2014
Clinical Vignette
and Research Competition

Army Chapter Army College of Physicians Meeting 2014
5 Dec 2014

1300-1305: Welcome and introduction from the Army Chapter Meeting Coordinator, MAJ David Callender, MD, FACP. Broadcast from Walter Reed National Military Medical Center, Bethesda, MD

1305-1405: 2014 Updates in Infectious Disease by COL(ret) Glenn Wortmann, MD, FACP. Broadcast from WRNMMC, Bethesda, MD

1405-1430: Update on Army General Medicine by COL Jeanne Tofferi, MD, MPH, FACP, Consultant to the Surgeon General. Broadcast from Walter Reed National Military Medical Center, Bethesda, MD

1430-1445: KETAMINE BY CONTINUOUS INFUSION FOR SEDATION IN SEPTIC SHOCK, CPT Victoria Sullivan, Madigan Army Medical Center, Tacoma, WA

1445-1500: DETERMINATION OF REFERENCE VALUES FOR CARDIOPULMONARY EXERCISE TESTING IN AN ACTIVE DUTY POPULATION, MAJ Daniel Weinstein, San Antonio Military Medical Center, San Antonio, TX

1500-1510: Break

1510-1525: SIMEPREVIR AND SOFOSBUVIR COMBINATION THERAPY IS SAFE AND WELL TOLERATED IN POST LIVER (LT) TRANSPLANT PATIENTS WITH RECURRENT HEPATITIS C (CHC), CPT Diana Dougherty, Walter Reed National Military Medical Center, Bethesda, MD

1525-1540: AUTOMATED URINE FLOW RATE AND VOLUME MEASUREMENTS: A NEW DEVICE ACCURACY TESTING, CPT Robert Broughton, Dwight D. Eisenhower Medical Center, Augusta, GA

1540-1555: ELECTROCARDIOGRAPHIC MONITORING OF NONCRITICAL HOSPITAL INPATIENTS AT WBAMC: A TELEMETRY UTILIZATION REVIEW PERFORMANCE IMPROVEMENT PROJECT, CPT Michael Switzer, William Beaumont Army Medical Center, El Paso, TX

1555-1610: Presentation of Chapter Awards from Walter Reed National Military Medical Center, Bethesda, MD

1610-1655: Doctor's Dilemma Competition, Proctored by CPT(P) Rohul Amin, Chief of Medical Residents, Walter Reed National Military Medical Center, Bethesda, MD

1655-1700: Close and thank you

Clinical Vignette Poster Competition

1st: A Dab Of Danger: A Case Of Severe Respiratory Failure Following Inhalation Of Butane Hash Oil**,** CPT Michael McMahon, MD, WRNMMC

2nd: The Kiss Of Death: A Rare Instance Of Anaphylactic Reaction To The Bite Of *Triatoma Rubrofasciata,* The "Red Margined Kissing Bug," CPT Caleb Anderson, MD, TAMC

3rd: Sarcoidosis Related Pleural Effusion Treated with Infliximab Monotherapy, CPT Zorana Mrsic, MD, DDEAMC

Research Podium Competition

1st: Ketamine By Continuous Infusion For Sedation In Septic Shock, CPT Victoria Sullivan, MD, MAMC

2nd: Electrocardiographic Monitoring Of Noncritical Hospital Inpatients At WBAMC: A Telemetry Utilization Review Performance Improvement Project, CPT Michael Switzer, WBAMC

3rd: Determination Of Reference Values For Cardiopulmonary Exercise Testing In An Active Duty Population, MAJ Daniel Weinstein, SAUSHEC

CONTENTS

Clinical Vignettes

Dwight D. Eisenhower Army Medical Center

Madigan Army Medical Center

San Antonio Uniformed Services Health Education Consortium

Tripler Army Medical Center

Clinical Vignettes (continued)

Research

Clinical Vignettes

DDEAMC

Dwight D. Eisenhower Army Medical Center

Clinical Vignettes

ECTOPIC ACTH SECRETION RESULTING IN ICU ADMISSION

Crystal Breighner MD[1] (ACP associate), Zorana Mrsic MD[1] (ACP associate), Christopher Colombo MD (FACP)[3], David Gaitonde MD (FACP)[2]

[1]Department of Internal Medicine, Eisenhower Army Medical Center, Fort Gordon, GA
[2]Department of Endocrinology, Eisenhower Army Medical Center, Fort Gordon, GA
[3]Department of Intensive Care, Eisenhower Army Medical Center, Fort Gordon, GA

Ectopic secretion of ACTH (EAS) from a non-pituitary tumor causes only a minority of Cushing syndrome cases and the diagnosis is often overlooked, particularly when the patient presents in the intensive care setting. However, EAS can present acutely with severe hypertension, electrolyte abnormalities, and multi-organ dysfunction. Prompt recognition is important in order to appropriately treat the metabolic complications and prevent the opportunistic infections associated with EAS.

A 78-year-old female presented with anuria, obstipation, fatigue and generalized weakness. Physical exam was remarkable for hypertension with BP 197/71 and the absence of dorsocervical hump, supraclavicular fat pads, Cushingnoid facies and striae. Initial laboratory evaluation revealed hyponatremia (124 mmol/L), hypomagnesemia (1.6 mg/dL), hypokalemia (1.6 mmol/L), hypochloremia (67 mmol/L) with metabolic alkalosis. The patient was admitted to the intensive care unit (ICU) for hypertensive urgency and severe electrolyte abnormalities. On further evaluation, the patient was found to have a new right middle lobe lung mass and multiple hepatic masses concerning for metastatic lung cancer. Due to the degree of hypertension and hypokalemia in the setting of a lung mass, ectopic ACTH syndrome was suspected. Since cortisol is often elevated in severe illness due to reasons other than Cushing syndrome, the diagnosis is challenging to make. A random serum cortisol level in the ICU and again on the medical ward was elevated (>62 ug/dl). Serum cortisol following a 1 mg overnight dexamethasone suppression test was 71.5 ug/dl (normal <5 ug/dl), and an ACTH level was elevated at 117 pg/ml. Liver biopsy was consistent with metastatic small cell lung cancer. The patient was diagnosed with Cushing syndrome secondary to EAS from small cell lung cancer. She was started on treatment with spironolactone, trimethoprim-sulfamethoxazole for Pneumocystis jirovecii prophylaxis and basal-bolus insulin for hyperglycemia.

This case highlights the need for physicians to maintain a broad differential diagnosis. Although Cushing syndrome as the direct cause for severe illness requiring ICU admission is rare, it does occur. Diagnosis is challenging to make, especially in patients with severe illness that can have elevated cortisol levels for reasons other than Cushing syndrome. If the diagnosis is suspected, prompt treatment may be needed prior to confirming the diagnosis in order to avoid acute complications such as severe metabolic derangements, perforated viscous and opportunistic infections. Therefore, high suspicion for and recognition of this syndrome in the ICU is crucial as it can be fatal if left untreated.

RHABDOMYOLYSIS AS PRESENTING SYMPTOM OF ACUTE HIV INFECTION IN A SOLDIER

Rob Gaeta, CPT MC USA, PGY2 Internal Medicine, DDEAMC, FT Gordon GA

Rhabdomyolysis is a condition caused by muscle breakdown due to traumatic or muscle compression, nontraumatic exertional, or nontraumatic nonexertional. The latter may be due to drugs or toxins, infections, or electrolyte disorders. Although acute viral infections are known to cause rhabdomyolysis, this syndrome is rare as the initial presentation of acute HIV infection. We report an Active Duty Soldier found to be HIV positive who presented with non-exertional rhabdomyolysis.

19y male with remote history of hypothyroidism with 24h of muscle soreness, cramping and "Coke-colored urine" with no history of any strenuous activities. Prior to that episode he had not been doing any heavy exertion as well. Endorsed recent URI within a week of his current presentation but denied fevers/chills/cough/sore throat/lymphadenopathy/malaise or trauma associated with episode of muscle soreness and dark urine. He had an initial CK level of 204,000 without oliguria/anuria or AKI. Patient denied taking any supplements or OTC medications.

Vital signs were stable and unremarkable. Physical exam was non-focal. Initial laboratory studies were remarkable for CK 204887, UA significant for large hemoglobin with 4 RBC. His renal function remained stable without evidence of AKI and he did not demonstrate symptomatic hypocalcemia or hyperkalemia on serial renal panel monitoring. His myoglobinuria resolved on HD#2 and his CK continued to trend down to 4529 at the time of discharge. UDS and EtOH were negative, he had normal TSH and FT4 levels. The following labs were all unremarkable: mononucleosis, sickle cell, ANA, ENA, Flu A/B, coxsackie titers, G6PD, nasal swab viral culture, carnitine deficiency, exercise intolerance, JO-1 ENA. HIV-1/O/2 was found to be positive. All imaging was unremarkable.

Rhabdomyolysis results from cell death due to many possible inciting events. As the patient denied injury or exertion, as well as medication/toxin/supplement use, an underlying disorder for the etiology of his rhabdomyolysis was suspected. Although rhabdomyolysis has been associated with a number of viral infections, the exact mechanism has never been completely elucidated. Specifically, rhabdomyolysis has been associated with advanced HIV where HIV RNA is localized to lymphoid cells surrounding muscle fibers but not to myocytes, toxicity of antiretroviral therapy via hepatic CYP450, or rarely the manifestation of HIV seroconversion. Notably, in this patient with a remote history of hypothyroidism, hypothyroidism is frequently accompanied by myalgias and mild to moderate serum CK elevations but not to the extent seen in this presentation.

This case is notable for the florid presentation of non-traumatic rhabdomyolysis with an extensive, unremarkable laboratory workup and the value of a complete history. Although this initial manifestation of HIV infection is rare, recognition of this presentation is critical to providing timely therapy.

PRIMARY TESTICULAR FAILURE IN A 46, XX MALE

Patrick Mastin, MD (Associate); David Gaitonde, MD (Fellow), DDEAMC

Introduction: Low testosterone in men is an increasingly recognized condition that frequently results in testosterone supplementation without first performing an appropriate laboratory evaluation to determine primary versus secondary causes. It is critical to distinguish between primary and secondary hypogonadism in order to determine the underlying etiology. Certain etiologies require more extensive counseling regarding gender definition and possible lifelong infertility. One such etiology, 46,XX male, disorder of sexual development, is rare and occurs in 1 in 20,000 live births. The disorder is most often due to translocation of sex determining region Y (SRY) to an X chromosome. Patients typically have complete aspermatogeneis and should be counseled that they are not females. We describe a 46, XX male, and review the salient presenting features and cornerstones of management.

Case: A 23 year old male presented to his primary care provider with progressively worsening symptoms of depressed mood, sleep disturbance, decreased libido and fatigue. A serum testosterone level was drawn and found to be low at 145ng/dL. On physical exam he was found to have low testicular volume bilaterally less than 4mL, penis with mild hypospadias, decreased facial hair and a normal visual field on direct confrontation. Serum LH was elevated at 30.3miu/mL and FSH was elevated at 53.9miu/mL consistent with primary testicular hypogonadism. Karyotype testing revealed a normal female karyotype 46, XX and PCR amplification showed the presence of the SRY gene. The patient was started on transdermal testosterone replacement therapy with an appropriate response in serum testosterone levels to 524ng/dL and clinical improvement.

Conclusion: Hypogonadism in males presents with a constellation of non-specific symptoms such as decreases in libido, vitality, body hair and muscle mass. Symptoms of androgen deficiency in men should prompt a serum testosterone analysis and if low, further evaluation should be performed to determine the etiology. Among the causes of primary hypogonadism, Klinefelter's syndrome is the most common congenital abnormality with the most common karyotype being 47, XXY. An important subset of Klinefelter's syndrome consists of 46, XX karyotype individuals. The cornerstone of treatment consists of testosterone replacement therapy with regular monitoring of hematocrit, liver function, lipid profile, and bone densitometry scanning. Despite a 46,XX genotype patients should be counseled that that they are not females and they do not have a gender identity disorder.

SARCOIDOSIS RELATED PLEURAL EFFUSION TREATED WITH INFLIXIMAB MONOTHERAPY

CPT Zorana Mrsic, MD (Associate), MAJ Samuel Burkett, MD (Member)
D.D. Eisenhower Army Medical Center, Ft. Gordon, GA

Introduction:
Pleural effusions are a rare manifestation of pulmonary sarcoidosis with a prevalence of 1-2%. The treatment of sarcoidosis related pleural effusions is not well defined and recommendations mirror that of other manifestations of sarcoidosis. We present a rare case of a sarcoidosis related pleural effusion treated with Infliximab monotherapy.

Case Presentation:
A 42 year-old female with biopsy-proven, stage I pulmonary sarcoidosis presented with one month of right sided, pleuritic chest pain. The patient denied fever, chills, night sweats, or cough. The patient received an empiric course of Levofloxacin for presumed pneumonia without symptomatic improvement. A computed tomography (CT) scan of the chest was obtained and demonstrated a right sided pleural effusion with hilar lymphadenopathy. A diagnostic thoracentesis revealed a lymphocyte predominant, exudative pleural fluid with cultures and cytology being negative for infection or malignancy. A presumptive diagnosis of a sarcoidosis related pleural effusion was made. The patient refused treatment with corticosteroids or methotrexate for symptomatic pleural sarcoidosis. Alternatively, Infliximab was initiated with 5mg/kg infusions at 0, 2, 6, 10, 18, and 26 weeks. Her symptoms resolved quickly with near complete radiographic resolution of her pleural effusion at three months.

Discussion:
Sarcoidosis is multisystem, immune-mediated inflammatory disorder of unknown etiology characterized by the formation of noncaseating granulomas in affected organs. Tumor necrosis factor (TNF)-α plays a critical role in the pathogenesis of granulomatous inflammation and the literature supporting the treatment of sarcoidosis with TNF-α antagonists is growing. While TNF-α antagonists are commonly used as an adjuvant therapy to corticosteroids or cytotoxic agents in refractory cases of sarcoidosis, we report this case to demonstrate that Infliximab can be effective as monotherapy in the treatment of sarcoidosis in patients whom corticosteroids or cytotoxic agents are either ineffective or are associated with unacceptable side effects.

MAMC

Madigan Army Medical Center

Clinical Vignettes

A CASE OF PROFOUND BACLOFEN TOXICITY MASKED BY ACUTE ILLNESS.

CPT Robert Bruce, MD (Associate), CPT Evelyn Slaughter, MD (Associate), CPT Nikhil Huprikar, MD (Associate), LTC Cristin Mount, MD (FACP). Madigan Army Medical Center, Tacoma, WA

INTRODUCTION: Baclofen, a gamma-aminobutyric (GABA) agonist, is used as an antispasmodic agent. Toxicity can manifest with loss of brainstem reflexes mimicking global anoxic brain injury and should be suspected in any patient on baclofen presenting with neurologic changes.

CASE: A 38-year-old woman with cerebral palsy and spastic quadriplegia presented with acutely decreased respiratory drive and decreased responsiveness. Eight days prior she underwent outpatient implantation of an intrathecal baclofen pump with subsequent improved muscle tone. On presentation to the emergency room, she was hypothermic and hypopneic. Examination revealed a flaccid patient with decreased breath sounds, absence of pupillary, gag, or cough reflexes, fixed midline gaze with Doll's eye maneuver, and no response to noxious stimuli. Glasgow coma scale was 3. Labs were notable for leukocytosis and elevated serum creatinine of 5.07 mg/dL. Cerebrospinal fluid analyses were within normal limits. Chest imaging revealed complete left lung atelectasis and right pneumonia. The patient experienced acute cardiopulmonary decompensation while in the ED, requiring intubation and blood pressure support with norepinephrine. She was transferred to intensive care, and the delivery rate of her Baclofen pump was reduced. The patient's renal function rapidly improved but neurologic exam remained unchanged. Head CT showed no acute intracranial abnormality, an EEG revealed findings concerning for anoxic brain injury. By hospital day 3, however, the patient exhibited increased responsiveness and was successfully extubated. She returned to home on hospital day eleven, with complete resolution of her neurological symptoms. Baclofen level sent on admission was reported as 1480 ng/mL (therapeutic range 80-400 ng/mL).

DISCUSSION: While case reports exist of intentional overdose and overdose in hemodialysis patients, Baclofen toxicity can also occur with sudden decrease in creatinine clearance. In baclofen patients with renal failure, common methods of evaluating neurologic response may be unreliable, until baclofen levels return to therapeutic range.

ARTICULAR DIFFUSE LARGE B CELL LYMPHOMA DIAGNOSED DURING TOTAL KNEE ARTHROPLASTY

CPT(P) Jennifer Creamer, MD (Associate), CPT Chase Dukes, MD, MAJ Haines Paik, MD. Madigan Army Medical Center, Tacoma, WA.

Introduction: Primary articular non-Hodgkins lymphoma (NHL) is a rare entity, with only a handful of case reports described throughout the literature. All of these cases have occurred in the setting of either an inflammatory spondylopathy or other rheumatologic condition. While up to 25% of patients with NHL will have musculoskeletal involvement, to date no other cases of primary articular NHL have been described in the setting of primary knee osteoarthritis.

Case presentation: We present a case in which Diffuse Large B Cell Lymphoma (DLBCL) was diagnosed in an 88-year-old man undergoing left total knee arthroplasty (TKA) for osteoarthritis. Abnormal appearing synovium was resected during the procedure and sent to pathology. Histological and immunohistochemical examination confirmed a diagnosis of DLBCL. Post-surgical work up was significant only for a soft tissue focus with intense metabolic activity within the lateral joint space on PET/CT. DLBCL therapy consisted of three cycles of R-CHOP followed by consolidation radiation therapy to the left knee. Subsequent PET/CT was negative for active malignancy recurrence or metastatic disease.

Discussion: The average age at diagnosis for DLBCL is 64. Survival is directly correlated with stage of disease at presentation and 60% of patients have advanced disease, stage III or IV, at the time of diagnosis. Non-Hodgkins lymphoma involving the synovium is rare, with only a few reported cases. This case is unique in its presentation, as the patient was asymptomatic at the time of presentation and his TKA was being done for primary knee osteoarthritis. Most reported cases of Non-Hodgkins lymphoma involving the synovium have been associated with chronic inflammatory states, commonly rheumatoid arthritis and seronegative spondyloarthropathies. Early diagnosis is critical to patient outcomes and therefore any suspicion for occult disease in patients undergoing TKA should prompt a preoperative discussion about possible tissue resection for pathologic examination at the time of surgery.

