, and elevated GGT. Antinuclear antibody testing, C3, C4, and autoimmune serologies were negative. Differential diagnosis of his disease process included oncologic process such as lymphoma; lymphoproliferative disorders including autoimmune lymphoproliferative syndrome; infections including Epstein-Barr virus, cytomegalovirus, Mumps virus, and tuberculosis; autoimmune adenopathies such as Kikuchi syndrome and Rosai-Dorfman syndrome; as well as autoimmune diseases including Sjogren’s syndrome, sarcoidosis, lupus, and IgG4-related disease. Magnetic resonance imaging of the abdomen showed multiple hepatic hypoechoic foci without intra- or extrahepatic ductal dilation. Liver biopsy revealed marked interface hepatitis with bile duct injury with IgG4 plasma cells representing more than 40% of the IgG plasma cell infiltrate. The patient was diagnosed with IgG4-related disease with superimposed autoimmune hepatitis/sclerosing cholangitis overlap syndrome. The patient was started on Azathioprine and Prednisolone with improvement in his neck swelling and cholangitis.

**Discussion:** IgG4-related disease is a newly-recognized rare fibroinflammatory condition that is characterized by infiltration of IgG4 plasma cells in any organ system (1). Pediatric IgG4-related disease is even rarer, and systemic review of existing case reports suggests that ocular and pancreatic disease are the most reported manifestations in the pediatric age group (2). We describe a child with IgG4-related disease with salivary and hepatic involvement. These disease manifestations have been reported separately in the literature: a 3 year-old girl with acholic stools and jaundice (3), and an 11 year-old boy diagnosed with Kuttner tumor (4), but not in the same patient. We observed similar favorable response to treatment in our patient with oral steroids and Azathioprine.

**Significance:** IgG4-related disease is a newly recognized pediatric condition, and manifestations may include bilateral sialoadenitis and cholangitis.
Title: Lumbar Spinal Tophaceous Gout: An Uncommon Cause of Paraparesis

Authors: Uchechi C. Egbehuzo, Iziegbe Ehiorobo, Lynda Tilluckdharry, Sharon Dowell, Gail Kerr

Howard University Hospital

Case Description: A 59 year old male with chronic kidney disease, hypertension and diabetes mellitus referred to rheumatology clinic with a 2-year history of progressive lower extremities weakness, concerning for myositis. Examination revealed proximal muscle weakness and decreased reflexes of the lower extremities. Laboratory investigations revealed elevated inflammatory markers, leukocytosis, normocytic anemia, but normal creatine kinase. CT scan of the lumbosacral spine reported a soft tissue mass at L2-L3, with MRI revealing compression of the posterior thecal sac with near obliteration of the central canal. Lamina bone biopsy of L4 was performed, followed by L3-L5 decompressive laminectomy. Histopathology showed amorphous material with monosodium urate (MSU) crystals. Serum uric acid was elevated at 9.1 mg/dl (4.0-8.5 mg/dl). The patient was prescribed urate lowering therapy (ULT) with allopurinol and underwent rehabilitation with marked improvement of his lower extremity weakness.

Case Discussion: Gout is an inflammatory arthritis caused by the deposition of MSU crystals in the appendicular skeleton. Rare case reports (<150 cases) of axial skeleton involvement exist. Tophaceous gout of the spine may mimic septic arthritis of the facet joints, epidural abscess, and malignancy. Symptoms include localized back or neck pain, radicular pain, or neurological deficits. Conventional imaging studies (plain radiographs, CT scan and MRI) are often non-diagnostic and tissue biopsy is usually necessary for diagnosis. The emerging imaging modality, Dual energy CT (DECT) scan allows effective differentiation of MSU crystals from other pathology. Non-urgent treatment of spinal gout is generally limited to anti-inflammatory medications and ULT. Surgical intervention is required in patients with neurological compromise.

Case Conclusion & Significance: Spinal gout is likely under-reported due to under-diagnosis. It should be considered in patients with tophaceous gout or less commonly, with hyperuricemia, who present with back pain and/or neurological symptoms. DECT scan is seminal to the diagnosis of tophaceous gout of the axial skeleton.

T2 weighted MRI Sagittal View of the Lumber Spine: Image demonstrating spinal stenosis created by an invading mass into the posterior thecal sac. Biopsy of this mass confirmed tophaceous gout by presence of negatively birefringent crystals under polarized light.
Title: Disappearing Bones: A Case of Massive Osteolysis of the Hips and Shoulder

Authors: Corey Ephrussi

Georgetown University Hospital

Case Description: A 65 year old male with a history of GERD, Barrett’s esophagitis presented to the hospital with progressively worsening shortness of breath and anasarca of one week duration. He was admitted to the hospital with a diagnosis of volume overload. NT pro-BNP was 832, chest radiograph demonstrated cardiomegaly and interstitial edema. Echocardiogram showed an intact ejection fraction and moderate pericardial effusion. He was admitted to the medical ICU for close monitoring and gentle diuresis, a pericardiocentesis was offered but declined by the patient. He admitted to hip pain and radiographs of the hips and pelvis revealed massive osteolysis of the femoral heads bilaterally with complete resorption of the femoral neck and head. Rheumatology was consulted for possible etiology. He denied any recurrent swollen joints, fever, rash or sensory disturbance. He admitted to drinking moonshine for the past year. After agent orange exposure in the Vietnam war, he was given prednisone for ten months. Labs revealed a normal glucose, negative RPR and normal markers of bone health. MRI of the spine did not reveal syringomyelia. Review of old radiographs documented the hip findings to be chronic and also showed severe left glenohumeral joint destruction. Considering he did not have evidence for rheumatic disease, neuropathic process or malignancy we did not think he had severe osteonecrosis even though he had prior glucocorticoid and alcohol use. The degree of osteolysis and bone resorption was out of proportion for osteonecrosis and thus the diagnosis of Gorham’s disease was considered the most likely diagnosis.

Case Discussion: Rheumatologists will often uncover osteonecrosis involving the hips, knees and shoulder joints with the frequent ordering of plain radiographs. Diseases like systemic lupus erythematosus and the frequent use of glucocorticoids for the treatment of rheumatic diseases may contribute to osteonecrosis. Common causes of osteonecrosis including glucocorticoid use, alcohol, sickle cell disease and trauma should be considered. However, when there is massive osteolysis and destruction of a joint, a neuropathic joint should be considered. Diabetes mellitus, leprosy, syphilis and syringomyelia are frequent causes of neuropathic arthropathy. Gorham’s disease or massive osteolysis, also known as vanishing bone disease is a rare condition characterized by spontaneous and pronounced bone resorption. The exact etiology is poorly understood and the mechanism of bone resorption/osteolysis is thought to be caused by hemangiomatosis. The most commonly affected sites include the shoulder and pelvis. Clinical manifestations vary. Treatment includes bisphosphonates and radiation therapy.
Figure 1. A. CT Pelvis. B. CT Pelvis. C. Pelvis Radiograph D. Shoulder Radiograph
Title: An International Consensus Exercise to Develop Candidate Items for Classification Criteria in Relapsing Polychondritis

Authors: Marcela Ferrada, Keith Sikora, Clint Allen, Jeffrey Kim, Robert Colbert, James Katz and Peter C Grayson on behalf of the Relapsing Polychondritis International Working Group

National Institutes of Health, NIAMS

Background/Purpose: There are no validated classification criteria for relapsing polychondritis (RP). Given that some manifestations of RP are organ- or life-threatening, it is imperative that classification criteria in RP have adequate sensitivity to identify cases early during the disease. The objective of this study was to use consensus procedures to select a set of items with potential utility to classify RP. An international, multidisciplinary group of physicians with experience managing RP was formed. Based on a systematic review of the literature, combined with clinical experience, a list of potential candidate items was generated. All group members were invited to participate in an online Delphi exercise for item reduction. Survey participants rated each potential candidate item on a scale of 1-10 (ranging from 1=completely inappropriate to 10=completely appropriate for inclusion as a potential classification criteria item in RP). Items with a median response score of ≤4 were eliminated from further consideration. Items with a median score of ≥7 were retained. Items with a median score >4 and <7 were included in a second and third Delphi. After the Delphi, factor analysis was performed to further reduce the number of items within each organ system domain.

