# Proceedings from the 2016 Annual Meeting of the American College of Physicians, Wisconsin Chapter

The following abstracts were presented during the 61st Annual Meeting of the Wisconsin Chapter of the American College of Physicians in 2016. Internal medicine residents from each of Wisconsin's 5 residency programs presented their research and/or unusual clinical experience via case-and research-based vignettes and posters. All of the vignettes as well as the winning posters are published here. Additional poster presentations are available online in an appendix and can be accessed at https://www.wisconsinmedicalsociety.org/\_WMS/publications/wmj/pdf/116/5/16\_ACP\_Abstract\_Book.pdf.

#### **RESEARCH-BASED VIGNETTES**

#### 1st Place

#### Blood-Based Genomic Testing for Newly Diagnosed Lung Cancer Patients to Facilitate Rapid Treatment Decisions

Adithya Chennamadhavuni, MD, Jennifer Mattingley, MD; Gundersen Health System, La Crosse, Wis

Background: Despite advances in lung cancer treatment, its management remains challenging. Several patients present at an advanced stage where systemic therapy and biomarker testing are required. From studies on nonsmall-cell lung cancer (NSCLC), 21% of patients had biomarker results available at their initial oncology consultation, which led to shorter median time from consultation to treatment decision (0 vs 22 days, P=0.0008) and time to treatment start (16 vs 29 days, P=0.004). Of those patients with positive estimated glomerular filtration rate (eGFR) or ALK results, 19% started chemotherapy before biomarker results were available. Our institution's multidisciplinary team used blood-based genomic testing to expedite treatment decisions and facilitate more informed conversations with lung cancer patients.

Methods: Commercially available, bloodbased genomic testing was ordered for all clinical patients. Testing included genomic test GeneStrat, a targeted panel for eGFR sensitizing and resistance mutations, ALK fusions, KRAS and BRAF mutations.

Results: Of the patients (n=32) submitted for genomic testing, results were available within 72 hours of blood draw. Among this cohort of patients who were diagnosed with adenocarcinoma between January and June, 2016, approximately 28% (n=9) had a mutation identified by GeneStrat (KRAS G12D=4, eGFR T790M=4, EML4-ALK=1, eGFR L858R=1). One patient had dual eGFR L858R/EML4-ALK mutations. There was 1 patient for whom the test was not able to identify G719A (exon 18) as it looks only for exon 19, 20, and 21. The sample size was limited for positive predictive value but the negative predictive value is 94%.

Conclusions: Blood-based genomic testing provides valuable treatment information regardless of disease stage. Early identification of the mutations will benefit the patient with early initiation of specific chemotherapy.

#### 2nd Place

#### Utility of a Remote Image Acquisition and Feedback Tool in Promoting Point-of-Care Ultrasound Skills Among Critical Care Trainees

Kate Steinberg, MD, Pierre Kory, MD, University of Wisconsin Hospital and Clinics, Department of Internal Medicine, Division of Pulmonary, Allergy, and Critical Care Medicine, Madison, Wis.

Introduction: Point-of-care ultrasound

(POCUS) is increasingly incorporated into both clinical practice and training programs. Implementation of POCUS curricula is challenged by a limited number of experts available to teach ultrasound skills and oversee interpretation at the bedside. Recent image database software products now allow faculty members to remotely supervise and teach learners by reviewing recorded, interpreted studies followed by provision of feedback on the POCUS skill components of image acquisition, image interpretation, and clinical application skills. We sought to assess the level of basic critical care echocardiography (BCCE) skills attained among critical care trainees after introduction of a remotely supervised POCUS curriculum.

Methods: A POCUS curriculum incorporating hands-on training was introduced in July 2015. A structured BCCE exam with required image set was taught along with a process for using an ultrasound archiving and quality assurance software product to record, interpret, and submit performed exams. In September 2015, trainees began wirelessly submitting independently performed exams for remote over-read by a faculty member who was an expert in critical care ultrasonography. After a 6-month period, an analysis of all submitted and over-read studies was performed with a primary focus on appropriateness of clinical application of ultrasound findings. Image quality and interpretation scores were also evaluated.