MEDIAN ARCUATE LIGAMENT SYNDROME OF THE SUPERIOR MESENTERIC ARTERY.

CPT Stephen Curtis, MD (Associate), MAJ Peter Kreishman, MD, COL Mark Cummings, MD. Madigan Army Medical Center, Tacoma, WA.

Introduction: Median arcuate ligament syndrome is a cause of post prandial abdominal pain, weight loss and presents similar to chronic mesenteric ischemia. Superior mesenteric artery (SMA) compression causing median arcuate ligament syndrome, although previously documented in prior case reports, is especially rare.

Case Description: A 58-year-old man with past medical history notable for hypertension, hyperlipidemia, s/p low anterior resection of sigmoid colon due to massive polyps/diverticulosis presented to the GI clinic with 1.5 year history of consistent post prandial epigastric pain and weight loss. His history was concerning for chronic mesenteric ischemia. Mesenteric duplex was performed which showed high grade stenosis of the SMA as well as possible stenosis or occlusion of the celiac artery. CT Angiogram was obtained which showed that celiac and superior mesenteric arteries arose within close proximity from the aorta and were being compressed by the median arcuate ligament. On surgical exploration he was found to have dense muscular tissue from the median arcuate ligament clearly compressing the root of the celiac and closely located superior mesenteric artery. The numerous collaterals around the celiac artery suggested his symptoms were more likely from SMA artery compression. After surgical release, his post prandial symptoms completely resolved.

Discussion: Median arcuate ligament syndrome (MALS), also known as Dunbar syndrome, is a fairly rare syndrome with symptoms that often include post prandial abdominal pain, food avoidance, weight loss, and dyspepsia. It is a diagnosis of exclusion and usually only suspected after workup for more common causes of abdominal pain have been investigated. It is most commonly caused by compression of the celiac artery or celiac ganglia by fibers of the median arcuate ligament which traverse the abdomen. Although most commonly a syndrome affecting younger women, it can be seen in other demographic groups.

FEVER OF UNKNOWN ORIGIN: AN UNLIKELY CULPRIT

CPT Ijagha Eme, MD (Associate), LTC George Mount, MD (FACP), Christina Schofield, MD (FACP). Madigan Army Medical Center, Tacoma, WA.

Introduction: Mesenteric panniculitis is a rare inflammatory condition manifested by chronic and nonspecific inflammation of the adipose tissue of the intestinal mesentery. It is an uncommon presentation for a fever of unknown origin.

Case: A 46-year-old female presented with a 2-year history of recurrent fevers up to 38.9°C, fatigue, and frequent urination. Her fevers were associated with muscle weakness, joint stiffness, and extreme headache lasting approximately 30 hours. Her past surgical history was notable for gastric sleeve and hysterectomy complicated by pelvic abscess that required an interventional radiology drain. On exam, she was a well appearing obese female in no acute distress with normal vital signs. Laboratory data revealed a microcytic anemia, whereas comprehensive metabolic panel, HIV assay, inflammatory markers, quantiferon, blood cultures, LDH, ANA and SPEP were all within normal limits. CT of the abdomen and pelvis showed a misty appearance of the mesentery in the left hemiabdomen with multiple enlarged mesenteric lymph nodes. The CT findings were felt to represent chronic mesenteric panniculitis. Findings of mesenteric panniculitis on CT scan prompted gastroenterology consultation where the patient is currently being evaluated.

Discussion: Mesenteric panniculitis is a rare inflammatory condition manifested by chronic and nonspecific inflammation of the adipose tissue of the intestinal mesentery. There is a 2-3:1 predilection for men versus women with incidence increasing with age. A precise etiology remains unclear although a history of abdominal surgery or trauma has been reported. Fever, abdominal pain and malaise are common symptoms although the disease is usually asymptomatic. Therapy is individualized with drugs such as steroids, thalidomide, cyclophosphamide, progesterone, colchicine, azathioprine, tamoxifen, antibiotics or radiotherapy used with various degrees of success. This case suggests that mesenteric panniculitis should be considered as a rare etiology in a patient with a fever of unknown origin.

AN UNUSUAL CAUSE OF INTRA-OPERATIVE ST ELEVATION

CPT Nupur Garg, DO (Associate), LTC Sean Javaheri, MD (FACP). Madigan Army Medical Center, Tacoma, WA

Introduction: Flecainide is a class 1c antiarrhythmic used in the treatment of atrial fibrillation and ventricular dysrhythmias. This drug has a use-dependent effect, in that its effect on the sodium channels of the heart becomes more pronounced with an increase in heart rate. This case report describes an elderly male on flecainide who was administered ephedrine during surgery and shortly after exhibited QRS widening, similar to a left bundle branch pattern and ST elevation in anterior leads that was misinterpreted as an acute ST elevation MI.

Case: A 65-year-old Caucasian male with a history of paroxysmal atrial fibrillation and dilated cardiomyopathy (EF of 35%) was admitted for nasal polypectomy. While undergoing anesthesia, the patient became hypotensive and required administration of ephedrine. A few seconds after the ephedrine was administered, ST elevation was noted on telemetry and the surgery was aborted. Upon review of the EKG, QRS widening and a left-bundle branch pattern with ST elevation in leads V2-V5 was noted to be new in comparison to old EKGs. The patient was admitted for further cardiac workup. Serial troponins were negative. During the myocardial perfusion exercise stress test, while at peak exercise (heart rate of 106), widening of the QRS interval and non-specific ST changes were noted. These changes were similar to those seen when ephedrine was administered during his planned surgery.

Discussion: ST elevation due to a flecainide toxic effect is an under recognized EKG abnormality and can easily be mistaken for an acute myocardial infarction. Flecainide is a class 1C antiarrhythmic drug that functions to block sodium channels in the heart, slowing conduction in the AV node as well as in the downstream ventricular conduction system. In this patient, the ST elevation and QRS prolongation presenting in a left-bundle branch pattern occurred after the patient was administered ephedrine and again when the patient was exercising. Flecainide exhibits a use-dependent effect in which an increase in heart rate causes flecainide's effect to be more pronounced. It is imperative to understand that patients with structural heart disease are at greatest risk for flecainide toxicity. Flecainide toxicity is an important consideration in the differential diagnosis when approaching patients presenting with new-onset ST elevation on EKG.

AN UNUSUAL CAUSE OF STROKE IN A 72-YEAR-OLD MALE

CPT Joseph W. Howells, DO (Associate), LTC David Trowbridge, MD. Madigan Army Medical Center, Tacoma, WA

INTRODUCTION: Primary cardiac masses represent a rare cause of cerebrovascular accidents (CVAs) in the adult population. We present a case of non-bacterial endocarditis (NBE) in the setting of secondary polycythemia in an adult with a subacute CVA.

PRESENTATION: 72-year-old man with past medical history significant for COPD and tobacco / alcohol abuse presented with a 24 hour history of aphasia. MRI on admission revealed cerebral infarcts along the left temporoparietal lobe and left insular cortex. Initial labs were notable for a secondary polycythemia, with hemoglobin / hematocrit of 21.9 / 65.8 g /dL and low-normal EPO of 4.3 mIU / mL. Further workup, including CT chest / abdomen / pelvis and liver MRI, suggested a multifactorial etiology, with untreated COPD, active smoking, and hepatic hemangiomas all likely contributing. Transthoracic echocardiography (TTE) revealed non-specific thickening of the anterior mitral valve leaflet. Transesophageal echocardiography (TEE) demonstrated a 1.1cm X 1.1cm mass, adhering to the atrial side of the anterior and posterior leaflets of the mitral valve, devoid of stalk or prolapse, with preserved valvular function. Surgical excision of the mass revealed an organized thrombus with no evidence of infection, consistent with the diagnosis of non-bacterial endocarditis (NBE).

DISCUSSION: NBE should be considered in any patient with valvular vegetations in the clinical context of malignancy, autoimmune disease, or hypercoaguable states. Although reports of NBE associated with secondary polycythemia are lacking, there have been experimental animal studies which demonstrated hypoxia-induced polycythemia predisposed rats to cardiac thrombus formation. On echocardiography, organized thrombi are sessile, heterogeneously echoreflectant, and generally lack independent mobility. In this case, the features were somewhat atypical given the size and mobility of the lesion, leading to initial concerns for papillary fibroelastoma (PFE) - the most common primary cardiac valvular tumor. Treatment for NBE generally consists of systemic anticoagulation (preferably with Unfractionated Heparin or Low Molecular Weight Heparin), with surgery offered to selected patients where the benefits outweigh the risks. In our patient, given the size of the lesion, concerns for PFE, and his overall functional status, surgery was the recommended treatment.

A RARE CASE OF CATECHOLAMINE PRODUCING PARAGANGLIOMA FOUND INCIDENTALLY ON CHEST CT

CPT Matthew H. Kemm, MD (Associate); LTC Walter S. Leitch, MD. Madigan Army Medical Center, Tacoma, WA.

Introduction: Paragangliomas are rare neuroendocrine tumors with an annual incidence of 2 out of every million people. Paragangliomas are the cause of high blood pressure in less than 0.2% of cases. While rare, they can cause serious health problems like stroke, MI, and even death due to release of catecholamines in uncontrolled bursts. We present a case of a non-metastatic catecholamine producing extra-adrenal paraganglioma found incidentally on CT.

Case: A 59-year-old woman with hypertension was found to have a retroperitoneal mass on chest CT. I-123 labeled MIBG SPECT-CT demonstrated a 2.1 x 2.4 cm solitary mass, inferomedial to the left kidney. She had been experiencing six months of episodic headaches and diaphoresis with a persistent tachycardia. Lab testing revealed a 24 hour urine normetanephrine level 2.8 times the upper limit of normal (ULN) and a serum norepinephrine level 6.1 times the ULN. The patient underwent robotic assisted laparoscopic excision of the mass with pathology confirming an extra-adrenal paraganglioma. The patient recovered well with resolution of her prior symptoms, normalization of urinary normetanephrine levels and improvement in her blood pressure.

Discussion: Paragangliomas are mostly sporadic tumors with only 25% of sympathetic paragangliomas associated with a hereditary syndrome and malignancy. Patients with excessive catecholamines can be symptomatic. Diagnosis can usually be made by measurements of urinary and/or plasma fractionated metanephrines and catecholamines, followed by imaging to localize the tumor. Surgical cure is possible for non-malignant tumors with combination medical and surgical options available for malignant cases. Biochemical testing is indicated for all patients with a paraganglioma, even if they present without symptoms, to determine risk of recurrence and follow-up care.

MECHANISMS AND MANAGEMENT OF DIFFICULT-TO-TREAT ASTHMA

CPT John L Kiley MD (Associate), COL Alexander S Niven MD (FACP), Madigan Army Medical Center, Tacoma, WA

Introduction: IgE-mediated atopy has been described as one mechanism among increasingly varying pathways of disease affecting asthma. The monoclonal antibody inhibitor omalizumab has been found in clinical trials to be effective in treating persistent severe asthma in patients for whom other therapies have failed.

Case: A 59 year old obese female with poorly controlled, severe persistent asthma presented off therapy with worsening symptoms. She was previously controlled with methotrexate and prednisone during treatment for orbital myositis, and most recently with high dose fluticasone, salmeterol, and omalizumab. Past history included vocal cord dysfunction (VCD), OSA, and GERD. Exam showed stigmata of allergic rhinitis and wheezing. Spirometry demonstrated moderate, reversible obstruction, with a 21% drop in FEV1 since 2008. CXR, CBC, CMP, TSH, allergy testing, aspergillus specific Abs, autoimmune and sinus evaluations were normal, and IgE was elevated (77.8 kU/L). The patient was treated with nasal and inhaled fluticasone, salmeterol, tiotropium, omalizumab, fexofenadine and albuterol, with weekly follow up to enhance compliance. Theophylline was added after spirometry failed to improve with 2 weeks of prednisone.

Discussion: Difficult-to-treat asthma is associated with poor medical adherence, inhaler technique, or continued exposure to tobacco, occupational or environmental triggers. Confounding factors include allergic rhinitis, obesity, VCD and hypothyroidism. Rare conditions including allergic bronchopulmonary mycosis and allergic granulomatosis must also be considered. There is increasing recognition of varying asthma phenotypes due to IgE, cytokine, and T helper cell mechanisms. Chronic oxidative stress can cause corticosteroid resistance due to PI3Kd activation, decreased HDAC2 activity, and increased proinflammatory kinases. Theophylline, nortriptyline, azithromycin, omalizumab, and other targeted biologic treatments have been used with variable success. Bronchial thermoplasty is a promising but controversial management option until further proven targeted therapies are available.

HENOCH-SCHÖNLEIN PURPURA IN AN ELDERLY MAN

CPT John Kiley, MD (Associate), MaryAnne McDonald, MD. Madigan Army Medical Center, Tacoma, WA.

INTRODUCTION: Henoch-Schönlein purpura is an IgA mediated leukocytoclastic vasculitis that more commonly affects children. It is significantly less common in adults and when it does occur usually has more serious sequelae and is often accompanied by underlying infection or malignancy.

CASE: A 68-year-old man with a history of diabetes and very little contact with healthcare providers presented to the emergency department complaining of a rash and swelling in his wrists and ankles along with a left necrotic toe. Palpable purpuric lesions extended from his lower abdomen to his proximal anterior thighs and his distal calves. His left toe was amputated and he underwent a skin and kidney biopsy. Both biopsies were consistent with IgA leukocytoclastic vasculitis confirming a diagnosis of Henoch-Schönlein purpura. His creatinine at admission was 1.5 and continued to rise until it peaked at 3.5 around 1 month later. He was started on high dose prednisone 1 mg/kg shortly after his kidney function began to worsen. His purpuric lesions and ankle and wrist swelling and pain resolved over the next two weeks. On the third week of hospitalization he developed abdominal pain with symptomatic hematochezia and hemodynamic instability. He underwent upper and lower endoscopy with subsequent embolization of a branch of his superior mesenteric artery by interventional radiology. He subsequently developed a ruptured small bowel secondary to necrosis, thought to be caused by the embolization procedure. The patient died on hospital day 68 from complications related to his GI bleed, renal failure and prolonged hospital course.

DISCUSSION: Henoch-Schönlein purpura, while typically a vasculitis requiring supportive treatment in younger patients, puts older patients at risk of developing long term serious complications including renal and GI involvement. The most serious of these is usually advancement of renal disease to the point of requiring dialysis or transplant. Abdominal pain is a common complaint associated with IgA vasculitis. Gastrointestinal hemorrhage, especially to the point requiring intervention is much less common. A review of the primary literature suggests that ischemic gastrointestinal complications from arterial embolization procedures are very rare, however overall mortality is increased in elderly patients.

A COMPLICATED CASE OF CHYLOTHORAX AFTER DELIVERY

CPT Tessa Klinkhardt, MD (Associate), MAJ Anita Shah, MD. Madigan Army Medical Center, Tacoma, WA.

Introduction: Chylothorax is a complication from damage to the thoracic duct or its branches which results in the accumulation of chyle or lymphatic fluid from the abdomen into the pleural space. Peripartum chylothorax secondary to traumatic delivery represents a rare cause with few reported cases.

Case: A 32-year-old woman presented with a 48-hour history of non-productive cough and dyspnea on exertion 4-days after delivering her first child. The birth was complicated by shoulder dystocia requiring aggressive adjunctive measures to include abdominal/thoracic pressure and episiotomy. Her exam was notable for complete absence of breath sounds on the right and chest imaging showed a large layering pleural effusion. Thoracentesis showed LDH 261 units/L, triglycerides 1,280 mg/dL, amylase 36 units/L, pleural total protein 2.8 g/dL, WBC 1.9 x109/L with 79% lymphocytes, serum total protein 4.7 g/dL She was treated with multiple therapeutic thoracenteses and dietary restriction, but due to worsening shortness of breath, she underwent a VATS procedure which was converted to open thoracotomy. A chylous leak superior to the diaphragm was identified and the thoracic duct was ligated. She continued to have high chylous output from her chest tubes (>2L/day) and underwent a lymphangiogram which did not identify tracer uptake within the thorax or pleural effusion. A right thoracoscopy with pleurectomy and chemical pleurodesis was performed which led to the development of chylous ascites. Her nutritional status declined and she underwent a peritoneovenous shunt placement with successful resolution of her symptoms and clinical improvement.

Conclusion: Etiologies for chylothorax can be divided into two categories: nontraumatic and traumatic. Review of the literature shows very few cases of chylothorax during pregnancy. Our patient's case is unique in that her traumatic event was secondary to complications of shoulder dystocia. Although a rare etiology for shortness of breath in the postpartum period, consideration of damage to the thoracic duct or abdominal collaterals should be considered in the setting of a new pleural effusion.

WITHOUT GUILE: A CASE OF DRUG-INDUCED ASEPTIC MENINGITIS IN A PATIENT WITH IDIOPATHIC CD4 LYMPHOCYTOPENIA

CPT Jason J. Nam, MD (Associate)[1], CPT Benjamin Vipler, MD (Associate)[2], MAJ David Callender, MD (FACP) [2], Christina M. Schofield, MD (FACP) [1]. Madigan Army Medical Center, Tacoma WA[1], Walter Reed National Military Medical Center, Bethesda, MD[2]

Introduction: Idiopathic CD4 lymphocytopenia (ICL) is a rare condition characterized by depressed levels of T-cells without evidence of infection or defined immunodeficiency. Like HIV, patients with ICL are at risk for various infections including those of the central nervous system. This makes aseptic meningitis, specifically drug-induced aseptic meningitis (DIAM) a diagnostic challenge.

Case: A 62-year-old man with ICL whose last CD4 count was 120 cells/mm3 presented with fever, headache, and neck pain after one dose of trimethoprim-sulfamethoxazole (TMP-SMX) which was prescribed for pneumocystis prophylaxis. He had a fever to 102.8℉, hypotension, and neck stiffness. He was alert, oriented and without focal neurologic deficits. Empiric bacterial and HSV meningitis therapy was started. A non-contrast head CT scan showed no acute intracranial processes; a LP was not performed because of elevated INR. Cultures were without growth, and serum Cryptococcus antigen was negative. A LP was eventually performed, and demonstrated 210 WBC with negative cultures. On hospital day (HD) 3 the patient became acutely obtunded. He was transferred to the ICU and required intubation. The following day, he was extubated and was again alert and oriented. On HD 6, he was started on dapsone for pneumocystis prophylaxis and developed a fever of 101.5℉ without mental status changes. Dapsone was discontinued; he remained afebrile and was discharged.