Results: A list of 142 candidate items was generated related to patient-reported symptoms, physician-observed findings, laboratory, and imaging assessments in RP. Delphi respondents (n=32) were from 6 countries (United States=22; France=3; Japan=3; Canada=2; United Kingdom=1; India=1) representing multiple subspecialties (Otolaryngology=5; Pulmonology=3; Interventional Pulmonology=3, Adult Rheumatology=16; Pediatric Rheumatology=4 and Radiology=1). After 3 Delphi rounds (88% participant response rate), 46 items were eliminated. An additional 28 items were eliminated by factor analysis, leaving 68 potential candidate criteria items. The top 5 rated items were ear swelling sparing the lobe, ear deformity, subglottic stenosis, tracheomalacia, and periostochondritis on biopsy. Several retained items were representative of early disease features rather than damage including hoarseness, anterior neck pain, arytenoid inflammation, and costochondritis. The top-rated organ systems were ear, upper and lower airway, and musculoskeletal. The lowest rated organ systems were skin, gastrointestinal, and neurological.

Conclusion: This consensus exercise generated a preliminary set of candidate items for use in developing classification criteria for RP through prospective data collection. The final list of candidate items included features of early-stage disease activity and later-stage damage. Development of classification criteria that represent the broad spectrum of clinical presentations in RP will facilitate the design and implementation of clinical trials in this complex disease.
**Title:** Relapsing polychondritis in a pediatric population: results of a patient survey indicate significant disease burden, diagnostic delay, emergency room utilization, and negative impact on school attendance

**Authors:** Marcela Ferrada, Casey Rimland, Ninet Sinaii, Keith Sikora, Robert Colbert, Peter C Grayson and James D Katz

National Institutes of Health, NIAMS

**Purpose/Methods:** Relapsing polychondritis (RP) is a rare autoimmune disease characterized by recurrent episodes of chondritis. The pathogenesis of RP is poorly understood, and clinical manifestations can be variable resulting in diagnostic delays, especially in pediatric patients where the disease is under recognized. A survey based on known clinical symptoms of RP was developed. The Relapsing Polychondritis Awareness and Support Foundation administered the survey by posting the link to it on the Relapsing Polychondritis pediatric support group. The survey met criteria for exemption from IRB review per CFR 46 and was approved by the Office of Human Subjects Research Protections.

**Results:** 24 surveys were completed. Patients were predominantly male (62.50%, n=9) and Caucasian (70.83%, n=17). The mean age that symptoms of RP were first noticed was 8.0 (SD 6.0 yr), while the mean age at diagnosis with RP was 11.2 (SD 6.8 yr). The majority (62.5%, n=15) saw more than 3 doctors prior to diagnosis and were most commonly diagnosed by a Rheumatologist (45.8%, n=11) or ENT (33.3%, n=8). The most common symptom prior to diagnosis was ear pain/redness (87.5%, n=21). 58.3% (n=14) reported joint pain or swelling prior to diagnosis. 37.5% (n=9) reported symptoms suggestive of airway involvement. 16.7% (n=4) reported developing tracheomalacia requiring tracheostomy. 37.5% (n=9) of patients were diagnosed 1-3 years after symptom onset, however 3 patients (12.5%) were not diagnosed for more than 10 years. 66.7% (n=16) of patients went to the ER prior to diagnosis, with 33% (n=8) going 4 or more times. The top reasons for going to the ER were shortness of breath (37.5%, n=9) or ear pain (33.3%, n=8). Most reported no association between symptom worsening and diet (54.2%; n=13) or physical activity (70.8% n=17). In females, 57.1% (n=4) had worsening of symptoms with menses. 75% (n=18) missed school for more than a week and 54.2% (n=13) missed more than a month due to their disease. 41.7% (n=10) had been treated with steroids and the most common DMARD was methotrexate (41.7%, n=10).

**Conclusions:** Our data suggests that establishing a diagnosis was difficult with most patients seeing more than 3 doctors prior to diagnosis. The most common presenting symptoms were ear pain/redness, but joint pain was also common. The data reported in this cohort provides important descriptions of the presenting features and burden of RP in children including missed school, emergency room visits, joint arthritis, and pulmonary symptoms.
Title: Diagnostic Pitfalls: Syndromic Arthropathies Can Mimic JIA

Authors: Emily C. Gotschlich, Sara Sabbagh, Ann Marie Szymanski, Lawrence Jung, Tova Ronis, Hemalatha Srinivasaalu

Children’s National Medical Center

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic childhood rheumatic disease with a variable disease course and poorly understood pathogenesis. Diagnosis can be difficult and complicated by the fact that there are many syndromes with joint complaints and examinations that can mimic JIA. We present 4 cases of syndromes associated with arthropathy to illustrate this point.

Case Descriptions:

Case 1: H Syndrome
A 10-year old girl presented with polyarthralgia involving small joints of hands and feet associated with one year of flexion contractures responsive to NSAIDs. She had hairy plaques over extremities, proptosis, camptodactyly and hammer toes. She had a mass in the labial folds that on biopsy showed histiocytic infiltration with plasma cells on lymphoid nodules. A genetic analysis revealed homozygous mutation in SLC29A3 gene confirming the diagnosis of histiocytosis-lymphadenopathy plus syndrome or H-syndrome.

Case 2: COPA Syndrome
A 12-year-old boy with chronic lung disease, failure to thrive and seizures presented with months of joint stiffness, polyarthritis and nodules over the joints of the hands. Laboratory evaluation revealed a positive ANA, HLA-B27, rheumatoid factor and anti-CCP antibodies. Biopsy of nodules was consistent with rheumatoid nodules. Genetic evaluation revealed a p.W240R variant of the COPA gene giving diagnosis of COPA Syndrome (syndrome of autoimmunity characterized by high-titer autoantibodies, inflammatory arthritis and interstitial lung disease).

Case 3: CACP Syndrome
A 4-year old female presented with wrist and knee pain, stiffness and swelling along with flexion deformity of fingers and trigger fingers. The symptoms responded poorly to NSAIDs, Methotrexate and anti-TNF agents raising concerns for an alternate diagnosis. Genetic testing revealed homozygous mutation in the PRG4 gene coding human lubricin confirming a diagnosis of camptodactyly, arthropathy, coxa vara, pericarditis syndrome.

Case 4: MONA Syndrome
A 2-year old boy with congenital heart disease and coarse facial features presented with stiffness of bilateral hands and puffiness over hands and feet. He had evidence of polycythemia and diffuse osteopenia. Genetic testing for skeletal dysplasia revealed two mutations in the MMP2 gene, consistent with MONA (multicentric osteolysis, nodulosis and arthropathy).