Results: Eighty-one BCCE exams were performed and submitted for over-read; 72% of the submitted studies were graded as having good or excellent image quality. Overall diagnostic accuracy was 77%. Accurate interpretation of ultrasound exams was associated with appropriate clinical application in greater than 90% of cases. In cases of inac-

curate interpretation of ultrasound images, 25% were associated with inappropriate clinical application. Incorrect clinical applications included inappropriate fluid management (60%) and use of inotropic agents (40%).

Conclusions: After introduction of a POCUS curriculum founded upon remote image over-reading with written electronic feedback, critical care trainees achieved high levels of image acquisition, interpretation accuracy, and appropriateness of clinical application.

#### **Bias in the Eyes of Resident Physicians**

Abel Irena, MD, Kern Reid, MD, Richard Battiola, MD; Aurora Health Care, Milwaukee, Wis

Introduction: The utilization of patient characteristics can allow clinicians to arrive at diagnosis or decide on treatment options; however, the subjective nature of patient characterization can negatively affect patient care. A 2003 Institute of Medicine report, Unequal Treatment, recognized that bias or stereotyping may affect provider-patient communication or the care offered. We investigated residents' recognition of bias.

Methods: We indirectly assessed recognition of bias among resident physicians by asking their opinion in an anonymous manner about their fellow residents. We asked residents the following 2-step question; "Have you observed a colleague of yours SAY, PORTRAY, or ACT in a biased manner towards a patient while providing inpatient service?" If the answer was yes, we subsequently asked them to elaborate on the bias.

Results: The survey was sent to 39 postgraduate (PG) internal medicine residents in their 1st to 3rd year of training. Half of the respondents (20/39) were female. The response rate was 100%. Forty-six percent (18/39) reported observing their colleague(s) being biased toward patients. Of those who reported bias, 77.8% (14/18), reported one or more examples about the content of the perceived bias. The largest category, 42.8% (9/21), was about bias towards patients with past or current "drug/substance abuse" or "narcotic seeking" behavior; 14.3% (3/21) involved patients with repeated admissions or so-called "frequent fliers;" 9.5% (2/21) related to race/ethnicity; 14.3% (3/21)

indicated providers not wanting to care for patients who were perceived to be "difficult." Interestingly, another 9.5% (2/21) reported witnessing preferential service for "affluent/VIP" patients. Other examples included bias against obese patients, female patients, and general stereotyping with no specifics given.

Conclusions: Given the evidence that implicit bias can be recognized and improved upon, this study reinforces the need for implicit bias training/discussion to be included in residency programs.

#### Reducing Central Line-Associated Blood Stream Infections in Pediatric Oncology Patients

Ashley Quinn, BS, Lauren Ranallo, MSN, RN, Alyse Bartczak BSN, RN, Paul Harker-Murray, MD, PhD; Medical College of Wisconsin (Quinn, Harker-Murray), Children's Hospital of Wisconsin (Ranallo, Bartczak, Harkery-Murray), Milwaukee, Wis

Background: Central line-associated blood stream infections (CLABSI) are preventable, hospital-acquired conditions that increase morbidity, mortality, length of stay, and health care costs. Implementation of central line insertion and maintenance bundles have reduced but not completely eliminated these infections. Daily treatment with chlorhexidine gluconate (CHG) antiseptic has been shown to reduce them in a variety of populations including adult, pediatric, and neonatal intensive care, burn, adult medical and surgical, and long-term acute care units. We hypothesized that daily CHG treatments would reduce the incidence of CLABSIs in pediatric oncology and bone marrow transplant (BMT) patients.