Conclusion: This case demonstrates the fulminant and rapidly resolving nature of DIAM after a single dose of TMP-SMX. His rapid recovery, neurologic symptoms, and the recurrence of fever with administration of dapsone, a sulfa moiety, strongly support this diagnosis.

WHAT'S A MASS GOT TO DO WITH IT: TURNER'S SYNDROME AND SARCOIDOSIS

CPT Jason J. Nam, MD (Associate), LTC David B. Trowbridge, MD (Fellow). Madigan Army Medical Center, Tacoma, WA

Introduction: Turner's Syndrome is a relatively common chromosomal disorder that features short stature and gonadal dysgenesis. The most serious clinical aspect of Turner's is the potential for congenital cardiovascular anomalies such as aortic coarctation and dissection. Venous anomalies can include persistent left superior vena cava and partial anomalous pulmonary venous return.

Case: A 32-year old white Turner's Syndrome (45X) patient with past medical history of low back pain presented for physical examination for fertility evaluation. She reported recent exertional dyspnea. Otherwise, she denied chest pain, cough, pleurisy, or constitutional symptoms. Physical exam was remarkable for short stature and webbed neck. Pulmonary function tests demonstrated normal baseline spirometry and DLCO. Her electrocardiogram showed a prolonged QTc consistent with left anterior fascicular block. Initial transthoracic echocardiogram demonstrated an inability to determine the number of aortic leaflets, normal aortic root, and no coarctation of aorta. To confirm a normal aorta, she was sent for cardiac and aortic MRI. She was found to have a bicuspid aortic valve, normal size aortic root, partial anomalous pulmonary venous return with two right pulmonary veins draining into the superior vena cava, and dilated pulmonary varix originating from the left upper lobe pulmonary artery. A CT pulmonary angiogram confirmed the presence of these vessels, multiple mediastinal masses, and an anterior left upper lobe 2.7cm mass abutting the pleura. Because the mediastinal mass was concerning for lymphoma, a PET CT was obtained which noted highly PET avid diffuse mediastinal and hilar adenopathy and a left upper pleural based nodule. CT-guided biopsy of the left upper lobe nodule and mediastinoscopy of lymphadenopathy revealed no evidence of malignancy and presence of non-caseating granuloma, negative for AFB and fungal stains. These findings were highly suggestive of sarcoidosis.

Conclusion: This case demonstrates an interesting presentation of sarcoidosis in a Turner's Syndrome patient with exertional dyspnea that was also found to have venous anomalies. Though Turner's Syndrome is often associated with autoimmune and endocrine disorders like Hashimoto's thyroiditis and Grave's disease, sarcoidosis is rare.

PARALYSIS BY HYPOKALEMIC ANALYSIS: AN INTERESTING CASE OF SJÖGREN'S SYNDROME

CPT Jason J. Nam, MD (Associate), LTC George R. Mount, MD (Fellow), COL David P. Vetter, MD (Fellow). Madigan Army Medical Center, Tacoma, WA

Introduction: Sjögren's Syndrome (SS) is a systemic autoimmune disorder that predominantly affects the exocrine glands. Renal tubular acidosis is an under-reported complication of Sjögren's. Furthermore, diagnosing Sjögren's from periodic paralysis remains a challenge in a patient especially without typical glandular manifestations.

Case: A 55-year-old female with no remarkable past medical history presented with periodic flaccid paralysis. Family history was not remarkable for autoimmune disorders or any hepatic disease. A year prior, the patient was noted to have hypokalemia on an annual physical examination and started on potassium supplementation. Several months thereafter, she presented to an emergency room with flaccid paralysis and a potassium of 1.6 mEq/L. She was admitted to the ICU, underwent electrolyte repletion, and discharged. She was thought to be suffering from congenital hypokalemic periodic paralysis. Subsequently, following discontinuation of her potassium supplement, she experienced recurrent fatigue, periodic twitching and cramping of muscles, as well diplopia. Her physical exam was remarkable for diminished strength in both her lower and upper extremities. A lab evaluation demonstrated a normal potassium 4.0mEq/L. However, she had a chloride of 116mEq/L and bicarbonate of 19mEq/L consistent with a non-anion gap metabolic acidosis. Her urine pH was 6.5, consistent with a type I distal renal tubular acidosis (RTA). Further analysis to explore the etiology of her RTA revealed a positive nuclear antibody, in a titer of 1:2560 with a speckled pattern. Serology also showed high titer positive SS-A (Ro) and SS-B (La) autoantibodies. These findings were highly suggestive of Sjögren's Syndrome.

Conclusion: This case demonstrates a rare presentation of Sjögren's Syndrome without the typical sicca symptoms. What was originally thought due to congenital hypokalemic periodic paralysis, her repeated episodes of hypokalemia and non-specific weakness were actually caused by a type I RTA secondary to Sjögren's.

A RARE CASE OF GASTROINTESTINAL INVOLVEMENT IN A PATIENT WITH GRANULOMATOSIS WITH POLYANGIITIS

CPT Brian C. Pomerantz, MD, (Associate), LTC George Mount, MD, (FACP). Madigan Army Medical Center, Tacoma, WA

Introduction: Granulomatosis with polyangiitis (GPA) is a rare condition and gastrointestinal (GI) involvement in patients with GPA is very uncommon. We present a case of GPA with vasculitic involvement of both the upper and lower gastrointestinal tract.

Case: A 38-year-old woman with a history of GPA, manifest by pulmonary, renal, sinus, and ocular involvement, which was in remission for three years off therapy, presented with complaints of postprandial abdominal pain. The pain was primarily periumbilical and developed over several months with accompanying anal pain on defecation, fatigue, malaise, night sweats, weight loss, and arthralgias in the context of decreased oral intake. Exam was notable for abdominal tenderness, supraclavicular lymphadenopathy, and a perianal ulceration. Initial workup revealed a new onset anemia and a positive fecal occult blood test. Upper and lower endoscopy was remarkable for patches of erythematous mucosa with erosions in the gastric body, antrum, duodenum, terminal ileum, and descending colon as well as a large ulceration at the splenic flexure. All endoscopic biopsies except those from the terminal ileum revealed neutrophilic infiltration and reactive capillary endothelitis without granulomata, consistent with active gastrointestinal GPA. Interestingly, left anterior cervical lymph node biopsy revealed low-grade follicular lymphoma, which was also noted in the terminal ileum. She was treated with high-dose glucocorticoids with pending transition to rituximab.

Discussion: GPA is an ANCA-associated vasculitis, and most commonly presents with upper respiratory, pulmonary, and renal manifestations. Cutaneous, ocular, and nervous system manifestations are less common but still seen regularly. GI involvement is not commonly seen. Most of the described cases of intestinal involvement have been noted intraoperatively during surgery for bowel perforation, although a few have been identified endoscopically. Given the potential severity of unidentified or inadequately managed GI involvement in GPA, this disease manifestation must be maintained in the differential in at-risk patients with GI symptoms, and an appropriate endoscopic workup with biopsies performed when clinical suspicion warrants.

DIAGNOSIS AND MANAGEMENT OF THE INCIDENTAL LIVER LESION: A RARE CAUSE OF A COMMON CLINICAL PROBLEM.

CPT Matthew J. Robles, DO (Associate); COL Alexander S. Niven, MD (FACP). Madigan Army Medical Center, Tacoma, WA

Introduction: Incidental liver lesions are common, but biliary hamartomas are rare in adults. We present a case of multiple, incidental biliary hamartomas and discuss the current evidence and recommended diagnostic approach to these patients.

Case: A 72 year old Asian female presented for evaluation of a lung nodule identified on CXR during an evaluation for weight loss. She had no other complaints, and physical exam was normal. CT chest demonstrated characteristics of a hamartoma, and incidentally identified multiple liver masses. A liver MRI revealed numerous small T2 hyperintense lesions without enhancement, consistent with biliary hamartomas. Liver function tests were normal, and no prior imaging was available for comparison.

Discussion: The incidence of small benign liver lesions has been reported to be 52% in autopsy series, with biliary hamartomas accounting for 0.69 - 2.8% of these findings. Differential diagnosis includes cystic tumors, CT imaging is frequently nonspecific; ultrasound can demonstrate multiple hyper- and hypoechoic areas described as “comet tail echoes”. MRI and MRCP are the imaging modalities of choice, and can verify the presence or lack of communication with the biliary tree. Von Meyenberg Complex (VMC) is a rare genetic condition associated with extensive hepatic involvement with multiple, small hamartomas, which are generally asymptomatic. VMCs are the result of ductal plate malformations which have occurred during embryonic development, and appear on pathological assessment as cystic, dilated bile ducts. They will not enhance with gadolinium, differentiating this entity from Caroli's disease. There is no currently available genetic test to confirm this diagnosis. VMC rarely exhibits malignant transformation and does not require biopsy confirmation in typical cases, but periodic serial imaging is recommended due to this concern.

ACHALASIA LEADING TO ACUTE RESPIRATORY FAILURE

CPT Victoria Sullivan, MD (Associate), Bernard Roth, MD (FACP). Madigan Army Medical Center, Tacoma, WA

INTRODUCTION: Achalasia is an esophageal motility disorder characterized by absence of esophageal peristalsis and impaired relaxation of the lower esophageal sphincter (LES). It can lead to severe esophageal dilation and compression of the posterior aspect of the trachea. Respiratory distress and respiratory failure can follow. We report a case of respiratory distress attributed to an exacerbation of COPD and HCAP before the precipitating etiology of achalasia and mega-esophagus was identified.

CASE: An 81 y/o female with COPD presented with increasing shortness of breath, hypoxia and fever. She was tachycardic, tachypneic, with diffuse wheezes and rhonchi. She had recently been discharged after a 3 day hospital stay for COPD exacerbation. Chest x-ray revealed a left lower lobe infiltrate and the patient was treated for a presumed healthcare associated pneumonia. On hospital day 2, she had three episodes of post-prandial desaturations. Due to an underlying anxiety disorder and the development of stridor, ENT was consulted to rule out vocal cord dysfunction (VCD). During a swallowing evaluation, she developed respiratory failure and was emergently intubated. VCD was ruled out. GI was consulted when a naso-gastric tube could not be inserted. EGD revealed food in the esophagus and dilation of the entire esophagus. Subsequent history from family members revealed that the patient had a history of dysphagia, including increased dyspnea following meals.

DISCUSSION: The initial absence of typical symptoms associated with achalasia; dysphagia, regurgitation, chest pain, pyrosis and weight loss, and the patient's history of COPD and anxiety were confounding factors that led to a delay in diagnosis. In acute respiratory failure secondary to achalasia, it is important to immediately decompress the esophagus. Induced vomiting, E-wald tube lavage or EGD can be therapeutic. Definitive treatment requires pneumatic dilation or botulinum toxin injection of the LES. Younger patients who do not respond to pneumatic dilation or older patients who fail dilation and botulinum toxin injection should be referred for laparoscopic cardiomyotomy with partial fundoplication which improves dysphagia over 90% of the time.

CHALLENGES IN COPD MANAGEMENT: THE ALPHA-1-ANTITRYPSIN PiMZ HETEROZYGOTE

CPT Victoria F. Sullivan, MD (Associate), COL Alexander S. Niven (FACP). Madigan Army Medical Center, Tacoma, WA

Case: A 60-year-old Caucasian female PiMZ alpha-1 antitrypsin (A1AT) heterozygote with severe COPD and significant prior tobacco abuse demonstrated progressive decline in exercise capacity, lung function, and increasing hospitalizations over several years despite escalating management with budesonide / formoterol, tiotropium, roflumilast, azithromycin, pulmonary rehabilitation and oxygen therapy. Pulmonary function testing demonstrated severe airflow obstruction (FEV1 990 ml, 41% predicted) with evidence of hyperinflation and a reduced diffusing capacity (9.62 ml/min/mmHg, 40% predicted). Six minute walk on 3L NC O2 was 324 m (71% predicted) but maximum exercise capacity was only 10.5 ml/kg/min with evidence of a ventilatory limitation. Quantitative lung perfusion scintigraphy demonstrated diffuse, heterogeneous radiotracer distribution only.

Discussion: Alpha-1 antitrypsin (A1AT) deficiency is a recognized risk factor for COPD, and current Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines have been shown to also perform well to identify high risk homozygous A1AT patients. Approximately 6 million (10.5 per 1,000) individuals in the U.S. are PiMZ carriers, and those who smoke have higher IL-8-related neutrophilic burden, elastase activity, risk of COPD, hospitalization, and mortality. Diffusing capacity and HRCT may be more sensitive predictors of lung function decline than spirometry in these patients. Besides tobacco cessation, the proportional benefits of common COPD management options including new bronchodilators, long term macrolide therapy, and selective phosphodiesterase-4 inhibitors, and lung volume reduction surgery are unclear. Current recommendations include early, aggressive diagnosis and management, and these patients represent an ideal population for research on current and future COPD therapies.

THINKING OUTSIDE OF THE BLACK BOX: A CASE OF FLUOROQUINOLONE-INDUCED MYOSITIS

CPT Victoria Fernandes Sullivan, MD, (Associate), LTC George Mount, MD, (FACP)
Madigan Army Medical Center, Tacoma, WA

Background: Fluoroquinolone antibiotics are well-known inducers of tendinopathies, usually involving the Achilles tendon. There is a black-box warning regarding this side effect. Less known side effects of fluoroquinolones are complications of the cartilage, bone and muscle. There are a handful of reports describing fluoroquinolone induced myalgias and myositis.

Case Description: A 73-year-old man with a remote history of Guillan-Barre Syndrome presented with complaints of muscle pain, weakness, and diffuse body stiffness. Three days prior to symptom onset, he completed a 10-day course of levofloxacin for sinusitis and bronchitis. He initially noticed myalgias involving the bilateral hip and shoulder girdles. He had difficulty climbing up stairs and standing from a seated position. He had bilateral knee swelling and pain. ESR, CRP and creatine kinase level were normal. Autoantibody serologies were negative. An MRI of the bilateral lower extremities revealed asymmetrical muscle signal abnormality of the bilateral thighs. It also showed a tendon abnormality of the bilateral hamstring attachments. The patient was diagnosed with fluoroquinolone induced myositis. His statin therapy was discontinued and he was instructed to avoid fluoroquinolones in the future. The patient's symptoms gradually resolved.

Discussion: Fluoroquinolone antibiotics can cause damage to tendons, cartilage, bone and muscle. This is thought to be secondary to alterations in cell signaling proteins and toxic effects on musculoskeletal tissues. Although an exact etiology is not known, there is evidence that the fluorine atom in fluoroquinolones may reveal pre-existing muscular anomalies. There have been case reports of myalgias, severe rhabdomyolysis and myositis associated with fluoroquinolones. The cases described typically involved patients that developed symptoms within 1 week after starting a fluoroquinolone and usually resolved within 1 month after discontinuation of the offending agent. The most common symptoms were diffuse muscle pain, without or without weakness, and usually the proximal muscles were most affected. Statins are thought to potentiate these side effects.

SEVERE INFECTION WITH CYTOMEGALOVIRUS IN IMMUNOCOMPETENT HOSTS

CPT Erin Tompkins, MD (Associate), Christina Schofield, MD (FACP). Madigan Army Medical Center, Tacoma, WA

INTRODUCTION: Infection with Cytomegalovirus (CMV) is highly prevalent in the general population, but rarely causes severe illness in immunocompetent hosts. There are examples of severe illness and reactivation disease in immunocompromised populations in the intensive care setting, however, serious infections in adult, immunocompetent hosts are rarely described in the medical literature. This is a case series of three patients hospitalized due to fever of unknown origin, subsequently diagnosed with acute CMV infection. The course of CMV infection was protracted, and caused significant morbidity.

PRESENTATION: Case 1: a 61 y/o female with a history significant for hereditary spherocytosis and splenectomy presented with weeks of fatigue, headache, joint pain and swelling, fevers, and transaminitis. She was treated with supportive therapy and symptoms resolved over the following month. Case 2: a 55 y/o healthy woman presented with low back pain, fatigue, intermittent fevers. She was treated for back pain with resolution of symptoms over several weeks. Case 3: a 33 y/o male with two weeks of right upper quadrant pain, night sweats, malaise and fevers. Splenomegaly had incidentally been discovered on imaging for nephrolithiasis. The patient was admitted for diagnostic splenectomy and supportive care. He had a prolonged, six month course, complicated by a post-operative abscess. All three cases had lymphocytic predominant leukocytosis on presentation, were found to have serologically confirmed acute CMV, and had prolonged recovery times with functional limitations lasting from several weeks up to six months.

DISCUSSION: Severe CMV infection with prolonged disease course in otherwise healthy adults is unusual. With acute infection, disease is most commonly localized to a single organ system. Presentations with severe multisystem involvement are rare. Acute CMV infection should be on the differential diagnosis for immunocompetent patients presenting with fevers of unknown origin. Though there are few treatments outside of supportive care for this infection, close hospital monitoring is important as fulminant CMV can cause significant illness burden, even for patients without additional comorbidities.

PRIMARY MYELOFIBROSIS AT AN UNUSUAL AGE

CPT Erin L. Tompkins, MD, (Associate), Anthony Fadell, MD. Madigan Army Medical Center, Tacoma, WA.

Introduction: Myeloproliferative disorders are a group of conditions that cause abnormal clonal proliferation and abnormal development of cell lines. Primary myelofibrosis (PMF) is the least frequent among the chronic myeloproliferative diseases, and occurs with an overabundance of collagen production as well as disordered hematopoiesis. PMF arises mainly in middle aged and elderly patients with the median age of 67 years. Roughly 5 percent of patients with PMF are diagnosed before the age of 40 years. We discuss a case of severe, early-onset PMF in an active duty male.