Significance: These syndromes each have features of arthropathy that mimic JIA. Each syndrome manifests with systemic features often involving other organs. Some of these syndromes are
characterized by a non-inflammatory arthropathy and normal inflammatory markers. Differentiation from JIA is crucial given the different management for inflammatory versus non-inflammatory arthropathy, particularly given the side effects of treatment in JIA.
Title: Features of IF-ANA Negative Systemic Sclerosis

Authors: Mayce Haj-Ali, Sean McNish, Derek Jones, Victoria K Shanmugam

George Washington University

**Background:** Systemic Sclerosis (SSc) is an autoimmune disease characterized by inflammation, fibrosis, and vasculopathy. More than 90% of patients with SSc test positive for anti-nuclear antibodies using immunofluorescence (IF-ANA) as well as for scleroderma specific extractable nuclear antibodies such as topoisomerase (Scl-70), centromere, THTO, U3RNP, U1RNP and RNA Polymerase III. However, a small subset of scleroderma patients test negative for anti-nuclear antibodies. The purpose of this study was to investigate whether scleroderma patients with negative IF-ANA had different characteristics when compared to scleroderma patients with positive IF-ANA.

**Methods:** This study was IRB approved and all patients consented to be included in the study. At the time of data lock, 65 patients fulfilled diagnostic criteria for systemic sclerosis. Data was collected on patient demographics, autoantibody profile, and disease characteristics.

**Results:** Of the 65 patients, 49 had positive IF-ANA and 16 had negative IF-ANA. There was no significant difference in age, sex, race or scleroderma subtype (sine, limited, diffuse, or localized) between the IF-ANA positive and negative groups. The IF-ANA negative group were more likely to have positive U3RNP (p=0.009).

**Conclusion:** The U3RNP is one of the nucleolar antibodies which is known to be missed using direct ANA testing; however, this study shows that this antibody subtype may also be missed using the IF-ANA test. This is an important finding since scleroderma patients with U3RNP are at higher risk for life threatening complications of scleroderma including pulmonary hypertension and pulmonary fibrosis.
**Title:** Prophylactic treatment of Amyopathic Dermatomyositis without ILD to prevent future development of ILD

**Authors:** Arash Hassantoufighi1, Sunita Dia2, Christopher Collins1

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**Case Description:** Amyopathic dermatomyositis is characterized by the typical symmetric skin rash but without muscle involvement. Despite the lack of muscle weakness, many patients complain of debilitating fatigue. Previous findings suggest that patients with amyopathic dermatomyositis have increased risk of developing interstitial lung disease. We present a case of amyopathic dermatomyositis in a young Asian male who presented with acute onset of unilateral right sided periorbital edema, redness and typical Gottron like papules without any pulmonary symptoms. His work up did not show any signs of interstitial lung disease (ILD). However, given that majority of patients with this diagnosis eventually develop ILD and have a poor prognosis with high mortality, we decided to treat him prophylactically with pulsed dose steroids followed by either tacrolimus or rituximab or both.

**Discussion:** No treatment guidelines have been established to help clinicians treat clinically amyopathic dermatomyositis patients especially those without interstitial lung disease at diagnosis. Current treatment principles are based largely on physicians experience and are extrapolated from protocols suggested to treat interstitial lung disease associated with systemic sclerosis. Initial management involves treatment with high dose prednisone or methylprednisolone pulse plus steroid sparing agents such as methotrexate, hydroxychloroquine, cyclosporine, cyclophosphamide, azathioprine, or tacrolimus. Rituximab is used increasingly in patients with myositis that is refractory to other therapies. With respect to ILD, some patients treated with rituximab have demonstrated improvement in forced vital capacity (FVC), DLCO and regression of ground glass opacities (GGOs) on follow up HRCT. Given association with RP-ILD and high mortality, should we treat these patients aggressively before development of lung disease? And, would this early and intensive treatment will alter prognosis and progression of disease to interstitial lung disease? This has not been established or reported. Our patient is currently four month out of initial diagnosis and is doing well. Only time will tell if this patient will develop ILD in the future, or will early treatments with tacrolimus/rituximab will prevent development of ILD in this patient.

**Conclusion:** A prompt diagnosis of anti MDA-5 antibodies and awareness of its association with rapidly progressive interstitial lung disease in amyopathic dermatomyositis patients is important in disease management. Interstitial lung disease carries a worse prognosis and associated with high mortality, and therefore early and aggressive therapy is warranted. There are neither guidelines nor any prior studies showing how these patients without ILD at diagnosis should be managed. It will be interesting to follow response to early aggressive treatment in our patient to see if our interventions alter progression and/or development of ILD.
Figure 1. Manifestation of amyopathic dermatomyositis as right periorbital edema and erythema (Panel A) and pruritic papular rash on dorsum of his hands (Panel B) that developed after 1 month of his initial presentation.
Title: Acute Calcific Periarthritis

Authors: Suneetha Jasty, Paloma Alejandro

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Introduction: Acute periarticular calcification is a condition associated with juxta articular deposits of calcium hydroxyapatite. Although it is a self-limited disease, it is often misdiagnosed and over-treated. The following is a case of acute calcific periartthritis (ACP) involving metacarpophalangeal (MCP) joint of left 5th digit.

Case Report: 38-year-old female patient with history of asthma and gastroesophageal reflux disease presented to emergency department due to severe left-hand pain and swelling. Symptoms developed three days prior to presentation. She denied any trauma, fever, or systemic complaints. She works as a patient transportation technician. On examination, she had redness, swelling and tenderness localized to the left fifth MCP joint. The range of motion at the left fifth MCP joint was restricted both actively and passively.

Radiographs showed a curvilinear calcific density adjacent to radial aspect of the MCP joint of left fifth finger (Fig. 1). Laboratory investigation revealed normal leukocyte count, normal serum uric acid, calcium, phosphorus, parathyroid hormone levels and normal inflammatory markers (ESR and CRP). Blood cultures and nucleic acid amplification tests (NAATs) for Chlamydia trachomatis and Neisseria gonorrhoeae were negative. Based on these findings, a diagnosis of ACP was made. Nonsteroidal anti-inflammatory drugs (NSAIDs) were administered to the patient along with ice packs and rest. Two weeks later patient had complete resolution of symptoms with no further recurrence.

Discussion: ACP is a form of calcium deposition disease that can present with acute, severe periarticular pain in the hand1. It has been described by a variety of terms, such as calcific tendinitis, peritendinitis, calcareous tendonitis, peri arthritis calcarea and hydroxyapatite rheumatism2. It most commonly affects the shoulder followed by the hip and knee joints. Though less common, it has also been described in the interphalangeal, metacarpophalangeal and dorsal wrist joints3,4,5. The pathogenesis of the disease is not fully understood but associations with alterations in vascularization, hypoxia, trauma and metabolic disorders have been postulated3,6. An association with repetitive micro trauma has been reported7. Acute presentation of this condition includes, as in our case, pain, swelling, erythema and...
restriction of motion of the involved joint. Diagnosis requires both clinical and radiological findings. Based on the clinical presentation, infection must be ruled out. The presence of calcification in the radiograph makes infection unlikely. ACP is a self-limiting disease and usually resolves in 3 to 4 weeks even if not treated. Recurrence is uncommon. Treatment involves conservative measures such as splinting and non-steroidal anti-inflammatory drugs.