Methods: All pediatric oncology and BMT patients received daily treatment with 2% CHG-impregnated cloths during the 1-year intervention period unless contraindicated. All primary blood stream infections in patients with a central line during this period (wCHG) and the preceding 12 months (pre-CHG) were recorded as a CLABSI. CLABSI rate was calculated as events per 1,000 central line days. Cultured pathogen, microbe sensitivity, and CHG compliance were also collected. Patient characteristics were evaluated to determine relationship to mucosal barrier

injury (MBI) per the Centers for Disease Control and Prevention criteria.

Results: Compliance with CHG treatment remained >90% over the wCHG period. The CLABSI rate did not improve with CHG use (2.90 preCHG vs 3.39 wCHG). Most patients affected were undergoing treatment for hematologic malignancy (hematologic 11 preCHG vs 15 wCHG, BMT 2 preCHG vs 3 wCHG, solid tumor 3 preCHG vs 2 wCHG). There was no alteration in the type of pathogens isolated (Gram positive 6 preCHG vs 6 wCHG, Gram negative 7 preCHG vs 13 wCHG, Fungus 3 preCHG vs 0 wCHG) or incidence of antibacterial-resistant infections (Vancymycin resistant enterococcus 1 preCHG vs 0 wCHG). A large proportion of CLABSIs qualified as an MBI in both intervention periods (11/16 preCHG vs 15/20 wCHG). The non-MBI CLABSI rate still remained unchanged with CHG use (0.91 preCHG vs 0.85 wCHG). However, 100% of non-MBI CLABSIs in the wCHG period had mucositis or neutropenia and were not classified as an MBI based only on growth of nonintestinal organisms (mucositis or neutropenia 100% all MBIs, 40% preCHG Non-MBI, 100% wCHG Non-MBI).

Discussion: CHG did not appear to reduce CLABSIs based on strict infection-source definitions. However, all patients with CLABSIs in the wCHG period had severe neutropenia and/or mucositis. There were few CLABSIs in immunocompetent patients receiving CHG treatment, specifically, patients undergoing chemotherapy for a solid tumor. This suggests an endogenous source of bacteremia in severely immunocompromised patients.

#### **CASE-BASED VIGNETTES**

#### 1st Place

#### Platypnea-Orthodeoxia Secondary to Patent Foramen Ovale: A Rare But Dramatic Cause of Respiratory Failure

Sarah Doleeb, MD, Raj Patel, MD, Tonga Nfor, MD, MSPH; Aurora Health Care, Milwaukee, Wis

*Introduction:* Platypnea-orthodeoxia syndrome is a rare disorder characterized by both dyspnea (platypnea) and arterial desaturation (orthodeoxia) in the upright position with improvement in the supine position.

Case: The patient is a 73-year-old woman with a past medical history significant for sudden cardiac death status post single chamimplantable cardioverter-defibrillator, mitral regurgitation, patent foramen ovale (PFO), and chronic lymphoid leukemia who was sent from the primary care clinician for evaluation of hypoxia and chest discomfort. She reported dyspnea when she is upright, improved when she lay flat. Initial evaluation showed oxygen saturation of 85% on room air; this did not improve with nasal cannula or non-rebreather mask necessitating admission to intensive care unit (ICU) on bilevel positive airway pressure. Physical examination was benign, electrocardiogram showed left atrial enlargement, computed tomograpy (CT) angiogram ruled out pulmonary embolism. Cardiology was consulted, transthoracic echocardiogram was remarkable only for a positive bubble study. Transesophageal echocardiogram demonstrated a PFO with large right-to-left shunt, aneurysmal interatrial septum, and a prominent eustachian valve directing blood towards the PFO. Right and left heart catheterization ruled out pulmonary hypertension and Eisenminger syndrome or other cardiac pathology. The patient underwent percutaneous PFO closure under guidance of fluoroscopy and intracardiac echocardiography via the right femoral vein using a 30mm Gore septal occluder. She had immediate and complete resolution of her symptoms, normal oxygen saturation on room air, and was discharged home in 2 days. Discussion: Platypnea-orthodeoxia is a rare manifestation of PFO, and closure of the atrial defect is curative. Few cases are reported in the literature, but the severity of presentation is rarely as dramatic as this case.