Case: The patient is a previously healthy 38-year-old active duty male who presented in October 2011 after experiencing exertional chest pain and bloating for one week in the setting of a longer history of midthoracic back pain, fatigue and episodic pruritus. He was found on CT scan to have an ill-defined infiltrating mass in the porta hepatis with associated intrahepatic and extrahepatic biliary ductal dilatation, early termination of the portal vein consistent with portal vein thrombosis, esophageal varices, and massive splenomegaly. Labs were significant for a profound iron deficiency anemia, unexplained leukocytosis, and moderate thrombocytosis. Genetic analysis was performed and the patient was homozygous positive for JAK2 V617F mutation, a classic clonal marker found in patients with PMF. Analysis for BCR-ABL was also sent, and was negative. Subsequent bone marrow biopsy revealed erythroid hyperplasia, and increased megakaryocytes with atypical hyperlobulated forms. Over the next few years, it became evident that the primary disease involvement in this patient involved his biliary system. He has undergone several stenting attempts as he is extremely prone to biliary obstruction. He also has had at least one episode of significant cholangitis thus far. Often, his hospital course is complicated by *E.coli* bacteremia and *C.difficile* infection. Despite these difficulties, the patient continues to be self-sufficient, ambulatory, and completes ADLs and IADLs independently.

Discussion: We present a case of a young man with a rare form of clonal disease, who is both outside of the expected age group for this condition, and has a less commonly seen form of myeloproliferative neoplasm. In cases of unexplained splenomegaly, and/or intrahepatic obstruction, even in relatively young and healthy patients, PMF should be considered. Genetic analysis along with symptomology and hallmark signs on microscopy will aid in diagnosis.

CAPECITABINE INDUCED ARRHYTHMIA.

CPT Bernadette Villarreal, DO (Associate), COL Eric Shry, MD. Madigan Army Medical Center, Tacoma, WA

Introduction: Capecitabine is an oral prodrug of 5-fluorouracil (5FU) that has become integrated into the treatment of multiple cancers due to its ease of administration and favorable balance of efficacy and toxicity. Cardiotoxicity is a well described adverse event reported with 5FU, but has been rarely reported with capecitabine.
Case: An 87-year-old male with history of hypertension, but no other cardiac history was diagnosed with low rectal T3N1 adenocarcinoma. The patient was started on neoadjuvant capecitatbine and local radiation. Four days into therapy he presented with substernal chest pain consistent with angina, which resolved prior to presentation. Initial CXR was unremarkable, troponins were negative, and EKG demonstrated peaked T waves with resolving ST segment depression. The patient had 4 additional episodes of chest pain associated with dynamic EKG changes in a pattern consistent with posterior ST elevation and hyper-acute T waves which degenerated into sustained ventricular tachycardia with fusion beats captured on telemetry. The patient underwent cardiac catheterization which demonstrated mild large vessel coronary disease and branch-vessel disease without a culprit lesion. An echocardiogram demonstrated left ventricular hypertrophy with normal systolic function. Based on temporal association with starting capecitabine, his angina, EKG changes, and ventricular tachycardia were felt to be due to capecitabine induced vasospasm. The capecitabine was stopped and he was started on metoprolol, amlodipine, and isosorbide mononitrate without recurrence.
Discussion: Capecitabine is a prodrug which is orally administered and is converted to 5FU primarily in tumor cells and the liver. It has a milder toxicity profile as compared to 5FU; however cardiotoxicity has been observed including MI, angina, dysrhythmias, EKG changes, and cardiomyopathy. Chest pain is reported in approximately 6% of patients and dysrhythmias are reported in <5%. The mechanism of the symptoms and dysrhythmias are unclear; both coronary thrombosis and vasospasm are proposed causes. Capecitabine should be considered to have cardiotoxic potential and warrants further investigation into the exact mechanism.

HYPEREOSINOPHILIC SYNDROME MASQUERADING AS AN ACUTE CORONARY SYNDROME

CPT Kimberly Zibert, DO (Associate), MAJ Shaun Miller, MD. Madigan Army Medical Center, Tacoma, WA.

Introduction: Hypereosinophilic syndromes are rare disorders that can result in multi-organ failure secondary to infiltration and inflammation caused by sustained eosinophilia. Presenting symptoms are driven by the effected organ with dermatologic, pulmonary, and gastrointestinal involvement being the most common. Cardiac involvement is seen less frequently but has been shown to have significant morbidity and mortality secondary to its rapid progression.

Case: A 62-year-old black male presented with a 2-week complaint of intermittent chest pain and dyspnea. He was noted to have elevated biomarkers and nonspecific changes on EKG. An echocardiogram demonstrated a pericardial effusion without tamponade physiology as well as a mildly depressed ejection fraction with questionable anterior hypokinesis. Labs were notable for mildly elevated inflammatory markers and a CBC showing an absolute eosinophilia count (AEC) of 19,000. He was taken for coronary angiography which revealed only mild atherosclerotic disease. The patient was treated for myopericarditis with NSAIDS and colchicine with some clinical improvement in symptoms. The patient underwent an extensive workup to include evaluation for parasites, T lymphocyte phenotyping, bone marrow aspirate and biopsy, and molecular testing for the *FIP1L1/PDGFRA* mutation, all of which were negative. The patient was treated with high doses of prednisone, tapered as tolerated. His AEC subsequently declined to 7000.

Discussion: The prevalence of hypereosinophilic syndromes is unknown but estimated to be anywhere from 0.36 to 6.3 per 100,000. While the majority of cases are idiopathic, several can be explained by T-cell lymphomas or by parasitic and neoplastic etiologies. Treatment is guided by the presence or absence of the fusion of Fip1-like 1 (*FIP1L1)* and platelet-derived growth factor receptor alpha *(PDGFRA)* genes. In *FIP1L1/PDGFRA*-negative disease, treatment consists of high dose glucocorticoids. In patients intolerant to glucocorticoids or requiring more than 10mg/day after initial therapy, a second-line agent is added. Allogeneic hematopoietic cell transplant is an option when pharmacologic therapy fails or is not tolerated, however, it is associated with higher morbidity with limited data on long term remission.

SAUSHEC

San Antonio Uniformed Services Health Education Consortium

Clinical Vignettes

A RARE TRANSFORMATION: MYELODYSPLASTIC SYNDROME TO MAST CELL LEUKEMIA

Kathryn Bello, CPT, MC, USA (ACP Associate), Matthew Shupe, Capt, USAF, MC (Associate), and William N. Hannah Jr., LtCol, USAF, MC (FACP); SAUSHEC Internal Medicine, San Antonio, TX

Introduction: Less than five cases of myelodysplastic syndrome (MDS) transforming into mast cell leukemia (MCL) have been reported. MCL is a rare form of systematic mastocytosis representing less than one percent of all patients with mastocytosis. Mast cell leukemia is diagnosed by the fulfilling the criteria for systematic mastocytosis and additionally having twenty percent or greater atypical mast cells in bone marrow or greater than ten percent in blood. Treatment for mast cell leukemia is divided into two strategies: controlling mast cell release symptoms or limiting mast cell burden.

Case Report: An eighty year old female with known refractory anemia with excess blast type 2 was requiring frequent hospitalizations for platelet transfusions. Over two months, she developed fatigue, weakness, anorexia, diffuse abdominal pain, nausea, and vomiting. The patient recently finished cycle eighteen of azacitidine for her MDS. On physical exam, the patient had diffuse abdominal tenderness worse in the mid-epigastrium and a faint maculopapular rash on her back, arms, and legs with significant excoriations. Her pancytopenia was at baseline; however, there was a new basophil count of twenty-four percent. Lipase, amylase, urinalysis, and fecal occult blood were all unremarkable. A computed tomography of the abdomen and pelvis did not show any intra-abdominal process. Given her increased frequency of platelet transfusions, basophilia, and her constitutional symptoms, a bone marrow biopsy was performed and a serum tryptase was obtained. Her tryptase was 600 mcg/L (2.2-13.2 mcg/L). Her bone marrow showed 100% cellularity with aggregates of interstitial, perivascular and paratrabecular mast cells in fibrotic stroma. Her marrow showed CD2 and CD25 positivity and mast cell aggregates with spindling. She was treated with prednisone 50 mg, ranitidine 150 mg, cetirizine 10 mg, and esomeprazole 40 mg with good control of symptoms.

Discussion: Clinical suspicion for MCL was considered due to the patient's rash, abdominal pain with negative lab and imaging, nausea, and basophilia. On manual differential and cell count, basophils have a similar appearance to mast cells. Bone marrow biopsy can definitively identify mast cells and with stereotypical immunohistochemistry, the diagnosis can be established. In patients with MDS having symptoms of mast cell release, it is important to have mast cell leukemia on the differential. Overall prognosis is poor with six month expected mortality; primary treatment is antihistamine therapy which will greatly improve symptoms.

SEVERELY ELEVATED HEMOGLOBIN AND HEMATOCRIT IN POLYCYTHEMIA VERA WITHOUT THROMBOSIS

Nicholas Cosentino, CPT, MC, USA (Associate), Ryan Devine Maj, USAF, MC (Member); SAUSHEC Internal Medicine, San Antonio, TX

Introduction: Polycythemia vera is a myeloproliferative disorder resulting from a hematopoietic progenitor mutational event that results in increased red blood cell production. One major cause of morbidity in PV is due to thrombosis. We present a case of PV with markedly elevated hemoglobin and hematocrit without evidence of thrombosis on imaging or exam.

Case Presentation: A 43 year old African American male with no significant medical history presented to the emergency room with left ankle pain for several days after undergoing diagnostic arthroscopy six days earlier. Pre-admission labs revealed significantly elevated hemoglobin of 24.3 g/dl with an undetectable hematocrit, likely higher than 70%. He also had a leukocytosis of 11.9 x 10^3 and mild thrombocytosis of 563 x 10^3. The only previous blood count evaluation for the patient was eight years earlier with elevated hemoglobin of 16.8 g/dl, hematocrit 49.7% and platelet count of 698K. He had no other complaints on admission to include aquagenic pruritus, headache, erythromelalgia or shortness of breath. Patient reported no significant medical history and denied smoking or history of pulmonary disease. Family history was negative for malignancy. CT chest angiography and lower extremity venous Doppler ultrasounds were negative for pulmonary embolus and deep vein thrombosis. JAK2 V617F mutation was detected along with subnormal erythropoietin level. BCR-ABL returned negative for chronic myelogenous leukemia. According to the revised WHO criteria, results were diagnostic for primary polycythemia disorder due to PV. He was started on aspirin as well as therapeutic phlebotomy. With intervention, the patient's platelet count rose from 563k to 1344k at its peak over a period of one week, leading to the addition of hydroxyurea. Since initiation of therapy, hematocrit and platelet count have decreased to 47% and 471k respectively within 3 months.

Discussion: The unusual presentation of this case was an asymptomatic presentation despite the significantly elevated hematocrit. Even postoperatively, there was no evidence of thrombosis despite an estimated annual risk of thrombosis in patients with hematocrits >60 % to be over 75%. The median survival for patients with untreated symptomatic PV is 6-18 months, whereas treated patients have good long term expected survival. The rise in platelet count likely was reactive, either to worsening iron deficiency with phlebotomy and/or post-surgical thrombocytosis.

EXTENDED SPECTRUM BETA LACTAMASE *ESCHERICHIA COLI* MANDIBULAR INFECTION IN A RHEUMATOID ARTHRITIS PATIENT

Daniel M. Kaplan, CPT, USA, MC (Associate), Michelle R. Newkirk, Capt, USAF, MC (Associate), Jay B. Higgs, Col (Ret), USAF, MC (Member). SAUSHEC Internal Medicine, San Antonio, TX

Introduction: *Escherichia coli* (*E. coli*) is a facultative anaerobic Gram negative rod that is commensal in the human gut but is also a common cause of morbidity when it escapes its normal habitat. Variants of *E. coli* have developed many forms of antibiotic resistance. We present a case of extended-spectrum beta-lactamase (ESBL) *E. coli* abscess of the mandible of a gentleman with rheumatoid arthritis being treated with methotrexate, hydroxychloroquine, and adalimumab.

Case Report: A 59 year old male with a past medical history of rheumatoid arthritis controlled with methotrexate, hydroxychloroquine, and adalimumab developed a mandibular infection in December 2013 requiring dental surgery. Patient had several relapses of bleeding and infection between December 2013 and August 2014. He underwent multiple debridements and tooth extractions, had a bone graft for resorbed bone, and was placed on numerous antibiotic regimens. The patient had never been on a bisphosphonate, nor did he have a history of radiation to the jaw. His rheumatoid arthritis symptoms flared during this period as his methotrexate and adalimumab were held, but were successfully managed with tramadol, naproxen, and later, low-dose prednisone (5-10 mg daily). In July 2014, it was believed the infection was completely eradicated, so his adalimumab therapy was restarted. Eight hours later, he developed another mandibular abscess requiring drainage and additional tooth extraction. Culture of the abscess was positive for ESBL *E. coli* sensitive to ciprofloxacin. He was treated with oral ciprofloxacin., The patient continues to be followed by oral surgery for repeat wash-outs and prolonged antibiotic therapy.

Discussion: *E. coli* is generally considered a benign and even protective organism in the gut, as it pre-vents the growth of more virulent flora. However, *E. coli* can acquire genes that make them more likely to become pathogenic, such as an ESBL. Concurrently, immunomodulatory drugs are increasingly used for diseases such as rheumatoid arthritis. Our patient was on immunosuppressants that placed him at increased risk of infection. His repeated infections suggest that the pathogen may have never been entirely cleared, and his multiple rounds of antibiotics may have played a role in selecting ESBL *E. coli*. The oral cavity is an unusual location for infection with *E coli*, which does not typically colonize this location. Immunomodulatory drugs may have predisposed to this atypical presentation.

LINEZOLID TOXICITY MIMICKING MYELODYSPLASTIC SYNDROME

Maurice Khayat, CPT, MC, USA (Associate); Wilfred dela Cruz, Maj, USAF, MC (Associate); Dale Selby, Col, USAF, MC; SAUSHEC Internal Medicine, San Antonio, TX

Introduction: Linezolid is an oxazolidone antibiotic that interferes with protein synthesis through inhibition of the 70s ribosomal subunit. It is indicated for most Gram positive infections, most notably for treatment of methicillin resistant *Staphylococcus aureus*. Common reported hematologic toxicities include anemia, thrombocytopenia and leukopenia. The proposed mechanism of activity is mitochondrial damage leading to the reduction in hematopoietic cell lines.

Case Report: The patient is a 55 year old African-American male status post a left total knee arthroplasty 4 months prior to evaluation complicated by methicillin resistant *Staphylococcus aureus* surgical site infection requiring multiple surgical revisions and treatment with linezolid for over 90 days. He initially presented 1 month prior at the Ophthalmology clinic for the evaluation of blurry vision bilaterally. At that time, he was noted to have hypotension, poor appetite an unintentional 30 pound weight loss. A CBC obtained at that time, revealing a worsening anemia, requiring a 2 unit red blood cell transfusion. His symptoms were attributed to linezolid-induced bone marrow toxicity. Dysplastic leukocytes and rare nucleated red blood cells were noted in his peripheral smear leading to a bone marrow biopsy, which showed ringed sideroblasts. Concern was raised for myelodysplastic syndrome (refractory anemia with ringed sideroblast). Subsequent analysis revealed a normal flow cytometry and cytogenetics and a normal karyotype. Linezolid was discontinued and repeat CBC several weeks later demonstrated a recovery of his red cell line. This suggests that the patient's anemia and bone marrow findings which mimic MDS are consistent with linezolid toxicity.

Discussion: Linezolid's inhibition of protein synthesis may present with reduction in cell lines and demonstration of ringed sideroblasts through damage incurred to the mitochondria of erythopoetic cells. This phenomenon has been described in prior case reports as well as a retrospective review of linezolid-related sideroblastic anemia in the University Hospital of Lille, France. The combination of anemia and these pathologic findings may mimic myelodysplastic syndrome, causing a potential for overdiagnosis of MDS. Of note, the anemia produced by linezolid toxicity appears to be reversible with discontinuation of the offending drug, a repeat CBC demonstrating recovery would help to differentiate linezolid toxicity versus myelodysplasia.

DIFFERENTIATION OF STILL'S DISEASE WITH MACROPHAGE ACTIVATION SYNDROME FROM PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

Tyler Powell, CPT, MC, USA (ACP Associate), Anthony J. Oliva, MD; SAUSHEC Internal Medicine, San Antonio, TX

Introduction: Still's disease is a systemic inflammatory process characterized by the presence of persistent daily fevers and arthritis that can rarely be complicated by the development of the macrophage activation syndrome (MAS), a secondary form of hemophagocytic lymphohistiocytosis (HLH), at presentation. This condition is associated with hemophagocytosis of the bone marrow and liver leading to hepatitis and cytopenias identical to primary genetic HLH.

Case Report: A 29-year-old female presented to our hospital with a complaint of daily fevers to 104^{o}F, arthralgias, sore throat, pruritus, and generalized malaise for 3 weeks. Initial laboratory studies showed transaminitis with an AST of 670 IU/L and ALT of 378 IU/L, leukopenia with white blood cell count of 3.2 and thrombocytopenia of 99,000. Following admission the patient experienced progressively higher fevers to maximum of 105.3^{o}F despite broad spectrum antibiotics and negative infectious work-up. Concern for potential Still's disease arose and Rheumatology was consulted for further assistance. A ferritin level returned at >6200 supporting the diagnosis and the decision was made to initiate therapy with high dose intravenous methylprednisolone 1000mg daily for 3 days followed by oral prednisolone 60mg daily and subcutaneous anakinra for potential Still's disease. Despite this treatment, the high fevers continued and the patient's liver function tests continued to elevate with AST reaching >2200 IU/L over the ensuing week. Leukopenia worsened to 2.2 and DIC subsequently developed with INR 1.6, fibrinogen 74, and platelet count of 72,000 requiring transfusions of cyroprecipitate. Bone marrow and liver biopsies were performed which were significant for the presence of hemophagocytic invasion consistent with primary HLH vs. MAS. Given the poor response to steroid therapy, there was high suspicion for primary HLH and the patient was started on the HLH-94 protocol with etoposide and dexamethasone. Fevers resolved and LFTs gradually improved over the ensuing week with decrease in ALT to less than 300 IU/L. Follow-up labs as an outpatient showed continued improvement in ALT to less than 200 IU/L and resolution of thrombocytopenia further supporting the diagnosis of primary HLH.