Though ACP is a common entity, its relatively uncommon occurrence in the hand can lead to misdiagnoses, resulting in unnecessary treatments including surgeries and antibiotics. A detailed history together with diagnostic imaging allows for an adequate diagnosis in most cases avoiding unnecessary treatments.

Figure 1. Posteroanterior radiograph of left hand demonstrating periarticular calcium deposition at little finger metacarpophalangeal joint
**Title:** A Curious Case of Aortopathy

**Authors:** Alyssa Johnson, Erica McBride, Arman Majumder, Saira Bilal

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**Background:** Cystic Medial Degeneration (CMD) is a disorder of typically large arteries, particularly of the aorta, and can be associated with congenital vascular diseases such as Ehlers Danlos or Marfan syndrome. CMD can be a diagnostic challenge for rheumatologists as it is a known vasculitis mimicker, thus PET scan is a vital diagnostic tool in differentiating between vasculitic and non vasculitic etiologies when evaluating large vessel aneurysms. Here we present a case of a dilated aortic aneurysm and new onset Deep Venous Thrombosis (DVT) in a young patient where radiotracer uptake was noted on PET with initial concern for vasculitis, however histopathology revealed cystic medial degeneration.

**Case Presentation:** A 28-year-old African American male with past medical history significant for surgically-managed congenital patent ductus arteriosus presented to an outside hospital with right lower extremity pain and swelling with Venous Dopplers revealing a large occlusive distal DVT extending from the common femoral and popliteal veins. CT angiography revealed a 5.9 cm mid ascending thoracic aneurysm, and a 3.2 cm pulmonary artery dilatation. The patient was transferred to our institution for further surgical management of his aortic aneurysm.

Laboratory Evaluation revealed an ESR of 0, and CRP 37.1. HIV, RPR, Hepatitis B surface antigen, Hepatitis b Core antibody, Quantiferon Gold, ANA-IFA, Anti-dsDNA, Rheumatoid Factor, anti-CCP, ACE, C3, C4, HLA-B27, HLA-B51, and ANCA panel were all within normal limits. PET/CT revealed increased radiotracer uptake throughout the right lower extremity vasculature and a small focus in the ascending aorta. MRI/MRA of the brain revealed enlarged bilateral internal carotid artery aneurysms. Pulse dose methylprednisolone therapy was initiated following results of PET and patient underwent successful surgical aortic root aneurysmal repair. Surgical Pathology of aortic tissue revealed cystic medial degeneration without evidence of prominent lymphocytic infiltrate in the intima and tunica media; though a small focal lymphoplasmacytic infiltrate was identified in the aortic adventitia “without strong morphologic evidence of vasculitis.” Familial genetic aortopathy panel returned positive for a heterozygous missense mutation in the Smooth Muscle Alpha Actin Protein (ACTA2).

**Discussion:** This case illustrates the necessity of maintaining a broad differential when considering the etiology of arterial aneurysms in varying size vessels in a young patient. In our patient, radiotracer uptake was noted in the aorta and lower extremity vessels, but histopathology of aortic tissue was consistent with cystic medial degeneration. Mutations in the ACTA2 protein are associated with familial syndromes of Thoracic Aorta Aneurysms, premature Coronary Artery Disease and Moya Moya Disease.
Title: The Many Faces of Livedo Reticularis

Author: Maryann Kimoto

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Introduction: Livedo reticularis (LR) can be benign, or secondary to systemic disease, most commonly antiphospholipid syndrome with and without associated systemic lupus erythematosus. Rare manifestations of LR taken from cases observed at the Veteran Affairs Medical Center and Medstar Georgetown University Hospital observed between 2/2018-3/2018 are reported here.

Case 1: A 30-year-old female with a history of new-onset, idiopathic pancreatitis presented to our clinic for evaluation of a rash, which began one week following her first episode of pancreatitis and is improving. The rash was coarsely reticulated and non-palpable along the anterior thighs on examination. Laboratory studies demonstrated a borderline positive ANA of 1:80 and mildly elevated sedimentation rate of 21, but an otherwise negative work-up for antiphospholipid syndrome and connective tissue disease. Rare case reports suggest LR can be associated with pancreatitis, possibly due to vascular damage from circulating trypsin, and resolving with resolution of pancreatitis.

Case 2: A 66-year-old female with a history of diabetes, heart failure, chronic kidney disease and a non-healing wound for the past month presented with worsening skin lesion and pain of the right calf. An ulcer with eschar was noted without drainage, warmth or odor, in addition to a mild, coarsely reticular rash on the left posterior calf. Rheumatology was consulted due to concerns for livedoid vasculopathy, and a negative vasculitis work-up was completed. A skin biopsy was performed and diagnostic of calciphylaxis. LR can be an early skin manifestation of nonuremic calciphylaxis. Our patient was continued on aspirin and initiated sodium thiosulfate infusions.

Case 3: A 66-year-old female with limited scleroderma, anti-centromere and anti-La antibodies, long-standing Raynaud’s phenomenon and sicca symptoms presented to our clinic to establish care. An incidental finely-reticulated, red skin discoloration was noted on the upper and lower extremities bilaterally, which began years ago following treatment for a multi-drug resistant jaw osteonecrosis. Her exam demonstrated dry oral mucosa and sclerodactyly of the 2nd and 3rd digits bilaterally. Laboratory work-up demonstrated expected positive antibodies for Ro, centromere and ANA, but was otherwise negative. LR has been reported as a skin manifestation of hypersensitivity vasculitis following antibiotic exposure and certain infections, and as a non-vasculitic skin feature associated with Sjögren’s syndrome. LR is not commonly reported with scleroderma.

Conclusion: We discuss three recent cases that presented to our Rheumatology service, with skin manifestations consistent with livedo reticularis, with rare underlying etiologies attributed to pancreatitis, nonuremic calciphylaxis and Sjögren’s syndrome.
Title: A unique and rare case of overlap of three uncommon diseases: sarcoidosis, polymyositis and systemic sclerosis, further complicated by severe restrictive lung disease.

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Background and Objective: Multisystem autoimmune/inflammatory diseases are uncommon and their overlap is rare. Here we present an interesting but challenging case of an overlap between three uncommon diseases.

Method and Analysis: This is a 61 years old African-American male with history of pulmonary sarcoidosis that was diagnosed in 2016 with trans-bronchial lung biopsy and EBUS Lymph node (LN) biopsy showing non-caseating granulomas. CT chest showed pulmonary fibrosis that had progressed. At that time, he refused treatment including methotrexate and mycophenolate. He was subsequently diagnosed with cardiac sarcoidosis based on cardiac MRI showing focal transmural late gadolinium enhancement within the basal anterior wall and atrial arrhythmias requiring ablation. Echocardiogram showed ejection fraction of 35%. A follow up CT chest in 2017 was unchanged with extensive honeycombing, traction bronchiectasis and lymphadenopathy. Pulmonary function testing showed a severe restrictive lung disease with FVC of 37%, TLC of 48% and DLCO of 33%. Pulmonary artery pressure was inestimable in ECHO due to lack of tricuspid regurgitation.

He was also diagnosed with scleroderma by positive skin biopsy and features of systemic sclerosis including dysphagia, GERD, recurrent (pseudo) bowel obstruction, sclerodactyly and Raynaud phenomenon. Colonoscopy showed abnormal appearing mucosa without folds in transverse colon. Further work up revealed a high titer ANA (1:640, speckled), and strongly positive anti-SSA antibody but scleroderma specific antibodies were negative. He was subsequently diagnosed with polymyositis due to mild weakness in his bilateral thigh flexors (4/5), high CPK at 873, high aldolase at 11.8 and positive anti-Jo1 antibody at 2.1. He however did not follow up to complete MRI of thighs.