Discussion: This case illustrates the difficulty in differentiating primary HLH from Still's disease with MAS at presentation. Both conditions are associated with elevated serum ferritin levels and persistent fevers as well as elevated liver function tests and cytopenias when hemophagocytosis is present. Therefore, failure of presumptive MAS to improve with immunosuppressive therapy warrants consideration of primary HLH and institution of an appropriate chemotherapeutic regimen.

CHIKUNGUNYA IN THE MILITARY HEALTH SYSTEM

William J. Wadzinski, CPT, MC, USA (ACP Associate), Shane Patterson, Capt, USAF, MC (ACP Associate), Heather C. Yun, LtCol, USAF, MC, FACP, SAUSHEC Internal Medicine, San Antonio, TX

Introduction: A 25-year-old female dependent with no significant past medical history presenting with acute onset of diffuse joint pains.

Case Report: The patient presented within hours after returning from recent travel to Puerto Rico complaining of diffuse, disabling arthralgia, subjective fevers, fatigue, headache, and rash. Symptoms began the day prior to presentation as acute onset arthralgia occurring two days following multiple mosquito bites. The patient's past medical history and past surgical history were unremarkable. She was afebrile and hemodynamically stable at presentation. Her physical exam was significant for a blanching erythematous macular rash on her arms, legs, and abdomen. The remainder of her physical exam was benign. Laboratory analysis included: a complete blood count, renal function panel, liver associated enzymes, coagulation panel, CRP, ESR, beta-HCG, RA antibody, anti-CCP antibody, dsDNA antibody, ANCA panel, Dengue IgG and IgM, GC/Chlamydia NAAT, iron panel, CK, and peripheral smear. All were unremarkable. Dengue serologies were negative. The patient's constellation of symptoms following mosquito exposure in Puerto Rico was most concerning for chikungunya. She was treated symptomatically and blood was obtained for polymerase chain reaction (PCR) and serologies. Acute sera were negative; PCR was positive, and seroconversion by IgM occurred by day 10.

Discussion: Chikungunya is a mosquito-borne, RNA virus that causes fevers, arthralgias, and a variable maculopapular rash in infected individuals. The virus is classically transmitted by the *Aedes aegpytii* mosquito. *Ae. albopictus* is also an efficient vector. The virus has become epidemic in the Caribbean, Central, and South America. Cases are increasing among U.S. travelers returning from affected regions. Both vectors are present within the United States, particularly *Ae. alobopictus*, posing the potential for increasing autochthonous transmission throughout other U.S. states and territories. This case illustrates the growing number of chikungunya cases in returning travelers with patients now presenting in the Military Health System. Though the disease typically will not cause fatalities in the healthy young military population, it may result in a long course of disabling joint pains and fatigue thereby reducing the effectiveness of the individual. Early recognition of disease, patient counseling, and vector control can help to prevent epidemics within the military and civilian population.

TAMC

Tripler Army Medical Center

Clinical Vignettes

THE KISS OF DEATH: A RARE INSTANCE OF ANAPHYLACTIC REACTION TO THE BITE OF *TRIATOMA RUBROFASCIATA*, THE "RED MARGINED KISSING BUG"

CPT Caleb Anderson, MD (Associate), COL Conrad Belnap, MD, Tripler Army Medical Center, Honolulu, HI

Introduction: Triatoma (kissing bugs), a predatory genus of blood-sucking insects of the family Reduviidae, is a well-known vector in the transmission of *Trypanosoma cruzi*, the causative agent of Chagas disease. However, it is less well appreciated that bites from these insects can cause symptoms ranging from a localized cutaneous reaction to generalized anaphylaxis. Anaphylactic reactions following bites have been reported with five of the eleven species endemic to the United States, with the majority of cases secondary to *Triatoma protracta* and *Triatoma rubida*. Reports of anaphylactic reactions to *Triatoma rubrofasciata*, endemic to Florida and Hawaii, are sparse in the literature with only one previously reported case in 1973.

Case Report: A 50 year old healthy female from a rural area of the Hawaiian island of Oahu suffered three separate bites from *Triatoma rubrofasciata* and experienced a generalized, anaphylactic reaction on each occasion. On the first occasion, the patient suffered the sudden onset of dizziness, systemic pruritus, and a feeling of "tightness" in her throat shortly after putting on her jacket. This progressed to whole body urticaria, dyspnea, and dizziness. Upon arrival to the Emergency Department she was hemodynamically stable and was treated with IV diphenydramine and methylprednisolone, with gradual amelioration of her symptoms. Evidence of an insect bite was noted two days later. One year later, she noticed two bites on her right forearm while lying in bed, shortly after which she developed dyspnea, urticaria, and dizziness followed by a witnessed loss of consciousness. A search of the bed revealed the insect *Triatoma rubrofasciata*, though it was not saved for official identification. The final reaction occurred nine months later and was again characterized by hives, dyspnea, and lightheadedness. On this occasion, the culprit insect was captured and identified as *Triatoma rubrofasciata* by a medical entomologist.

Discussion: Anaphylactic reaction to the bite of *Triatoma rubrofasciata* is a rare event. Currently, there is no commercially available skin test to determine allergy to Triatoma bites and the diagnosis is based on clinical presentation. Likewise, there is no immunotherapy to the insect bite. In individuals with known anaphylactic reaction, avoidance is the best strategy. Considering the insect is nocturnal and found in rural areas, viable strategies include using insect repellent, bed nets, wearing pajamas with sleeves, moving to a more urban area, and inspecting sheets before bed. Epinephrine is the only effective treatment for anaphylaxis and an epinephrine autoinjector should be readily available.

A UNIQUE PRESENTATION OF POLYCYSTIC LIVER DISEASE

Cory G. Madigan, MD (ACP Associate), James Y. Wang, MD (ACP Member), Tripler Army Medical Center, Honolulu, HI

Polycystic liver disease (PLD) is defined by the presence of greater than twenty hepatic cysts. It is most commonly associated with autosomal dominant polycystic kidney disease (ADPKD), but can also be witnessed in the absence of renal disease as an unrelated autosomal dominant process caused by mutations in SEC63 or PRKCSH. Most patients with PLD are asymptomatic, but complications may arise from cyst infection or bleeding, compressive hepatomegaly, or hepatic venous outflow obstruction. Even in extensive cases, synthetic function is generally preserved.

A 45-year-old male with no significant past medical history was admitted to a small community hospital for ascending cholangitis. After medical stabilization, he underwent cholecystectomy and was discharged with routine follow up with general surgery. He was eventually referred to gastroenterology for persistence of abnormal radiographic and laboratory findings first noted while hospitalized. The most curious finding was radiographic observation of the development and regression of a subcapsular hepatic cyst. The cyst peaked in size at 7.1cm x 3.9cm x 11.3cm, before resolving entirely. Imaging further revealed liver heterogeneity consistent with cirrhosis, portal vein thrombosis, and massive splenomegaly. The patient's laboratory values were remarkable for an elevated INR of 1.3, decreased albumin of 3.1 g/dL, ALT of 69 U/L, AST of 62 U/L, and platelets of 109,000/mm^3. Of note, neither radiographic nor laboratory studies revealed evidence of renal disease. Upon interviewing the patient, he endorsed painful breast enlargement and leg swelling which had been present for years. His family history was remarkable for a distant cousin with hemochromatosis, but negative for any other hepatic or renal disease. He denied a history of alcohol abuse. His physical exam was remarkable for painful gynecomastia, 1+ pedal edema, and splenomegaly, but lacked other typical stigmata of cirrhosis. The patient was evaluated for hemochromatosis, viral hepatitis, autoimmune hepatitis, and Wilson's disease. This workup returned negative except for H63D homozygosity, an uncommon hemochromatosis genotype typically associated with minimal iron deposition and rare clinical significance. Liver biopsy was performed, which revealed fibrosis, hepatocellular extinction, mild iron deposition, and numerous von Meyenburg complexes. These findings were determined to be most consistent with cirrhosis in the setting of polycystic liver disease.

This case showcases two helpful lessons about PLD. First, it captures the unique development and resolution of a hepatic cyst on multiple imaging studies. Secondly, it raises awareness of this disease's ability to progress to cirrhosis.

CALCIUM MAELSTROM – RECALCITRANT HYPOCALCEMIA EXACERBATED BY PREGNANCY FOLLOWING RAPID CORRECTION OF THYROTOXICOSIS

MAJ Terry Shin, MD (Associate), MAJ Arthur Guerrero, MD (FACP), Tripler AMC

Introduction: Thyrotoxicosis can have marked effects on bone known as thyrotoxic osteodystrophy. The removal of thyroid stimulation after thyroidectomy can induce serum hypocalcemia. Pregnancy in itself increases bone resorption and can exacerbate hypocalcemia. Herein we report the first case of recalcitrant hypocalcemia due to a combination of thyrotoxic osteodystrophy and pregnancy after surgical correction of Graves' disease complicated by postoperative hypoparathyroidism.

Case Report: A 29 year old pregnant woman with Graves' disease presented with severe persistent hypocalcemia after thyroidectomy. Six months prior to presentation she was diagnosed with Graves' disease and remained uncontrolled with methimazole. She was confirmed pregnant prior to radioactive iodine ablation (RAI), and underwent total thyroidectomy during her first trimester. After surgery, continuous IV calcium infusion and high doses of oral calcium and calcitriol was administered until delivery of the fetus allowed discontinuation at postoperative day 18. A total of thirty eight grams of oral and seven and a half grams of intravenous elemental calcium were administered.

Discussion: The combined effects of thyrotoxic osteodystrophy and pregnancy can induce persistent severe hypocalcemia. Increased vigilance and early calcium supplementation should be a priority in the management of these patients.

USU

Uniformed Services University

F. Edward Hébert School of Medicine

Clinical Vignettes

EPIDURAL ROPIVACAINE FOR ANALGESIA IN METASTATIC ADENOCARCINOMA OF UNKNOWN PRIMARY

2LT Cyrus Askin BS (ACP Medical Student), Lt Col Rechell Rodriguez MD, FACP, San Antonio Military Medical Center, Fort Sam Houston, TX

Metastatic adenocarcinoma of unknown primary is a disease that provides a unique challenge to physicians as it lacks specific targets for chemotherapy and often results in painful metastatic lesions.

A 59-year-old woman with known adenocarcinoma of unknown primary with metastatic disease to the brain presented to the ER complaining of progressive back pain over the previous month. An MRI revealed metastases throughout her inferior thoracic and lumbar vertebrae and a pathologic fracture. The decision was made to initiate radiation therapy. After two of the scheduled 14 radiation treatments, the patient's back pain intensified. She was unable to lay supine long enough to undergo radiation treatment despite use of hydromorphone and increasing doses were not tolerated due to refractory nausea. Oxycodone caused her excessive sedation and AMS. Peripheral IV access was lost and with it any avenue for IV pain management. A left upper extremity PICC line became necessary despite her recent history of PICC line associated RUE SVC syndrome, however, three days after its placement, she developed a new PICC line thrombus. The PICC line was removed and once again the patient was without IV access. With few options remaining, we collaborated with colleagues from anesthesiology, interventional radiology and the pain service. The MS-IV on the primary team presented the idea of placing an epidural for localized pain management until a more optimal, sustainable pain regimen could be determined. Although initially reluctant, the pain management service agreed that this was a complicated, unique scenario, and placed a tunneled epidural to enable the primary team to treat the patient's pain with Ropivacaine. Within a day, her excruciating pain improved to zero or one on a 10-point pain scale, which facilitated continuation of radiation therapy and a thoracic vertebrae kyphoplasty. IR subsequently obtained a femoral PICC line that remained patent throughout her admission.

To our knowledge, this case illustrates the novel use of epidural Ropivacaine as an interim, bridging therapy for pain management when alternatives are either contraindicated or poorly tolerated until a sustainable pain regimen could be elucidated. Furthermore, this case illustrates the importance of a multidisciplinary approach to treating cancer patients with very poor prognoses and significant tumor burden.

Medical Student, Eastern Virginia Medical School. Norfolk, VA.
Uniformed Services University of the Health Sciences, Bethesda, MD. *The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Department of the Air Force, Department of the Army, Department of Defense or the Uniformed Services University of the Health Sciences.

WBAMC

William Beaumont Army Medical Center

Clinical Vignettes

SILDENAFIL INDUCED ACUTE INTERSTITIAL NEPHRITIS

CPT Ryan Burkhart, DO (ACP Resident), Nina Shah, DO, William Beaumont Army Medical Center, El Paso, Texas

Introduction:
Acute interstitial nephritis (AIN) is characterized by an inflammation of the renal interstitium, most often mediated by a drug induced hypersensitivity reaction. Multiple medications are known to cause AIN. Drug induced AIN usually occurs in a temporal relationship with the medication and polypharmacy may complicate the diagnosis. We present the first case report of sildenafil induced AIN in an 81 year old male.

Case:
An 81 year old Asian male with a history of erectile dysfunction, chronic kidney disease stage 3a, hypertension, hyperlipidemia, coronary artery disease, gout with chronic allopurinol use for three decades, and osteoarthritis with remote NSAID use was admitted with generalized edema, rapid weight gain over the previous month, nephrotic range proteinuria (14.7 g/day recorded two weeks prior), and acute kidney injury. The patient reported an acute change in physical appearance and symptomatology the day after the ingestion of a single dose of sildenafil four days prior to his admission. A renal biopsy was performed in the setting of nephrotic range proteinuria and acute kidney injury with a peak serum creatinine of 6.1 mg/dL (baseline serum creatinine 1.4 mg/dL). The biopsy was notable for minimal change disease with acute on chronic interstitial nephritis. Renal replacement therapy was initiated simultaneously with glucocorticoid therapy. Renal recovery within six weeks permitted discontinuation of dialysis and steroid dose reduction.

Discussion:
The temporal association and the absence of any new drugs suggest that the AIN was most likely due to the sildenafil. AIN superimposed on minimal change disease is a known association of NSAID induced nephropathy. However, in this case NSAIDs are less likely to have caused the AIN given their remote use. The ease of steroid responsiveness would also suggest another cause as NSAID induced AIN is often steroid resistant. The chronic interstitial nephritis is likely due the allopurinol and remote history of NSAID use. Prior NSAID use may have contributed to the minimal change disease. Sildenafil use is common for the treatment of erectile dysfunction as well as pulmonary arterial hypertension. The true incidence of renal issues with sildenafil is unknown as there is minimal published data or post marketing renal adverse events. As the number of sildenafil prescriptions increases, more cases of AIN may be identified and physician awareness for this drug disease association is necessary.

TWO RARE CASES OF PAUCI-IMMUNE MEDIATED NECROTIZING AND CRESCENTIC GLOMERULONEPHRITIS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

CPT Ryan Burkhart, DO[1] (ACP Resident), Nina Shah, DO[1], LTC Michael Abel, MD[1], COL James D. Oliver III, MD[2], (ACP Member), Matthew Lewin, MD[3]
[1]WBAMC; [2]WRNMMC; [3]ProPath, Dallas, Texas

Introduction: Renal involvement in systemic lupus erythematosus (SLE) is usually immune complex- mediated and may have multiple different presentations. Pauci-immune necrotizing and crescentic glomerulonephritis (NCGN) refers to extensive glomerular inflammation with few or no immune deposits and results in rapid decline of renal function if left untreated. We present two rare cases of biopsy proven pauci-immune necrotizing and crescentic glomerulonephritis in two patients with inactive SLE.

Case 1: A 79 year old Hispanic male with mild dementia and a history of chronic kidney disease stage 2 with nephrotic range proteinuria (7.5 g/day fifteen years prior attributed to biopsy proven "secondary membranous nephropathy") presented with acute kidney injury (serum creatinine 9.2 mg/dL), active urinary sediment, and 500 mg/day proteinuria. Current serologic testing indicated equivocal ANA, negative anti-dsDNA antibodies, normal complement levels, and increased P-ANCA titer with positive myeloperoxidase antibodies. The renal biopsy was diagnostic for NCGN superimposed on secondary membranous nephropathy. Treatment included renal replacement therapy, glucocorticoid therapy, plasmapheresis, and weekly rituximab for four weeks. A diagnosis of SLE based on American College of Rheumatology criteria was discovered via review of Veteran's Administration records after completion of treatment for pauci-immune NCGN. The patient did not regain sufficient renal function and remains dialysis dependent at sixteen month follow up. Additionally, the patient remains free of systemic manifestations of vasculitis or SLE.

Case 2: A 61 year old Hispanic female with a history of SLE/scleroderma overlap syndrome with interstitial lung disease, chronic kidney disease stage 1 with proteinuria (400 mg/day), and baseline serum creatinine of 0.6 mg/dL was admitted for further evaluation after routine lab work indicated an increase in the serum creatinine to 2.4 mg/dL and proteinuria to 2.3 g/day. The biopsy was consistent with pauci-immune NCGN and acute tubular necrosis without evidence of lupus nephritis. The biopsy prompted additional testing and the results were notable for an elevated MPO antibody titer. Treatment consisted of glucocorticoid therapy and weekly treatments with rituximab for four weeks. On three month follow up, the serum creatinine improved to 1.1-1.3 mg/dL and the proteinuria decreased to 464 mg/day.

Conclusion: ANCA antibodies are detected in 20-31% of patients with SLE. It is increasingly recognized that there is an association between SLE and ANCA seropositivity. It has been suggested that there may be an overlap syndrome. In patients with SLE and biopsy findings of NCGN without significant immune complex deposition, ANCA testing should be considered.

EPTIFIBATIDE INDUCED THROMBOCYTOPENIA

Guy S. Dooley IV, DO (ACP Associate); Abu Mohanad Speitan, MD (ACP Associate); Chad B. McBride, DO, William Beaumont Army Medical Center, El Paso, Texas.

Introduction:
Limited case reports and clinical trials show an association between GP IIb/IIIa inhibitors and thrombocytopenia, however it has been difficult to isolate GP IIb/IIIa inhibitors as the causative agent since it is typically given in addition to heparin, a well-known cause of heparin induced thrombocytopenia. In the past with cases of thrombocytopenia both agents are discontinued and the patient is placed on a different class of anticoagulant. This case is unique in that we were able to continue heparin and prove that eptifibatide was the offending agent.

Case Presentation:
A 75yo male presented to the ER with severe chest pain, electrocardiogram showed ST segment depressions, troponins were elevated, and the patient developed hypotension. A diagnosis of right ventricular infarction and cardiogenic shock were made. He was started on a heparin and norepinephrine drip. Cardiac angiography revealed chronic high grade distal left main disease and a culprit high grade mid-RCA lesion. One bare metal stent was placed in the mid-RCA with plans for complete revascularization with coronary artery bypass surgery in the immediate future. Chest pain and hypotension resolved with placement of an intra-aortic balloon pump. Eptifibatide was given during the catheterization and an 18 hour infusion was started post coronary angiography. Four hours later a critical platelet count of 9000 was obtained, baseline on admission five hours previous was 263,000. The platelet count was repeated in a citrate tube returning at 10,000, effectively ruling out pseudo-thrombocytopenia. A heparin induced thrombocytopenia panel returned as negative. Eptifibatide was immediately discontinued and the patient was transfused two units of platelets. Heparin, ASA, and clopidogrel were continued. Each subsequent platelet count continually increased. The patient proceeded to CABG two days later where he received two more units of platelets and three units of packed red blood cells. Platelet count on discharge 13 days later was 436,000.

Discussion:
This case illustrates that eptifibatide causes a rapid and severe decrease in platelet count that can be life threatening in a patient that has never been previously exposed to this agent. Previous reports had difficulty in determining whether heparin or eptifibatide were the offending agent. The uniqueness of this case is due to the rapid onset of severe life threatening thrombocytopenia within 4 hours of giving the eptifibatide and proving that heparin was not the causative agent. Further research needs to be performed to see if the addition of heparin increases the chance of eptifibatide induced thrombocytopenia versus eptifibatide alone.

CHRONIC PANCREATITIS, A RARE ETIOLOGY OF HEMOBILIA

Johanna G. Hollweg, DO (ACP Associate), Michael E. Goldberg, DO, William Beaumont Army Medical Center, El Paso, Texas.

Hemobilia is an uncommon etiology of gastrointestinal bleeding. Hemobilia, bleeding from the hepatobiliary system, is most often a result of hepatic parenchymal or biliary tract disease due to instrumentation or injury. Much rarer etiologies are described in limited case reports and include pseudoaneurysms resulting from the hepatic and gastroduodenal arteries. Diagnosis is made through direct visualization of blood from the papilla; however establishing the etiology takes some investigative action. We present a rare complication of chronic pancreatitis resulting in a gastroduodenal pseudoaneurysm causing hemobilia.

53 year old male with chronic pancreatitis and pancreatic head lesion was scheduled to undergo an endoscopic ultrasound (EUS), however he presented one day prior to the planned procedure with melena and abdominal pain. Admission laboratory findings illustrated a hematocrit of 30.7 g/dL, bilirubin of 2.0 mg/dL, alkaline phosphatase of 885 IU/L and lipase of 21 U/L. Computed tomography (CT) showed new dilation of the intra and extra-hepatic bile ducts, evidence of chronic pancreatitis, and stable pancreatic head mass. Following admission, hematocrit decreased to 23 g/dL and the bilirubin continued to rise. Endoscopic gastroduodenoscopy (EGD) was planned with endoscopic retrograde cholangiopancreatography (ERCP) and EUS. The ampulla was visualized with blood draining from it. EUS illustrated an irregular mass in the pancreatic head however given evidence of hemobilia, fine needle aspiration (FNA) was not performed. ERCP was performed and a distal bile duct stricture was seen that was sampled. Balloon sweep of the duct showed hemobilia with blood clots and a biliary stent was placed with blood seen draining from the stent. CT angiogram was performed which illustrated a collection of contrast material at the pancreatic head with faint communication with the gastroduodenal artery, representing a pseudoaneurysm. Interventional radiology (IR) performed an angiogram and a branch of the gastroduodenal artery was embolized. After transfusion, he remained stable with no evidence of further bleeding and was discharged. Bile duct stricture samples showed no malignancy. Six weeks later he returned for repeat attempt at EUS. FNA was performed and showed only chronic pancreatitis with no malignancy.

Chronic pancreatitis and pseudoaneurysms are rare etiologies of hemobilia. We present a unique case of chronic pancreatitis causing a pseudoaneurysm in the gastroduodenal artery which eroded into the common bile duct causing hemobilia. This case illustrates the importance of multiple modalities including EGD, ERCP, EUS and IR evaluation in determining and treating rare etiologies of upper gastrointestinal bleeding.

PLASMODIUM VIVAX IN A SOLDIER RETURNING FROM THE DEMILITARIZED ZONE

Jason Lanning, DO (ACP Associate), Jeffrey Sherwood, MD (FACP), William Beaumont Army Medical Center, El Paso, TX

South Korea is often overlooked as a country with endemic malaria, with areas along the Demilitarized Zone (DMZ) still endemic for *Plasmodium vivax.* Malaria should be considered in travelers returning from South Korea.

A 21 year-old, active duty, Hawaiian male with a past medical history of asthma was admitted with symptoms including high grade fever, myalgias, nausea, headache, and diarrhea. His symptoms began nine days prior and were waxing and waning throughout that timeframe. He denied any history of sore throat, lymphadenopathy, or rash. The patient's complete blood count revealed thrombocytopenia with a platelet count of 30 K/ul. Mild splenomegaly was noted on bedside echocardiogram, and due to a positive Monospot, the patient was admitted with a suspected viral infection.

Upon further questioning, the patient noted that twelve months prior to his admission he was assigned to South Korea where he was stationed roughly fifteen minutes away from the DMZ. He described multiple outdoor military field exercises and reported that a member of his unit was diagnosed with malaria shortly after one of these exercises. Neither of these soldiers utilized personal protective measures against mosquitos, nor was either soldier given malaria prophylaxis medication. The patient was then stationed in Texas four months prior to presentation and denied any significant outdoor exposures. Also, the patient denied any additional international travel other than to his home in Hawaii before coming to Texas. However, he denied any sick contacts or fresh water swimming during his stay.

A malaria rapid antigen and a peripheral blood smear were obtained. The antigen test was positive for *Plasmodium vivax*, and the species was confirmed after identifying multiple stages of parasites on the blood smear. A literature review raised concerns regarding decreased chloroquine susceptibility due to mass chemoprophylaxis efforts by the Republic of Korea (ROK) Army. The patient was treated with oral atovaquone/proquanil for three days and a course of oral primaquine for presumptive anti-relapse therapy. At one week follow up, the patient was asymptomatic with a normal platelet count and no evidence of parasites on a repeat blood smear.

This case illustrates the need to recognize areas with resurgent malaria in order to provide appropriate pre-exposure prophylaxis and to initiate prompt treatment in febrile returning travelers. Although the ROK has conducted decades of anti-malaria campaigns, *Plasmodium vivax* infection is still occurring near the DMZ. Chloroquine resistance should be accounted for in patients returning from the Korean Peninsula.

BRAIN ABSCESSES CAUSED BY *NOCARDIA VETERANA* IN AN IMMUNOCOMPROMISED PATIENT

Dorothy Shum, DO, Member ACP, Department of Medicine, William Beaumont Army Medical Center, El Paso Texas
Jeffery Sherwood, MD, FACP, Department of Infectious Diseases, William Beaumont Army Medical Center, El Paso Texas

Nocardia veterana is a novel isolate that is mostly found in pulmonary infections. This is a case report of an immunocompromised patient presenting with brain abscesses attributable to *N. veterana* infection.

The patient is a 61 year old female with a kidney transplant secondary to end stage renal disease that was subsequently complicated by Cytomegalovirus enteritis and Pneumocystis pneumonia who presented to the emergency room with increasing lethargy and poor oral intake over the past week. Symptoms were associated with intermittent fevers, nausea, vomiting, and abdominal pain. MRI Brain demonstrated several ring enhancing lesions throughout the brain, with the largest located in the anterior corpus callosum. Blood cultures obtained demonstrated growth of *Nocardia veterana*. A lumber puncture was performed and initial lab results were suggestive for an infectious process. However, cerebral spinal fluid (CSF) cultures had no growth. The patient was started on trimethoprim/sulfamethoxazole for therapy, and subsequently developed renal failure and bone marrow suppression. The antibiotic regimen was transitioned to parenteral ceftriaxone and oral minocycline with successful resolution of symptoms.

Nocardia is an opportunistic pathogen that has the ability to cause a variety of infections and can disseminate to almost any organ in the body. *Nocardia veterana* is a rare isolate among the *Nocardia* species that has been recently recognized. It is important to identify species of *Nocardia* isolates as they can have different clinical disease presentations and antibiotic susceptibility. Most case reports of *N. veterana* appear to preferentially infect the pulmonary system. Signs and symptoms of central nervous system (CNS) nocardiosis are diverse and nonspecific because of its insidious onset. Immunocompromised patients have an increased risk for infection. There has only been one other reported case of *N. veterana* causing brain abscesses. Treatment is guided by retrospective experience and in vitro antimicrobial activity profiles.

WRNMMC

Walter Reed National Military Medical Center at Bethesda

Clinical Vignettes

ALPHA 1-ANTITRYPSIN DEFICIENCY IN A PATIENT WITH STAGE III FIBROSIS

Melanie J. Acevedo Valle, MD (ACP Member), Ryan Kwok, MD (ACP Member), Manish Singla, MD, Dawn Torres, MD
Department of Medicine, Walter Reed National Military Medical Center, Bethesda, MD

Alpha 1-antitrypsin (A1AT) deficiency is an autosomal recessive disease with codominant expression that can be associated with pulmonary disease such as emphysema as well as complications related to chronic liver disease and cirrhosis. Although clinically significant disease is rare, there are approximately 20 million individuals in the United States who carry at least 1 deficiency-associated allele. The highest risk phenotype for development of clinically significant disease is PiZZ though other allelic combinations such as PiMZ and PiSZ can also be associated with liver disease. The polymerization-prone conformation of variant Pi Z leads to the accumulation of abnormally folded proteins in the hepatocyte endoplasmic reticulum and can progress to end-stage liver disease.

A 52 year-old Caucasian male with obesity and diet controlled hyperlipidemia presented for evaluation of chronically elevated liver associated enzymes. The patient was noted to have an asymptomatic elevation in liver enzymes approximately 10 years ago during a routine physical evaluation. He denied any respiratory or gastrointestinal symptoms. Social history was notable for rare alcohol consumption and a remote history of smoking and was negative for high risk behavior or blood transfusions. Physical examination was remarkable for a BMI of 30 and hepatomegaly. Labs demonstrated mildly elevated aminotransferases (ALT 66 and AST 46), an elevated ferritin of 1248 and iron saturation of 31. Serologic workup was otherwise negative for infectious, metabolic, and autoimmune causes of elevated liver enzymes. A liver biopsy was performed which revealed mild activity steatohepatitis, stage 3 (bridging) fibrosis with minimal hemosiderosis and PAS positive, diastase resistant intrahepatic globules consistent with Anti-trypsin (AT) deposition. Biopsy was followed by low serum AT levels at 71 and PiSZ A1AT phenotype.

Diagnosis of hepatic A1AT deficiency can be challenging since most patients are asymptomatic and may only present with abnormal liver enzymes. Age, sex, alcohol consumption and obesity have been reported to worsen hepatic A1AT liver disease. Furthermore, A1AT deficiency might increase the severity of other existing liver disorders. Even with normal pulmonary function patients with hepatic A1AT should be referred to a pulmonologist for evaluation. Genetic screening of siblings of A1AT deficient patients of any phenotype is recommended. There is no proven therapy to reduce hepatic aberrant A1AT accumulation although strategies to reduce inflammation and fibrosis, however carbamazepine and rapamycin, are currently being investigated. Patients who develop decompensated cirrhosis or early-stage hepatocellular carcinoma, liver transplantation in the treatment of choice and is curative of hepatic A1AT deficiency.

NON-RESOLVING CELLULITIS – EXPANDING OUR DIFFERENTIAL TO INCLUDE MASSIVE LOCALIZED LYMPHEDEMA

Gilda Bobele, MD (ACP Resident /Fellow Member), Chin Hee Kim, MD, Walter Reed National Military Medical Center, Bethesda, MD.

A morbidly obese (BMI 67) 52-year-old female presented with several months of left medial thigh discomfort and firmness that increasingly interfered with her ability to ambulate. She denied any recent trauma or new environmental contact exposures, and denied associated fevers or chills, skin breakdown, or progression of skin involvement. Given an appearance similar to cellulitis, she had received multiple courses of antibiotics, all with minimal to no effect. Doppler ultrasounds of the lower extremities had been performed twice and ruled out venous thromboembolism.

Physical exam was notable for asymmetrically pendulous medial thighs disproportionately large when compared to the rest of her habitus. The skin had a brawny peau d'orange appearance with an underlying grapefruit-sized area of firmness with pebbly texture that seemed consistent with chronic lymphedema. However, her distal lower extremities were uninvolved and her clinical history did not support an apparent etiology for lymphedema. Laboratory workup was unrevealing with normal WBC, ESR, and CRP. The patient was treated with intravenous vancomycin for presumed non-resolving cellulitis, possibly from resistant gram-positive organisms or potential inadequate absorption of oral antibiotics, but her symptoms did not improve. An MRI of the extremity ruled out an underlying abscess as a source for persistent symptoms. Dermatology was consulted for superficial biopsy given her skin changes, and this demonstrated dilated lymphatic spaces and dermal fibrosis. With correlation between the clinical history and histopathology, the patient was diagnosed with Massive Localized Lymphedema (MLL).

There are several case reports of MLL in the dermatological and surgical literature, but there remains very little recognition among other specialties including Internal Medicine. The entity was first described by pathologists in 1998, and classically presents as an atraumatic, diffuse, ill-defined mass in the proximal and medial aspects of the extremities of morbidly obese patients. Given appropriate clinical context, providers should consider a dermatology or surgical consult for skin biopsy to support the diagnosis. Treatment is directed at weight loss and treatment of lymphedema - typically with compression devices - but there is little data regarding outcomes. Treatment is indicated for more than symptom relief due to the rare but serious risk of angiosarcoma development within regions of chronic lymphedema. After diagnosis with MLL, the patient was referred to a lymphedema clinic for specialized physical therapy.

In summary, MLL is an increasingly prevalent diagnosis that internists should consider in the morbidly obese population, particularly given its ability to mimic cellulitis.

GRANULOMATOSIS WITH POLYANGITIS: AN INSIDIOUS PRESENTATION LEADING TO A DELAYED DIAGNOSIS

Lee Jamison, MD Associate, Hector Medina, MD Associate, Rachel Robbins, MD Member, Jess Edison, MD FACP, Walter Reed National Military Medical Center, Bethesda, MD

Granulomatosis with polyangiitis (GPA) is a rare, multi-system, autoimmune vasculitis. Disease presentation is highly variable and often quite subtle with symptoms ranging in severity from chronic sinusitis to diffuse alveolar hemorrhage. This variability creates a diagnostic challenge for physicians who may initially attribute presenting symptoms to more common disease processes leading to delays in appropriate therapy.

A sixty-seven year-old male presented to an outside emergency department with acute on chronic dyspnea of eighteen months duration, recurrent epistaxis, and new onset cough with hemoptysis. Past medical history included cardiovascular and peripheral vascular disease, atrial fibrillation and hypothyroidism. On exam temperature was 38.2C, oxygen saturation was 90% on four liters. Labs were notable for a white cell count of 12,000, a hemoglobin of 9.3 g/dL, a creatinine of 2.4 mg/dL and an international normalized ratio of 4.2. Chest x-ray demonstrated bilateral infiltrates. The patient was diagnosed with community-acquired pneumonia, started on antibiotics, and his anticoagulation was discontinued. After failing to improve clinically after forty-eight hours, a computerized tomography scan of the chest was ordered revealing diffuse ground glass opacities, which were concerning for alveolar hemorrhage in the setting of persistent hemoptysis. Renal function continued to decline, with hematuria and proteinuria on urinalysis. At this time, the patient was transferred to our hospital for continued management. Physical exam was remarkable for saddle nose deformity, unmentioned on transfer summary. Biopsy of the nasal septum was performed, but was ultimately indeterminate. Anti-neutrophil cytoplasmic antibody (ANCA) testing returned positive for cytoplasmic-ANCA and myeloperoxidase antibodies. Hemoptysis and oxygen requirement persisted despite the administration of pulse dose corticosteroids. In response, oral Cytoxan was initiated the following day along with therapeutic plasma exchange. Treatment resulted in the resolution of his hemoptysis and return of kidney function to near baseline by the time of discharge 9 days later.

The typical organ systems affected by GPA are the upper and lower airways along with the kidneys. Our patient's insidious presentation, with an extensive cardiac and vascular medical history, made it easy for providers treating him over this time to anchor on these systems as the most likely etiologies for his symptoms. In hindsight his "saddle nose" deformity and epistaxis warranted earlier investigation for vasculitides.

CRITICAL MASS – A SEVERE PRESENTATION OF CROWNED-DENS SYNDROME

CPT Ryan M. Jones, MD (ACP Associate), LCDR Melissa Butts, DO (ACP Associate), LTC Jess Edison, MD, (ACP Fellow), CDR Robert O'Brian, MD (ACP Associate), Walter Reed National Military Medical Center, Bethesda, MD

Crowned dens syndrome is a rare manifestation of calcium pyrophosphate dehydrate (CPPD) crystal deposition at the cervical spine. Radiographically this crystalline deposition appears as a radiopaque density on the top or sides of the odontoid, hence forming a crown or halo. When crystalline deposition occurs at the cervicoaxial joint and 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.

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, however more weakness 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 mass lesion of left lateral mass of C1, as well as fracture of the odontoid process.

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 paraplegia. 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 did not show CPPD, hydroxylapatite or monosodium urate crystals, but did have 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.

Crowned dens syndrome is a rare phenomenon associated with CPPD and can often be misdiagnosed as an abscess, rheumatoid pannus or tumor. This case demonstrates the importance of early recognition of associated radiographic findings in CPPD, to prevent the catastrophic sequela demonstrated in this case.

KISS OF STREP: RECURRENT STREPTOCOCCAL PHARYNGITIS IN AN IMMUNOCOMPETENT FEMALE

CPT Zachary C. Junga, MD (Member), CDR Timothy Whitman, DO (FACP) and LTC Joshua Hartzell, MD (FACP), Walter Reed National Military Medical Center, Bethesda, MD.