Results: This patient was treated with prednisone 1mg/kg with a slow taper. A follow up PET CT while on prednisone showed an abnormal whole body 18FDG uptake showing widespread active disease involving multiple bones, widespread chest and abdominal LNs, bilateral pulmonary groundglass opacities and diffuse, patchy myocardial uptake involving multiple ventricular walls. Steroid-sparing treatment is planned.

Conclusion: Overlap syndrome with different multisystem inflammatory diseases is not common and poses a challenge in disease management. In our patient, it is difficult to find a specific steroid sparing agent to target all of his diseases. Moreover, his interstitial lung disease (ILD) can be related to any of the three diseases and response to a specific therapy might be different depending upon its etiology.
**Figure 1:** 18FDG PET: abnormal diffuse, patchy myocardial uptake involving multiple ventricular walls and metabolic activity coiling to interstitial infiltrate at right lung base.

**Figure 2:** CT chest WO Contrast: Bilateral (right more than left) basal interstitial fibrosis with bronchiectasis
Title: Baricitinib, a Janus Kinase Inhibitor, in the treatment of Rheumatoid Arthritis: A Meta-analysis of Randomized Controlled Trials

Authors: Sumit Kunwar, Christopher E. Collins, Florina Constantinescu

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Introduction/Objective: Tyrosine protein kinases including Janus Kinases (JAKs) are a part of intracellular signaling pathway which are activated by pro-inflammatory cytokines and are involved in pathogenesis of RA [1]. JAK inhibitors work by inhibiting these intracellular signaling pathways. Baricitinib is an oral, selective and reversible inhibitor of JAK1 and JAK2 [2]. This meta-analysis aims to aggregate currently available data to assess the overall efficacy and safety of baricitinib in RA.

Methods: We searched PubMed, EMBASE and Cochrane CENTRAL from inception through 05/25/17 without language restriction. Our eligibility criteria included human placebo-controlled RCTs in adults (≥18 years of age) that evaluated efficacy and safety outcomes of baricitinib in RA patients. We excluded meeting abstracts without full text publication. We used RevMan 5.3 to perform meta-analysis between groups on baricitinib 4mg per day and placebo using random effect model calculating odds ratio (OR) as well as 95% confidence interval (CI). I² statistic was used to identify heterogeneity between studies, and values of more than 50 was used to indicate significant heterogeneity. We measured efficacy using ACR20/50/70 and DAS28-CRP response criteria and safety with adverse events.

Results: Compared to placebo, 2mg of baricitinib was more effective in achieving ACR20 [54 vs. 36.6%; OR 2.09; 95% CI 1.60-2.71; p<0.00001; I² 0%], ACR50 [31.6 vs. 10.3%; OR 2.3; 95% CI 1.68-3.15; p<0.00001; I² 0%] and ACR70 responses [18.7 vs. 5.1%; OR 4.05; 95% CI 2.54-6.44; p<0.00001; I² 0%]. Similarly, 4mg of baricitinib daily was more effective than placebo. Baricitinib 2mg once daily did not increase any adverse events [65.3 vs. 62.4%; OR 1.03; 95% CI 0.80-1.34; p=0.8; I² 0%], serious adverse events [3.5 vs 5%; OR 0.68; 95% CI 0.37-1.27; p=0.22; I² 0%] and herpes zoster [1.2 vs. 0.4%; OR 2.34; 95% CI 0.27-20.47; p=0.44; I² 37%] as compared to placebo. Similarly, 4mg of baricitinib did not increase the risk of serious adverse events but increased herpes zoster infection [OR 3.88; 95% CI 1.36-11.06; p=0.01; I² 0%] when compared to placebo.

Conclusion: Baricitinib is effective in treatment of RA and did not appear to have significant safety concerns during the first six months of treatment.

References
Title: Two Cases of Sarcoidosis Involving the Spine

Author: Katherine Maher

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Introduction: Clinically significant neurosarcoidosis is present in 15% of cases. Generally, there is apparent sarcoidosis elsewhere and not just isolated to the spinal cord. This abstract presents two patients who presented with lower extremity weakness with a final diagnosis of sarcoidosis involving the spinal cord after supporting lymph node biopsy.

Case Descriptions:
Case #1: A 37-year-old African American gentleman with a prior history of HTN who initially presented to the ED with complaints of progressive lower extremity weakness, changes in sensation, and weight loss for two months. He was initially diagnosed with CIPD. However, on a CT of the chest he was noted to have lymphadenopathy concerning for lymphoma. Lymph node biopsy showed noncaseating granulomas and PET/CT scan also showed lymphadenopathy consistent with sarcoidosis. A MRI brain and spine was significant for circumferential enhancement of the spinal cord from T10 to the conus and of multiple nerve roots of the cauda equina, consistent with sarcoidosis. He was started on IV methylprednisolone, and eventually PO steroids and methotrexate.

Case #2: A 54-year-old African American gentleman with a history SVT, HTN who was originally diagnosed with longitudinal transverse myelitis in 2013 after presenting with increasing symptoms of lower extremity weakness and paresthesias. He underwent an extensive evaluation including neoplastic, paraneoplastic, infectious, and rheumatologic, all of which was initially unrevealing. MRI of the spine was significant for abnormal cord signal at C1-T2. His symptoms responded well to IV methylprednisolone; however, the patient was frequently lost to follow up and would present with recurrent symptoms. His treatments included IV methylprednisolone, PLEX, and rituximab. He had a lymph node biopsy in 2016, after complaining of neck fullness, which showed noncaseating granulomas. He was subsequently diagnosed with neurosarcoidosis and treated with methotrexate and infliximab.

Discussion of Cases: Sarcoidosis involving the spine is reported in roughly 5-15% of cases. Presenting symptoms are variable and nonspecific, (for instance weakness, paresthesias, and demyelinating syndrome), creating a diagnostic challenge. It can mimic multiple sclerosis, metastasis, and primary malignancies. When it does present it is most likely to be in the cervical spine (56%), as in Case #2, then in the thoracic spine (37%), and most rarely in the lumbar spine (7%) as in Case #1. It is most commonly seen in male (20-40yo) patients of Northern European or African descent.

Conclusion: Recognition that, while rare, sarcoidosis may only present with neurologic symptoms, with localized abnormalities to the spinal cord is important to recognize as to not delay treatment.
Case #1: Sagittal T2-weighted MRI lumbar spine
Title: RGS proteins in SLE

Authors: Mastin, P.¹, Edison, J.¹, Moratz C.²

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Background/Objectives: The regulators of G-protein signaling (RGS) proteins are a group of evolutionarily conserved proteins that modulate the duration and intensity of G-protein-coupled receptors (GPCR) signaling. In innate and adaptive immunity a subset of RGS isoforms modulate a cell’s responsiveness to chemoattractant receptor signaling. These proteins act to regulate the stop/stay/go response of immune cells during immune surveillance, infection, trauma, and inflammation. In the murine SLE model, animals have an elevated inflammatory background and a hyper-inflammatory response to tissue injury. We have previously shown a rapid and excess influx of immune cells into areas of tissue damage that do not recirculate out of the tissue, indicating a breakdown in normal resolution of immune responses/inflammation.