Recurrent pharyngitis including streptococcal infections in adults is unusual. The most common explanations include viral infection, non-compliance, unrecognized deep space infection, or an alternative bacteria such as *Fusobacterium necrophorum* or ***Arcanobacterium*** *haemolyticum*. Resistance to penicillin is rare although treating with clindamycin or amoxicillin clavulanate is reasonable after a relapse. Recurrent or "ping pong" infections related to spread from family members have been described and should be considered when alternative explanations are lacking. A case of recurrent pharyngitis is presented to demonstrate the importance of a thorough history in unlocking the etiology of the recurrence.

A 28 year old female presented to the infectious disease clinic for evaluation of recurrent episodes of streptococcal pharyngitis. During the preceding 2 months, the patient had been evaluated and treated 4 separate times for culture positive, non-group-A beta-hemolytic streptococcal (NGAS) pharyngitis. After each episode, her symptoms resolved and then recurred within 2-3 days of finishing the antibiotic. Since non-compliance, resistance, deep space infection and viral infection seemed less likely, further investigation into the patient's close contacts was undertaken. The patient's fiancé had been seen for culture-positive NGAS pharyngitis after the patient's first bout of pharyngitis. His symptoms had resolved without treatment. Upon culturing the fiancé, he was found to have NGAS colonization of the pharynx and was treated with antibiotics. The patient was treated simultaneously with her fifth course of antibiotics resulting in resolution of her symptoms. There was no recurrence of pharyngitis in either partner.

The current case highlights the importance of questioning patients about partners during episodes of recurrent pharyngitis. The simple step of questioning partners and treating concurrently if they are infected or colonized may avert multiple courses of antibiotics and complications from infection. As seen in this case, even if a partner is currently without symptoms, they may be colonized and hence repeatedly infecting their partner. Providers need to consider the importance of household contacts or partners when recurrent pharyngitis occurs.

RESTRAINT AND RESTRAINTS: A CASE HIGHLIGHTING DELIRIUM IN A CRITICALLY ILL PATIENT AND A BRIEF DISCUSSION OF ETHICAL CONSIDERATIONS IN THE USE OF MULTIMODAL RESTRAINTS

Jed Mangal M.D., Member ACP
Hana Zembruzska M.D., FACP
Walter Reed National Military Medical Center, Bethesda, MD.

Delirium is a psychiatric syndrome that is common among hospitalized patients, especially among elderly patients and critically ill patients with estimated prevalence of 15% to 55% and 30% - 80%, respectively. Delirium has many causes and may in fact be multifactorial, leading to a poor understanding of the pathophysiology behind the disease. However, it is known that the development of delirium has impact on patient outcomes, leading to development of permanent cognitive impairment and increasing mortality 3-to-5 fold.

A 75 year old Jamaican male smoker with small cell lung cancer and peritoneal carcinomatosis presented with dyspnea, abdominal pain, and confusion. He was found to be febrile, tachycardic, tachypneic and hypertensive. On exam, patient was oriented only to name but was able to answer some questions, needing reorientation and appearing somnolent. His abdomen was distended, tense, and diffusely tender with fluid wave and shifting dullness. He had no abnormalities on neurologic exam, although he had difficulty with instructions. Laboratory and other diagnostics were significant for leukocytosis, mild anemia, elevated anion gap metabolic acidosis, lactic acid 4.7 and peritoneal fluid WBC count 1057. He was diagnosed with bacterial peritonitis and delirium and admitted to the ICU for volume resuscitation, blood pressure and respiratory support and started on Piperacillin/Tazobactam. In the first 24 hours of admission his fever and abdominal pain improved however his hypotension and altered consciousness persisted. He frequently removed supplemental oxygen and tugged at intravenous lines. He required frequent attention from nursing staff, who placed the patient in mittens and wrist cuffs. The patient became increasingly agitated overnight until nursing requested Lorazepam as needed for chemical restraint and an order for physical restraints. At this time physical restraints were removed and the patient was started on low dose haloperidol and nonpharmacologic measures with improvement of his agitation. The patient's condition improved greatly over his remaining admission, haloperidol was discontinued and he was discharged home to his family.

Management of delirium usually involves nonpharmacologic measures, including sleep hygiene, frequent reorientation, familiarizing environment and mobilization, and can require antipsychotic medications. The use of physical or chemical restraints is not recommended in delirium unless the patient is at high risk for harm or violence; however prevalence of restraints use in ICU is estimated to be 13.6%. Key ethical concerns with the implementation of restraint are that they violate the patient's right to autonomy but can also worsen delirium, violating the principle of nonmaleficence.

A DAB OF DANGER: A CASE OF SEVERE RESPIRATORY FAILURE FOLLOWING INHALATION OF BUTANE HASH OIL.

Authors/Institution: Michael McMahon, MD (ACP Associate), Nikunj Bhatt, MD (ACP Associate), Michael Perkins, MD, Walter Reed National Military Medical Center

Introduction: Butane Hash Oil (BHO or Dabs) is a highly efficient delivery method for administering cannabinoids among marijuana abusers. We seek to illustrate a potential health risk of BHO by presenting a case of severe respiratory distress following its inhalation.

Case: A 19-year-old male with a history of daily marijuana use presented to the emergency department with worsening shortness of breath. Six days prior, he had smoked 2 "dabs" of BHO and immediately developed a burning sensation in his chest with chest tightness. He endorsed prior use of BHO, rare cigarette use, and moderate alcohol use, but denied other drug use. At presentation he noted dyspnea with exertion, cough, pleuritic chest pain, and trace hemoptysis. The patient's symptoms continued to progress and he was transferred to the Intensive Care Unit. Chest CT demonstrated worsened bilateral infiltrates and he was intubated for severe acute respiratory distress syndrome (ARDS) with hypoxemic respiratory failure. Bronchoscopy with bronchoalveolar lavage (BAL) was performed. The BAL cultures and gram stain were negative for bacterial, fungal, or viral infection and alveolar cell count revealed a non-specific alveolitis with eosinophils <10%. High dose corticosteroids were given for non-specific inflammatory inhalational injury and antibiotics were stopped. After 2 days, the patient was able to be extubated with slow improvement in hypoxia and clinical status. He was discharged home with supplemental oxygen.

Discussion: BHO is an increasingly popular form of cannabis with THC content upwards of 60-90%, giving the user a more intense intoxication. This concentrated resin is produced by passing butane through a container filled with cannabis, creating a THC-rich solvent, which is vacuum purged, eliminating the butane, and leaving a waxy substance that can be "dabbed" on a metal surface, vaporized, and inhaled by the user. To our knowledge, this represents the first reported case of ARDS following the inhalation of BHO. Rare cases of severe respiratory disease have been reported with marijuana use, including eosinophilic pneumonia and two cases of ARDS. Although the exact pathophysiological mechanism remains unclear, one hypothesis is that residual butane or other impurities in the BHO may have caused a direct inhalation injury. This case raises important questions about the potential life-threatening risks that may be associated with concentrating marijuana. Given recent legislation legalizing marijuana, it is likely reported toxicities from marijuana will increase.

T-CELL LYMPHOBLASTIC LYMPHOMA PRESENTING WITH RAPIDLY ACCUMULATING PERICARDIAL EFFUSION: A CASE REPORT

Hector Medina, MD (Member); Camille Costan-Toth, MD (Member); William Shimeall, MD (FACP)
Walter Reed National Military Medical Center, Bethesda, MD

Introduction:
Lymphoblastic lymphomas and leukemias usually present in late childhood to early adulthood, with a male predominance of two to one. T-cell lymphoblastic lymphoma is a common form of Non-Hodgkin's Lymphoma in this population. This malignancy can affect multiple organ systems, leading to a variety of urgent clinical presentations.

Case Report:
A healthy 25 year old male soldier deployed to Central Asia presented with new onset cough and shortness of breath. The patient's past medical history was notable for battle related trauma resulting in partial hepatic resection and right nephrectomy. Initial symptomatic treatment was unsuccessful, prompting further diagnostic work up revealing radiographic evidence of mediastinal lymphadenopathy as well as pleural and pericardial effusions. Infectious work up was largely negative. He was transferred to a U.S. military treatment facility via transcontinental flight in stable condition. Within 24 hours of arrival, the patient developed acute chest pain, tachycardia, and worsened dyspnea and cough. Immediate physical exam and bedside echocardiography were consistent with early cardiac tamponade physiology secondary to acutely worsened pericardial effusion with accompanying pleural effusions. Urgent pericardiocentesis and thoracentesis evacuated 700cc and 1000cc of amber fluid, respectively. Symptoms transiently resolved after the procedure, but returned within 48 hours due to recurrence of effusions. Preliminary pericardial and pleural fluid cytology analyses were concerning for lymphoma versus leukemia. While the diagnosis was being confirmed, the patient received initial empiric chemotherapy with daunorubicin, methotrexate, vincristine, and prednisone, which was appropriate for either diagnosis. The patient's symptomatic effusions resolved rapidly following chemotherapy initiation, eliminating the need for repeat pericardiocentesis and thoracentesis.

Discussion:
Pleural and pericardial effusions are fairly common signs of T-cell lymphoblastic lymphoma in younger populations, but symptomatic pericardial effusions with rapid accumulation are rare. This case emphasizes the importance of suspecting this complication and relying on physical exam to promptly guide the diagnostic approach and initiate appropriate therapy. Review of the literature reveals possible prognostic value in recognizing pleural effusions in patients with suspected lymphoma. Symptomatic pericardial effusions in cases of acute leukemia and lymphoma have been rarely reported, but early recognition of this manifestation is important in assuring prompt management and early definitive treatment in these aggressive diseases.

PROVOCATION CHALLENGE IN A MIDSHIPMAN WITH COLD URTICARIA

CPT Sarah M. Ordway, MD Internal Medicine (ACP Member), LCDR Taylor A. Banks, MD, Walter Reed National Military Medical Center, Bethesda, MD

Cold contact urticaria is subtype of physical urticaria characterized by development of hives and/or angioedema after cold exposure, caused by mast cell activation and release of inflammatory mediators. The incidence is estimated to be 0.05%. The most common method to confirm the diagnosis is an ice cube challenge test. Given the risk of anaphylaxis in cold environments, cold urticaria is considered a condition that may be incompatible with military service. We describe a case in which a midshipman with cold urticaria proved to be fit for military service after completion of a cold-water immersion challenge.

A 19-year-old female midshipman at the United States Naval Academy presented to the allergy and immunology clinic after noting swelling subsequent to cold exposure, over a period of one year. She initially noticed symptoms when applying ice to an injury. Within minutes, she developed urticaria and swelling of the skin in direct contact with the ice. During the winter, she developed hand and ear swelling, and hives on her extremities when exposed to the cold air. Her symptoms resolved within an hour of removing the cold stimuli and were well controlled with 10mg cetirizine daily. She denied known allergies. Her ice cube challenge was positive at five minutes, further titrated to two minutes. Over time, her symptoms gradually improved, she stopped her prophylactic antihistamine, and she began to tolerate exposure to cold environments, but her ice-cube test remained positive.

The midshipman desired a Marine commission, a career that often involves frequent and prolonged exposure to cold environments. Given her improved symptoms off antihistamines, we pursued a definitive cold-exposure challenge in a more realistic environment. For the challenge, the patient entered a pool with a temperate of fifty degrees Fahrenheit to shoulder level for approximately twenty minutes. Her skin at the water-air transition zone began to demonstrate urticaria and she developed signs of mild hypothermia, but did not develop systemic symptoms such as hypotension, respiratory symptoms or angioedema. Given the lack of a systemic hypersensitivity response to this provocation challenge, she later received a Marine Corps commission.

Provocation challenges are the definitive means of assessment for hypersensitivity reactions. This case raises the question of whether the ice-cube challenge alone is a sufficient test for patients with cold urticaria. In consultation with allergy-immunology, cold-water immersion challenge testing may allow for accession and retention of personnel with cold urticaria. Further study is needed to assess this testing modality.

A CASE OF SUPPLEMENT-ASSOCIATED ACIDEMIA AND ACUTE KIDNEY INJURY IN AN ACTIVE DUTY SOLDIER

Authors: CPT Cynthia Philip MD, MAJ Dustin J Little MD
Walter Reed National Military Medical Center, Bethesda, MD

INTRODUCTION:
We present a case of N.O.-Xplode-associated acidemia and acute kidney injury (AKI) in a previously healthy active duty soldier.

CASE REPORT:
A 31 year-old Caucasian male with a history of occasional tension headaches presented following the Army Physical Fitness test. He took 975 mg of aspirin for headache the previous evening, and consumed the dietary supplement N.O.-Xplode on the morning of the test. He developed dyspnea and leg and lower back pain during the run portion of the test, and lost consciousness. Initial evaluation revealed severe increased anion gap metabolic acidosis with pH of 6.9, serum bicarbonate of 6 mmol/L, lactate of 28 mmol/L, and anion gap of 41 mmol/L. Treatment included administration of isotonic sodium bicarbonate followed by 0.9% sodium chloride. Serum creatinine (SCr) at presentation was 1.9 mg/dL and peaked at 3.2 before decreasing prior to discharge. UA showed 100 mg/dl protein and small blood. Serum uric acid was 16.5 mg/dL and subsequently normalized; neither hyperkalemia nor hyperphosphatemia were present. The urine uric acid to creatinine ratio was 1.2. Peak creatine kinase was 788 units/L.

DISCUSSION:
This patient presented with life-threatening acidemia and nonoliguric acute kidney injury following heavy exertion, in the setting of N.O.-Xplode supplement use. Volume depletion likely contributed, and could have been exacerbated by methylxanthine, a diuretic in N.O.-Xplode. Cyclooxygenase (COX) inhibition by aspirin and rutaecarpine, a non-selective COX inhibitor in N.O.-Xplode likely caused renal afferent arteriolar vasoconstriction, contributing to pre-renal AKI. N.O.-Xplode contains creatine, which has been associated with AKI in case reports. Nicotinic adenine dinucleotide from the supplement may have contributed to lactic acidosis, by increasing substrate for the conversion of pyruvate to lactate. Although uric acid crystals were not directly visualized in our patient's urine, his marked elevation of serum uric acid and elevated urine uric acid to creatinine ratio suggests possible uric acid nephropathy. L-arginine from N.O.-Xplode could have contributed to increased uric acid production, particularly in the setting of strenuous exercise and salicylate use. In conclusion, there are several mechanistic possibilities to how N.O.-Xplode may have contributed to this soldier's severe illness. N.O.-Xplode has been associated with palpitations, dizziness, hepatotoxicity, and one other reported case of AKI, but remains on the market and available for purchase at our local Exchange store. Military providers should ask their patients about supplement use, and should consider counseling patients to avoid use of N.O.-Xplode, especially during times of heavy exertion.

ANTI-N-METHYL-D-ASPARTATE RECEPTOR (NMDA-R) ANTIBODY AUTOIMMUNE ENCEPHALITIS

CPT Rita Richardson, MD, PGY-2, Combined Internal Medicine Psychiatry, WRNMMC
LTC Shauna Scully, DO, Chief of Neurology, WBAMC

Autoimmune and paraneoplastic encephalitis is a heterogeneous group of disorders which present with a wide spectrum of non-specific symptoms leading to differential diagnosis including primary psychiatric disorder, malignant catatonia, viral or toxic-metabolic encephalopathy, and degenerative dementia. Anti-NMDA-R Ab encephalitis is characterized by onset of non-specific prodromal headache and fever which can progress to include acute onset psychiatric disorder including psychosis and catatonia, tonic-clonic seizure activity, autonomic instability, dyskinesias, and language dysfunction.

A 34-year-old woman presented to the emergency department with her husband after reported seizure accompanied by a myriad of symptoms including intermittent unsteady gait, hand tremor, anxiety, and irritability. Symptoms had been increasing in frequency since the birth of her fourth child four months prior. Patient was admitted to the general medicine service for evaluation of seizure activity. Work up, including CNS imaging, was unremarkable. Witnessed seizure activity was more consistent with non-epileptiform activity or panic attack. Additionally, patient was found to be experiencing visual hallucinations. Initial neurology and psychiatry evaluation concluded provisional diagnosis of moderate to severe post-partum. She was discharged to an in-patient psychiatric facility. Two weeks after discharge, patient returned to emergency department complaining of increasing frequency and severity of seizure activity and development of new onset fevers with weakness of all extremities. Patient was readmitted to general medicine service. Witnessed seizure activity noted to be significantly escalated from prior evaluation and more consistent with tonic-clonic seizure activity. During admission, patient developed fever of unknown origin, catatonia and seizure activity in response to slight movement of spinal column. MRI brain and entire spine were unremarkable. Extensive laboratory investigations were unremarkable except cerebral spinal fluid with marked elevation of protein, leukocytes with lymphocyte predominance, and total cell count. Patient was empirically treated for HSV encephalitis with some improvement of mental status and spasticity. CSF HSV PCR was negative and IV acyclovir discontinued after 10 day treatment. Patient was discharged to local facility for acute neurologic rehabilitation. One week later, CSF resulted positive for anti-NMDA-R antibody. Patient readmitted for immediate initiation of treatment including plasmapheresis, IVIG, and high dose steroids. Despite marked response over three weeks of treatment, patient suffered comprehensive brain injury due to the prolonged autoimmune response requiring extensive outpatient services to include neurocognitive rehabilitation.

This case illustrates the potential difficulty in diagnosis of autoimmune encephalitis as well as a novel combination treatment regimen. Correct and timely diagnosis is imperative to decrease mortality and morbidity.

A STORM'S BREWING: A CASE OF SUICIDE ATTEMPT BY MASSIVE LEVOTHYROXINE INGESTION

Shannon Wood, MD (ACP Member), James Clifford, MD (ACP Member), K.M. Mohamad Shakir, MD (MACP), Walter Reed National Military Medical Center, Bethesda, MD

Drug overdose is a leading cause of death among individuals 25-64 years old and prescription medications are often the culprit. Levothyroxine is one the most commonly prescribed medications with potential for great harm. We present a case of suicide attempt by massive levothyroxine ingestion and review management strategies in the setting of prior thyroidectomy.

A 19 year old female with a history of Graves' disease s/p thyroidectomy and post-procedural hypothyroidism on levothyroxine presented following ingestion of 90 tablets of levothyroxine 150 mcg (13.5 g total) in combination with ethanol, ibuprofen, aspirin, and vilazodone in an attempt to end her life. The patient reported fatigue, chest pain, and nausea prior to arrival, but was asymptomatic on initial evaluation. Exam was notable only for stable chronic right exophthalmos. She was not tachycardic, hypertensive, febrile, or tremulous. Labs were notable for T4 > 40 ng/dL, total T3 484 ng/dL, free T3 19.8 ng/dL, and TSH 4.56 uIU/mL. The patient was treated for thyrotoxicosis with activated charcoal, dexamethasone, cholestyramine, and propranolol. She was observed in the ICU and general medicine ward for 6 days without signs or symptoms of thyrotoxicosis prior to transfer to inpatient psychiatry.

Our patient remained relatively asymptomatic despite 13.5 g of levothyroxine ingestion, one of the largest ingestions reported in the literature. Although serious life threatening complications from thyroid hormone toxicity are rare, the onset of symptoms from overdose may be delayed necessitating prolonged observation. In our patient, dexamethasone was initiated to decrease peripheral conversion of T4 to T3 and cholestyramine was implored to enhance clearance through binding of free thyroid hormone. Propranolol was also utilized to reduce sympathetic stimulation that accompanies thyrotoxicosis. In severe cases, plasmaphoresis or charcoal hemoperfusion may be utilized for attempted extraction of thyroxine. Thionamides and iodine were not utilized in this case due to prior thyroidectomy, but could play a role in patients with intact thyroid glands. In the setting of thyroid hormone overdose, it is important for physicians to recognize the need for prolonged observation and prompt treatment for the reduction of morbidity and mortality. Our case illustrates successful treatment of a potentially lethal overdose of levothyroxine with prompt recognition, aggressive medical management, and prolonged observation.

Research

DDEAMC

Dwight D. Eisenhower Army Medical Center

Research

AUTOMATED URINE FLOW RATE AND VOLUME MEASUREMENT: NEW DEVICE ACCURACY TESTING

Robert O. Broughton MD[3], Max E. Stachura MD[2], Elena A. Wood MD, PhD[2], Amaya D George DO[3], Christopher J. Colombo MD1

[1] Medical Intensive Care Unit, Dwight David Eisenhower Army Medical Center

[2] Center for Telehealth, Georgia Regents University

[3] Internal Medicine Department, Dwight David Eisenhower Army Medical Center

Introduction: Accurate measurement of urine output rate and volume is essential for fluid balance and hydration management in numerous acute and chronic medical conditions in multiple clinical settings. Their current measurement is manual, time consuming, error prone, and costly. When limited numbers of healthcare personnel are responsible for multiple patients with complex medical problems, the error inherent in the current manual system becomes immediately apparent. The purpose of this collaborative project was to validate accuracy and precision of a new technology, UroSense™, that automates and improves the accuracy of urine output rate and volume measurement.

Materials and Methods: Ten UroSense™ containers, their wireless transmitters and the computer algorithms used to report results were tested simultaneously in a laboratory setting. In addition to the UroSense™ output report we captured hourly visual urine output readings from the embedded UroSense™ container urinometer. All containers were tested using variable speed pumps drawing from pooled human urine to mimic urine flow in a patient. The study consisted of three 10 hour shifts. One container accumulated urine throughout the three shifts. Nine containers were emptied at the end of each shift in order to test dry vs. wet sensor functions. Sensor sensitivity drift was evaluated by linear regression over the testing period. Total shift output (UroSense™ reading) was validated using visual graduated cylinder measurement. The main comparison was between UroSense™ and visual readings, including dry or wet sensors (initial and repetitive use). We also tested UroSense™ software data transmission modes: multiple collection systems (patients) to a single station/laptop vs. one-to-one system to station modes.

Results: Ten UroSense™ containers were tested and 201 measurement pairs were used in the analysis. The plotted data revealed clear linearity with UroSense™ measurements and visual readings strongly correlated, $r(201)=0.986$. Dry (initial use) and wet (subsequent use) readings were statistically different, based on paired t tests of absolute differences between hourly UroSense™ and visual readings: mean difference 37.76 ± 30.11 ml with dry and 75.52 ± 73.33 ml with wet containers ($P<0.0001$) lower in wet condition. No difference based on data transition mode (Container-laptop, Containers-laptop) were identified: ANOVA Single Factor "Data transmission mode" (all Containers dry) $F= 3.58$, $p>0.5$.

Conclusions: UroSense™ measurements are strongly correlated with visual readings. Repetitive sensor use (dry vs. wet) exhibits a statistically significant difference; however, clinically this has a minimal impact, and data transmission mode has no impact. Further clinical trials are warranted.

MAMC

Madigan Army Medical Center

Research

KETAMINE BY CONTINUOUS INFUSION FOR SEDATION IN SEPTIC SHOCK

Victoria Fernandes Sullivan, MD (Associate)[a]; Nathan Boyer (Associate)[b]; Jason Reese, MD (Associate)[c]; Cristin A. Mount, MD (FACP)[a] Madigan Army Medical Center, Tacoma, WA[a], San Antonio Uniformed Services Health Education Consortium, San Antonio, TX[b], Walter Reed National Military Medical Center[c]

Introduction: Sedating mechanically ventilated shock patients presents a management challenge. Most routinely used sedatives can cause hypotension, they do not have analgesic properties and many analgesics can also worsen hypotension. Ketamine is an NMDA receptor antagonist that acts as a dissociative sedative, providing analgesia and amnesia. Two additional effects of ketamine infusion are hypertension and bronchodilation. We hypothesized that use of ketamine as a sole sedative agent in adult patients in septic shock would decrease the required dose of vasopressor medication needed to maintain adequate perfusing mean arterial pressure.

Methods: This is a prospective, observational pilot study of adult septic shock patients requiring mechanical ventilation and sedation, admitted to the ICU from January 2012 until September 2014. Patients were started on a ketamine infusion at the time of enrollment and ketamine was continued for 48 hours or until the patient no longer required mechanical ventilation. The primary outcome was vasopressor dose over the first 96 hours of enrollment. Data on additional sedative and analgesic agents, APACHE II scores, use of corticosteroids and mortality was also collected.

Results: We conducted an interim analysis of data from 16 patients, compared with a retrospective cohort of 35 patients admitted for septic shock requiring mechanical ventilation who received usual sedation care. The average total dose of vasopressors in the control group at 48 hours was 20.5mg norepineprine versus 10.8mg norepinephrine in the ketamine group ($p = 0.09$). There was a trend towards significance in the amount of norepinephrine needed at all time periods measured and less use of a secondary pressor agent (vasopressin). Furthermore, the study group was older and sicker, based on APACHE II scores.

Conclusions: The interim results of this pilot study are inconclusive but the trend towards septic shock patients requiring less vasopressor dosing when ketamine is used as the sole sedative is promising. The higher age and illness severity scores in the ketamine group also lend strength to the hypothesis. To our knowledge, this is the first report of ketamine use for sedation in adult septic shock and mechanical ventilation. The preliminary results of this pilot study show a trend that could be further explored in a large, randomized, multi-centered trial. Sedation of septic shock patients in the ICU is challenging to manage, and ketamine could be another medication to add to the limited arsenal.

SAUSHEC

San Antonio Uniformed Services Health Education Consortium

Research

THE EFFECT OF NITRATE-RICH BEETROOT JUICE CONCENTRATE VS PLACEBO ON SUBMAXIMAL EXERCISE PERFORMANCE IN SYSTOLIC HEART FAILURE

Jerry Hu, CPT, MC, USA (ACP Associate); Adam T. Marler, Capt, USAF, MC; Kenneth L. Leclerc, LTC, MC, USA; SAUSHEC Internal Medicine, San Antonio, TX

Introduction: The goal of the current study was to measure the effect of acute ingestion of nitrate-rich beetroot juice concentrate vs nitrate-deplete beetroot juice concentrate (placebo) on oxygen consumption during submaximal steady-state treadmill walking as well as performance of a 6-minute walk test (6MWT) in patients with NYHA class II or III heart failure with reduced ejection fraction (HFrEF). Acute nitrate supplementation has been demonstrated to improve oxygen consumption and submaximal exercise performance in a healthy adult population but not in patients with heart failure.

Methods: Our study is a randomized, double-blind, placebo controlled trial. Twelve patients with NYHA class II to III heart failure with reduced ejection fraction (≤35%) underwent both submaximal steady state exercise with gas exchange analysis and six minute walk testing after taking nitrate-rich beetroot juice or placebo. All patients had serum nitrate and nitrite levels measured before and after ingestion of 70mLs of beetroot juice concentrate. The second exercise testing sessions were performed at least ten days later to allow for an appropriate wash-out period. Primary outcome measures were oxygen consumption and 6MWT distance.

Results: All twelve patients successfully completed both arms of the study. Serum nitrate levels were significantly increased in the treatment arm. The average oxygen consumption (VO2) was 12.19 mL/kg/min in the study group vs 12.20 mL/kg/min in the control group (NS). The average 6MWT distance was 1555 feet in the nitrate group vs 1539 feet in the control group. The difference between in 6MWT distance was not significant.

Discussion: In patients with heart failure with reduced ejection fraction who have ingested nitrate-rich beetroot juice concentrate there is no significant difference with regard to oxygen consumption during submaximal steady state exercise or six minute walk testing distance. The absence of treatment effect may be due to the low dose of nitrate provided in our study.

Conclusion: Our small patient population represents the first attempt at evaluating the effects of nitrate-rich beetroot juice in subjects with heart failure. Further study is warranted to determine the true efficacy of exogenous nitrate consumption in this population with consideration to further dosing adjustments or chronic ingestion.

DETERMINATION OF REFERENCE VALUES FOR CARDIOPULMONARY EXERCISE TESTING IN AN ACTIVE DUTY POPULATION

Daniel J. Weinstein, MAJ, MC, USA (Associate); Anthony Sidari, Capt, USAF, MC (Associate); Michael J. Morris, MD, FACP, SAUSHEC Internal Medicine, San Antonio, TX

Introduction: Cardiopulmonary exercise testing (CPET) may be a useful test in determining limitations to exercise due to deconditioning, cardiac disease, or respiratory disease. It is most useful in patients with known cardiac or pulmonary disease in whom the etiology of dyspnea is not clear. The reference values used to determine abnormalities are based on an older, sedentary population and do not reflect the expected values in a younger, athletic population such as the United States military.

Methods: Healthy active duty military between the ages of 20 to 40 with no pre-existing cardiac or pulmonary disease were asked to participate. Screening with a baseline EKG, spirometry, and chest radiograph were done to ensure normal baselines. Participants completed a maximal cardiopulmonary exercise test both a cycle ergometer and treadmill on two separate days. Treadmill was completed using a Bruce protocol to maximum exercise while cycle ergometry was completed with an increase of 20 watts per minute.

Results: Thirty participants (9 females, 21 males) have completed both the treadmill and cycle studies to date. Mean age for males was 29.2 ± 4.0 years; female age was 31.7 ± 4.3 years. Mean max VO_2 % predicted for treadmill (males vs. females) was 115.1% and 146.6% respectively. Mean max VO_2% predicted for cycle ergometry (males vs. females) was 106.6% and 135.1% respectively. Mean exercise times, workload and actual max VO_2 decreased on cycle ergometry compared to treadmill in this group of individuals.

Discussion: The ATS/ACCP consensus statement suggested normal values for VO_2 max, VAT, MVV-VE, RR, and VE/VCO2 were all based on the studies initially published by Hansen and Sue in 1984. Their patient population consisted of 77 asymptomatic, male, former or current shipyard workers who underwent CPET using cycle ergometry. This cohort included participants (mean age = 57) who were obese, sedentary, and actively smoking. Analysis by Sill et al. suggested different statistical comparison of predicted normals (reference vs. control) of maximal oxygen consumption (> 83% vs. 82%), ventilatory anaerobic threshold (> 40% vs. 53%) and other parameters. Treadmill studies allow participants to perform at higher workloads that cycle ergometry.

Conclusion: Preliminary data from this study shows significant discordance between cycle ergometry and treadmill values in a healthy active duty population. Treadmill studies are more reflective of a maximal exercise capacity.

WBAMC

William Beaumont Army Medical Center

Research

ELECTROCARDIOGRAPHIC MONITORING OF NONCRITICAL HOSPITAL INPATIENTS AT WBAMC: A TELEMETRY UTILIZATION REVIEW PERFORMANCE IMPROVEMENT PROJECT

Michael Switzer, CPT, MC, USA. Patrick Kicker, CPT, MC, USA. William Beaumont Army Medical Center, El Paso, TX

Purpose: The intent of this performance improvement project is to evaluate our facility's adherence to the 1991 American College of Cardiology (ACC) and 2004 American Heart Association (AHA) expert consensus guidelines for the use of telemetry monitoring for detection of arrhythmia among noncritical hospitalized medical and surgical patients. These guidelines stratify patients into three distinct classes on the basis of clinical conditions. Class I patients in which monitoring is indicated for almost all; Class II patients in which monitoring may be of benefit for some but is not essential for all; and Class III patients who are unlikely to benefit from monitoring, and for whom it is not indicated. It is my prediction that our facility over utilizes inpatient cardiac monitoring and that physicians likely overestimate the role of telemetry. Currently there is no hospital-wide policy regarding telemetry utilization and this decision is ultimately left to admitting physician discretion. Hospital wide WBAMC has 41 telemetry transceivers.

Design: This project consisted of a retrospective chart review of all patients admitted to WBAMC, El Paso, TX over a near three month time period from 4 July to 24 Sept 2013. All inpatients other than those admitted to the medical, cardiology, or surgical services were excluded from final analysis. The inpatient medical record review consisted of a review of clinical presentation and admission diagnosis and whether or not the patient was placed on cardiac telemetry monitoring appropriately based on ACC/AHA expert consensus guidelines. This data was reviewed to determine our facility's adherence rate to the ACC/AHA guidelines for in-hospital cardiac monitoring of adults for detection of arrhythmia.

Pre-Intervention Results: 2299 patient charts were reviewed from 4 July to 24 Sept 2013. After exclusion of pediatric, obstetric, and inpatient psychiatric admissions along with same day surgery discharges, 1001 inpatient admissions remained consisting of those admitted to medical, cardiology, or surgical services. Inpatient cardiac monitoring appropriateness was 81.3% with an inappropriate utilization rate of 18.7% when all medical, cardiology, and surgical admissions were reviewed. The appropriate utilization percentage fell to 60.8% and the inappropriate rate rose to 39.2% when only medical patients (452) were reviewed.

Intervention: On 14 May 2014 a new telemetry order set was activated in Essentris, the inpatient medical record system. The order set consists of pre-populated inpatient cardiac monitoring indications for detection of arrhythmia as deemed appropriate by the ACC/AHA expert consensus guidelines. Physicians select the indication from a list as opposed to free-texting the need for telemetry. Generic telemetry orders were also removed from existing general medicine order sets: Gen Med #1 and Gen Med Admit to motivate admitting physicians to reflect upon a patient's clinical need for telemetry as guided by the new order set. Order set availability was publicized to the WBAMC Internal Medicine interns and residents via e-mail on 14 May 2014.

Post-Intervention Results: Following the initiation of the new telemetry order set, 2441 patient charts were reviewed for 3 months. After the same exclusion criteria were applied, 1172 inpatient admissions remained. The results showed inpatient cardiac monitoring appropriate use was 94.5% when all admissions were reviewed. For all medical and surgical services, overall appropriate utilization of telemetry improved by 13.4%. Regarding only medical patients (531), the percentage was 92.3%. This was a dramatic improvement of 31.6% which was statistically significant ($p = 0.015$).

WRNMMC

Walter Reed National Military Medical Center at Bethesda

Research

SIMEPREVIR AND SOFOSBUVIR COMBINATION THERAPY IS SAFE AND WELL TOLERATED IN POST LIVER (LT) TRANSPLANT PATIENTS WITH RECURRENT CHRONIC HEPATITIS C (CHC)

Diana Dougherty, M.D., [1]Amilcar L. Morales, M.D., [2] Dawn M. Torres, M.D.,[2] John Bassett, MD[2], Maria Sjogren, MD.[2] Internal Medicine Service, Department of Medicine, Walter Reed National Military Medical Center, Bethesda, MD, [1] Gastroenterology Service, Department of Medicine, Walter Reed National Military Medical Center, Bethesda, MD.[2]

Introduction: Cirrhosis related to chronic hepatitis C (CHC) infection is the leading cause of liver failure requiring orthotopic transplant. Recurrent CHC is nearly universal in the absence of pre-transplant viral eradication, and frequent cause of graft failure. The current standard of care for genotype 1 CHC patients includes pegylated interferon (PEG) which leaves many patients ineligible for treatment secondary to comorbidities. The combination of simeprevir (150 mg daily) and sofosbuvir (400 mg daily) was used in the COSMOS trial in treatment naïve patients and in those with prior null response to PEG/ribavirin (RBV) with SVR 12 reported to be above 93% and SVR 24 close to 80%. In the new AASLD guidelines for management of CHC after LT, it is suggested that this combination could be used as first line therapy for this population; however this was based on expert consensus. This case series investigates the effectiveness and tolerability of a simeprevir/sofosbuvir based regimen in the transplant population.

Methods: Five patients post liver transplant with recurrent genotype 1a CHC were treated with once daily simeprevir and sofosbuvir for 12 weeks. Two of five patients were treated previously with PEG/RBV and failed therapy due to either neutropenia or anemia. Viral load, liver associated enzymes, renal panel, CBC, and tacrolimus trough were obtained prior to starting therapy as well as at four, eight and 12 weeks during treatment with plans to reassess viral loads at 4 and 12 weeks after completion of therapy.

Results: All five patients tolerated treatment without serious adverse events and without adjustment of tacrolimus required. All had undetectable viral load between 4-8 weeks of therapy. Four of five remain undetectable at 12 weeks post-treatment, with data forthcoming for the fifth patient.

Conclusion: The combination of simeprevir and sofosbuvir seems to be well-tolerated in this previously difficult to treat patient population. Undetectable viral load was noted in all patients between 4-8 weeks of therapy with SVR 24 data forthcoming. Simeprevir and sofosbuvir should be considered in liver transplant patients with recurrent CHC.