The function of RGS proteins is to modulate the strength and duration of GPCR signaling, such as chemokines and immune inflammatory mediators. The objectives of the current study are to determine if an alteration in RGS expression levels in the lymphocytes involved in tissue injury correlate with the hyper-responsiveness of these cells in the murine model of SLE. This data will determine if the RGS proteins can provide a mechanistic explanation of the hyper inflammatory background in SLE.

Methods: Using a superior mesenteric artery ischemia model, we compared the RGS proteins expression patterns in infiltrating lymphocytes using the mesenteric ischemia/reperfusion induced tissue injury between immune competent (C57BL/6) and autoimmune prone (B6.MRL/lpr) mice. Tissue sections were used in immunofluorescent staining analysis to determine RGS-1,2,10, and 13 expression in immune cells. We compared sham and ischemic groups of both strains to determine expression patterns.

Results: RGS1 and RGS10 expression was detected by immunofluorescent staining of tissue sections and RGS2 and RGS13 were not detected. RGS1 and RGS10 expression was only elevated in the B6.MRL/lpr autoimmune strain but not within the C57Bl/6 non-autoimmune strain.

Conclusion: Initial data indicate differential expression patterns of RGS1 and RGS10 after injury. An initial interpretation of this data is that in the B6.MRL/lpr animal’s expression of RGS1 and RGSS10 suggests that these immune cells will be resistant to egress chemotaxis signals. Completion of the analysis will determine if this expression pattern in the autoimmune animals is significantly different. Given that they act as a central control point in GPCR signaling cascades, RGS proteins are promising targets for drug development. Developing compounds that act as agonists or antagonists of GPCRs could provide an opportunity to target the protein-protein interactions that regulate intracellular signaling downstream of GPCRs.
Title: Fever of Unknown Origin and Symmetric Inflammatory Polyarthritis Prompting Transpacific Military Relocation to Tertiary Level Care Center

Authors: Hector Medina, Michael Loncharich, Robert O’Brian

Walter Reed National Military Medical Center,

Introduction: Adult rheumatoid arthritis (RA) as the cause of fever of unknown origin (FUO) is rarely reported in the literature, and fever in RA warrants exploration for alternative diagnoses. The differential includes infection, malignancy and other rheumatic disease. The anti-synthetase syndrome is a rare entity which may feature arthritis, myositis, interstitial lung diseases (ILD), fever, Raynaud’s phenomenon, and mechanic’s hands. The presence of autoantibodies against aminoacyltransfer RNA–synthetases are detected in association with the condition. The clinical features may be variably present and can be additive through time which may create a diagnostic challenge for clinicians.

Case Description: The patient is a 33 year old woman with a history of Raynaud’s phenomenon and seronegative, non-erosive RA with symmetric inflammatory synovitis of the proximal interphalangeal, metacarpophalangeal, wrist, and knee joints. Her ten-year disease course was notable for recurring flares despite multiple DMARD and biologic therapies. She developed FUO with several months of daily fevers up to 104°F. Extensive work up was negative for drug fever, infection, and malignancy. Her diagnosis of RA was deemed the culprit for her fevers and anti-IL 6 therapy was initiated, which resolved her fevers but not her arthritis. This prompted non-urgent trans-pacific military relocation to tertiary level care center where the diagnosis was revisited. Cessation of all medications resulted in worsening arthritis, proximal muscle weakness, and progressive dyspnea. Laboratory evaluation was notable for negative rheumatoid factor, negative anti-cyclic citrullinated peptide, elevated creatine phosphokinase, and elevated aldolase. Suspicion for myositis was confirmed with a myositis protocol MRI and muscle biopsy of the thigh, both consistent with inflammatory myopathy. High-resolution chest CT revealed Non-Specific Interstitial Pneumonitis. Serologic testing was positive for anti-Ro 52 Kd antibody and for the anti-synthetase antibody anti-Jo-1. Her clinical features and antibody profile were consistent with a diagnosis of anti-synthetase syndrome, prompting treatment with rituximab, methotrexate, and prednisone, with favorable response.

Discussion: This case illustrates the importance of a careful approach to the assessment of new symptoms in a patient with a known rheumatologic diagnosis. Rare manifestations of well-defined diseases should raise consideration for an alternative diagnosis. Anti-synthetase syndrome poses a challenge due to its rarity, heterogeneity within its clinical spectrum, and variable timing of symptom onset. Recognition of clinical inconsistencies in this case led to a more appropriate diagnosis of anti-synthetase syndrome and successful therapy with rituximab, which was chosen due to the presence of anti-Jo-1 and anti-Ro-52 kDa autoantibodies.
Title: EIEIO: Eye Inflammation and Ear Inflammation Overlap

Authors: Alaa Mohamed, Marcela Ferrada, James D. Katz, Peter Grayson

National Institutes of Health/NIAMS

Case description: A 44-year-old female with a past medical history of type 1 Diabetes Mellitus developed sudden unilateral hearing loss and vertigo. ENT evaluation revealed left-sided sensorineural hearing loss. Patient was treated with 60 mg of Prednisone with improvement of her symptoms. In the subsequent 5 months, she experienced red and painful eyes due to bilateral interstitial keratitis (IK). She was assigned a diagnosis of Cogan’s syndrome. Treatment with methotrexate for 6 months was unsuccessful, followed by unsuccessful treatment with Infliximab for another 6 months. Rituximab resulted in partial improvement of her hearing loss. In the subsequent 3 months she experienced severe, aching nose pain and pressure, followed by left ear pain and swelling. Upon evaluation at the NIH, her history confirmed intermittent episodes of shortness of breath, dry cough and voice changes. Visualization of ear inflammation on a PET CT scan (IMAGE 1), air trapping on dynamic CT scan, arytenoid swelling on direct laryngoscopy visualization, with synovitis on physical exam ultimately led to further reassignment of her diagnosis to that of relapsing polychondritis.

Case discussion/significance: Relapsing Polychondritis (RP) is a rare condition that can affect multiple organs other than the ear including the airway, inner ear, vasculature and the eye. Cogan’s syndrome (CS) is also a rare entity, characterized by the presence of non-syphilitic interstitial keratitis (IK) and bilateral cochlear and vestibular dysfunction that resemble Ménière-like attacks. The atypical form of Cogan's syndrome is defined by presence of eye and/or ear involvement of a different type than IK or Ménière-like attacks, or by the interval between onset of ocular and audiovestibular manifestations exceeding 2 years. Here we present a case of a patient with CS and RP.

Eye inflammation with ear inflammation overlap (EIEIO) presents a diagnostic challenge. Symptoms may present sequentially rather than simultaneously, thereby leading to diverse diagnoses. Distinguishing these various differential considerations requires longitudinal assessment while testing to rule out infectious causes (e.g., syphilis), vasculitic causes (e.g., GPA), genetic causes (e.g., Usher syndrome) and autoimmune causes (e.g., relapsing polychondritis). Overlap cases of CS and RP have been described in various case reports, raising the possibility that these two rare entities represent ends of a single spectrum of disease.
Title: Intravenous Immunoglobulin in Combination with Intravenous Methylprednisolone in the Treatment of Calcinitis Associated with Juvenile Dermatomyositis (JDM)

Authors: Marc Phillpotts, Eman Alshaikh, Yaseen Aleatany, Olcay Y Jones, Gulnara Mamyrova, Lisa G Rider, Rodolfo V Curiel

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

Methods: Retrospective medical record review of over 200 JDM patients seen from 2008-2017 at The George Washington Myositis Clinic was performed. 53 of JDM patients developed calcinitis, 15 had at least one follow-up visit and 11 were identified that received IVIG treatment for calcinitis. The number of anatomic areas with calcinitis (head, upper extremities, lower extremities, chest, back, abdomen and buttocks), and the number of joints with improved range of motion (ROM) at final visit were used to assess treatment response. Additionally, the areas with calcinitis were assessed for presence of inflammation.

Results: The median [IQR] age at baseline was 14 [12-16] years. The median [IQR] duration of IVIG treatment from baseline to final visit in calcinitis was 16 [9-60] months, with a dose ranging between 1g/kg- 2g/kg per month. At the time of the IVIG infusion, patients also received IV Methylprednisolone ranging from 100 mg to 1,000 mg. Treatment also included methotrexate (10 patients), oral prednisone (7 patients), rituximab (2 patients), infliximab (1 patient). The median [IQR] number of anatomic areas with calcinitis was 6.0 [1.0-7.0] pre- and 8.0 [2.0-8.0] post-treatment. The median [IQR] number of areas with inflammation was 2.0 [1.0-6.0] pre- and 1.0 [0.0-3.0] post-treatment. The number of restricted joints decreased in 7 out of 10 patients. 9 out of 10 patients with restricted joints movement at baseline demonstrated an improved ROM at the final evaluation visit (p=0.0011).

Conclusion: IVIG in combination with IV methylprednisolone may improve the level of functional disability and quality of life in JDM patients with calcinitis. Larger, controlled studies are needed to determine the effectiveness of immunosuppressive and immunomodulatory therapies for treatment of calcinitis associated with JDM.
Title: Biologics for the Treatment of Cardiac Sarcoidosis

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Background: Cardiac sarcoidosis is associated with significant morbidity and mortality and thus, is an indication for early treatment with immunosuppressive agents. There are currently no guidelines for the management of cardiac sarcoidosis. Corticosteroids remain the mainstay of treatment, with or without steroid sparing agents such as methotrexate, MMF or azathioprine. There are only a few case reports on the treatment of cardiac sarcoidosis with biologics, however it appears to be a reasonable option in severe or refractory cases. Here we present a case of cardiac sarcoidosis treated with adalimumab and methotrexate.

Case Description: 44 yo AAF with multisystem sarcoidosis, diagnosed per lymph node biopsy, presented to us for evaluation and management. Initially, her sarcoidosis was limited to skin, maxillofacial sinuses and lymph nodes. In 2016, she began to note irregular heartbeats, palpitations and chest discomfort. She was found to have recurrent PVCs. She subsequently had a cardiac MRI, which was consistent with cardiac sarcoidosis. She was started on prednisone and cellcept. She had a PET a few months later showing persistent active sarcoidosis involving LV walls and the aortic arch, multiple lymph nodes and the gastric wall. ECHO revealed normal left ventricular systolic function. Following review of her case, she was started on methotrexate 15mg weekly and adalimumab 40mg weekly and continued on prednisone 20mg daily, with the goal of tapering and following up with a PET in a few months.

Discussion: Sarcoidosis is a multisystem inflammatory disease of unknown etiology characterized by T-lymphocyte infiltration and formation of non-caseating granulomas. Cardiac involvement is a rare but potentially life-threatening complication of the disease. Although corticosteroids and other immunosuppressive agents such as methotrexate, mycophenolate mofetil or azathioprine are often used for treatment, those cases that prove refractory to standard therapy pose a dilemma. Given that TNF plays a central role in the formation and maintenance of granulomas, one would assume that anti-TNF biologics would be a good therapeutic option. However, there is limited data on their clinical effectiveness for cardiac sarcoidosis, especially due to concern for worsening/new-onset heart failure with their use. The published literature thus far consists of 3 case reports showing effective treatment of cardiac sarcoidosis with biologics such as adalimumab, infliximab and rituximab. There is a great need for more data, particularly prospective studies and RCTs, in order to be able to assuredly treat those with severe disease. Our patient is tolerating her treatment well and we hope to note improvement in disease activity on her repeat PET scan.

Conclusion: Cardiac involvement is diagnosed clinically in only 5% of patients with sarcoidosis but is associated with significant morbidity and mortality. Although biologics for treatment of cardiac sarcoidosis appear to be promising, there is a great need for more data, particularly prospective studies and randomized controlled trials, in order to be able to assuredly treat those with severe disease.
Title: Initial Presentation and Clinical Course of Anti-MDA5 Antibody-Positive Dermatomyositis

Authors: Nancy D. Sein, Robert J. O’Brien

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Case Description: Clinically amyopathic dermatomyositis (CADM) is a subtype of dermatomyositis (DM) and represents approximately 20% of DM. The myositis specific antibody anti-melanoma differentiation-associated protein 5 (MDA5) predicts CADM and may be associated with rapidly progressing interstitial lung disease (RPLID). Anti-MDA5 positive patients often present with distinctive palmar papules and unique mucocutaneous ulcers in addition to characteristic DM skin manifestations. In this clinical vignette, we describe the initial presentation and clinical course of two CADM patients with anti-MDA5 positivity.

Case Discussion:

Patient 1: A 42-year-old female presented with arthralgia, swelling of the fingers and around the orbits, and skin eruptions. Review of systems was positive for a 10-pound weight loss, oral ulcers, skin eruptions on the hands and elbows, and prolonged stiffness. Physical exam showed a heliotrope rash, Gottron’s sign on the elbows, palmar papules, abnormal nailfold capillaries, and hand synovitis. Further work up revealed positive anti-MDA5 antibodies concomitantly with anti-Ro52 antibodies. Ferritin was within normal limit. She was initially treated with tapered prednisone and methotrexate but methotrexate was discontinued shortly after initiation due to intolerance. We treated her with rituximab (RTX) and she will soon be receiving intravenous immune globulin.

Patient 2: A 51-year-old female presented with intermittent fevers, night sweats, a 10-pound weight loss, and a persistent cough for 3 months. Review of systems was positive for tongue ulcers, a rash on the face and hands, hoarseness, dyspnea on exertion, arthralgia, and weakness in the lower extremities. Physical exam showed periorbital edema, aphthous ulcers, palmar papules, Gottron’s sign on the elbows, abnormal nailfold capillaries, synovitis in the wrists and hands, and proximal muscle weakness. Further workup revealed normal CK and aldolase, a positive anti-MDA5 antibody, elevated ferritin, pulmonary fibrosis on high resolution CT revealed, and non-specific focal gluteal edema muscle edema on MRI. We initially treated her with high dose corticosteroid and started her on RTX.

Discussion: Both of our patients presented with palmar papules and mucocutaneous ulcers that are distinctive features of anti-MDA5 positive CADM. Studies have shown that ferritin is a predictor of ILD and high ferritin is associated with poor prognosis. Patient 2 has pulmonary fibrosis and high ferritin and this may suggest poor prognosis. Patient 1 has positive anti-Ro52 (also associated with ILD) in addition to anti-MDA5 which places her at increased risk of ILD though she has no clinically significant pulmonary manifestations currently. Different combinations of immunosuppression have been used for treatment but no consensus therapy has been identified.
Title: Radiographic Findings in Pseudogout: A Case Presentation and Review of Images

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Case Description: A 68 year old male with a history of hypertension presented to the rheumatology clinic for evaluation of left elbow pain. He first developed acute pain and swelling in the right elbow in the summer of 2017. After 5 days the symptoms resolved without intervention. In the fall he developed acute pain with redness and swelling in the right midfoot which similarly resolved in 5 days. In January 2018 he developed pain in the left elbow, which over the course of 24 hours spread to involve the left wrist and hand, and was marked by dramatic swelling. Again, these symptoms subsided within 5 days. At the time of his presentation to rheumatology clinic the following week he had only mild residual elbow pain. His prior work up between flares revealed a normal complete blood count, complete metabolic panel, and uric acid. Radiographs of the elbows and feet were ordered. The elbow radiographs revealed linear calcification along the triceps tendon. Radiographs of the feet revealed extensive linear calcification in the Achilles tendon proximal to its insertion point and along the plantar fascia (Figure 1), consistent with chondrocalcinosis. These results led to a diagnosis of calcium pyrophosphate deposition disease (CPPD).

Discussion: When evaluating patients for inflammatory arthritis, the presence of chondrocalcinosis can be a clue to a possible diagnosis of CPPD. This finding is commonly seen on wrist and knee radiographs, but the prevalence of chondrocalcinosis in the Achilles tendons and plantar fascia is not known. We reviewed radiographs of 29 patients from the Washington DC VAMC Rheumatology clinic with known crystal-proven CPPD. Of these 29 patients, 21 had foot radiographs available for review. 4 of the 21 patients had radiographic evidence of chondrocalcinosis along the plantar fascia (19.0%), and 6 of 21 had chondrocalcinosis of the Achilles tendon (28.6%). This small review demonstrates that radiographic chondrocalcinosis in the plantar fascia and Achilles is commonly found in patients with CPPD.

Conclusion: Acute monoarticular arthritis can present a diagnostic challenge when it occurs in an atypical joint with a normal serologic work up. Imaging studies can be pivotal in reaching the correct diagnosis. Our case is an example of the usefulness of radiography in reaching a diagnosis of CPPD, and a review of radiographs reveals that the finding of chondrocalcinosis in the Achilles and plantar fascia is common in patients with established CPPD.
Figure 1. Radiographs of the bilateral feet demonstrating extensive chondrocalcinosis of the plantar fascia of the right foot (top) and of the Achilles tendon of the left foot (bottom).
Title: Inflammatory Arthritis Associated with Immune Checkpoint Inhibitors (ICIs): A Report of 6 Patients.

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Background: Cancer immunotherapy aims to enhance the patient’s immune system to induce anti-tumor immunity and has shown benefit in the treatment of different cancers. One modality includes blocking immune checkpoints such as CTLA-4, PD-1 and PD-L1, which are intrinsic down-regulators of T-cell mediated immunity. Several agents targeting these checkpoints, known as immune-checkpoint inhibitors (ICIs), are now approved for the treatment of various cancers. Despite their successes, ICIs can promote inflammatory responses thought to be due to activation of the immune system with involvement of various organ systems.

Methods: We reviewed the medical records of patients who presented to NIAMS rheumatology consult service for ICI related joint manifestations. Demographics, clinical presentation, laboratory data and imaging studies were tabulated for purposes of discovering common characteristics and pattern of presentations.

Results: There were 6 patients who developed joint related symptoms during treatment with various ICIs. None of the patients had prior history of any autoimmune disease. Four patients presented with polyarticular inflammatory arthritis involving small and large joints with synovitis on examination. Two patients had polyarticular arthralgia with no synovitis. Most patients (4/6) developed symptoms within 4 weeks of the use of ICI. One patient had symptom onset after 11 months of ICI use. The total duration of symptoms after stopping ICI ranged from 3 months up to 10 months. Patients had elevated erythrocyte sedimentation rate (range: 34-100 mm/hr) and C-reactive protein (2.6-127 mg/l). All of the patients had negative autoantibodies (Rheumatoid factor, anti-cyclic citrullinated peptide antibody, antinuclear antibody). Joint x-rays did not show signs of erosions. MRI was available in two patients which revealed synovial thickening in one and tenosynovitis in another patient. The majority of the patients failed non-steroidal anti-inflammatory therapy and required systemic corticosteroids for symptomatic control with good response within 1 week of use. One patient was managed with intraarticular steroid therapy owing to an oligo-articular presentation. One patient was unable to taper oral steroids thereby requiring the addition of methotrexate, which was subsequently discontinued after 1 year. Persistent arthritis was the reason for discontinuation of ICIs in three patients.

Conclusion: Seronegative inflammatory arthritis and arthralgia may be a limiting factor in the use of ICIs. Rheumatologists should be aware of these adverse events for accurate diagnosis and early treatment. The underlying pathophysiology of arthritis is still unknown. Future studies are needed to further elucidate the mechanisms of such inflammatory arthritis.
Title: Eosinophilic Granulomatous with Polyangiitis as Immune Reconstitution Inflammatory Syndrome in HIV Infection

Authors: Victoria Fernandes Sullivan, Jeffrey Eickhoff, Jess Edison

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Case Description: Eosinophilic Granulomatous with Polyangiitis (EGPA) is a granulomatous vasculitis of small and medium-sized vessels. Immune Reconstitution Inflammatory Syndrome (IRIS) has many different clinical manifestations, including vasculitides and autoimmune diseases, and occurs in patients with Human Immunodeficiency Virus (HIV) after initiation of antiretroviral therapy. A 56-year-old Kenyan male with a recent diagnosis of HIV presented with tingling of his left hand, burning pain of the left wrist with numbness and muscle weakness. Past medical history was notable for adult onset asthma, pulmonary infiltrates, nasal congestion and discharge.

Physical exam demonstrated immobility of the left wrist and minimal volitional movement of the fingers. Diagnostic workup revealed an elevated ESR of 95 mm/hr, Rheumatoid Factor of 256 IU/mL, Immunoglobulin E of 4778 IU/mL and absolute eosinophil count of 3515 (45%). Infectious disease evaluation for parasitic and sexually transmitted infections was negative. An x-ray of the left wrist was normal. Electromyography (EMG) revealed sensory and motor nerve involvement in the left upper extremity, consistent with mononeuritis multiplex. A sural nerve biopsy showed scattered eosinophils involving the small and medium-sized vasculature and a brisk plasma cell infiltrate highlighted by CD138 immuno stain. A muscle biopsy of the left extensor carpi radialis showed eosinophil-rich granulomata adjacent to the perimysial small muscular artery and an eosinophilic infiltrate of the artery wall. The patient was treated with high dose prednisone and physical therapy, and gradually regained range of motion and strength in the wrist and hand and improvement in neuropathic symptoms.

Case Discussion: We report a patient who developed fulminant EGPA two months after initiation of antiretroviral therapy for HIV infection. His clinical picture was suggestive of EGPA years before his HIV diagnosis, with a peripheral eosinophilia of 6.4% dating back to 2011, adult onset asthma, and sinus congestion and coryza which developed one year prior to the HIV diagnosis. The temporal relationship of HIV infection and initiation of antiretroviral therapy are compelling enough to consider that this is IRIS. This patient had a decrease in viral load from 800 at diagnosis to 195 three months later and development of symptoms two months after starting ART. He also had the CD138 immuno stain on nerve biopsy that can be seen in IRIS.

Conclusion and Significance: We have found two prior cases of EGPA associated with HIV reported in the literature. The exact relationship between the two distinct disease entities remains unclear. Our case report supports that EGPA is a form of IRIS.
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