#### 2nd Place

### A Typical Presentation of an Atypical Problem

Steven Finstad, MD, Christopher Lowry, MD, Jennifer Mattingly, MD; Gundersen Health System, La Crosse, Wis

Introduction: Cryptogenic organizing pneumonia is a rare and diffuse idiopathic organizing form of interstitial pneumonia. The disease is characterized by acute to subacute

onset of vague systemic and pulmonary complaints often leading to a difficult clinical diagnosis of exclusion.

Case: We describe the case of a 77-year-old farmer with a 1-month history of a persistent minimally productive cough with associated fatigue, malaise, dyspnea, and orthopnea found to be hypoxic in clinic in the setting of previously failed macrolide and fluoroquinolone therapy. Admission review of chest x-rays indicated a progression from atypical infiltrates and pulmonary edema to bilateral peripheral infiltrates. A chest CT confirmed parenchymal reticulation, septal thickening, and ground glass opacities consistent with cryptogenic organizing pneumonia. Clinical diagnosis and treatment with high dose steroids led to improved pulmonary function and exercise capacity.

Discussion: Cryptogenic organizing pneumonia is characterized by a variable clinical course and a time to treatment dependent disease severity. Timely diagnosis and early intervention is key to abating a destructive and potentially reversible disease process. The induction of alveolar injury, recruitment of fibroblasts, and excessive proliferation of granulation tissue leads to intraluminal plugs and polyps. The resulting airway consolidation injury often led to the presenting clinical picture of a nonproductive cough, fevers, dyspnea, malaise, and weight loss. Further investigation frequently identifies peripheral pulmonary infiltrates on imaging as well as a reduction in oxygen saturation and functional capacity of the patient. Pulmonary function tests frequently indicate a reduction in diffusion capacity as well as a restrictive flow pattern. Treatment with glucocorticoids early in the disease course reverses identifiable pulmonary deficits in approximately 66% of patients. Overall prognosis remains positive with early recognition and treatment.

## 5-Oxoproline (Pyroglytamic Acid) Associated Increased Metabolic Anion Gap Acidosis: Role of Acetaminophen

Raviteja R Guddeti, MD, Aarti Narayan, MD, Jayanth Vedre, MD; Department of Internal Medicine, Marshfield Clinic, Marshfield, Wis

Introduction: Acute acetaminophen hepato-

toxicity is associated with anion gap metabolic acidosis secondary to lactic acidosis and renal failure. However, severe anion gap metabolic acidosis in patients consuming acetaminophen at therapeutic levels, secondary to 5-oxoprolinemia, is rare and seldom reported. Case: A 63-year-old severely malnourished woman with history of osteoporosis, chronic pancreatitis, Type 2 diabetes mellitus, anemia of chronic disease fibromyalgia, and depression was brought in unresponsive by emergency medical services. En route, she was intubated since she was found to have agonal breathing and unresponsiveness. She had elevated white blood cell count, acute kidney injury, elevated anion gap metabolic acidosis, and elevation in her beta-hydroxybutyrate of 4.04 initially consistent with diabetic ketoacidosis, as well as septic shock secondary to pneumonia diagnosed on a CT scan performed to rule out pulmonary embolism. She was started on vancomycin and levofloxacin for sepsis. Initial arterial blood gas analysis showed a pH of 6.81, partial pressure of carbon dioxide of 27, bicarbonate of 3 with an anion gap of 23. Rapid blood screen was negative for alcohol. Salicylate levels were 2.5 (2.0-29.9) and acetaminophen levels were slightly elevated at 13 (0-10). Patient had been taking acetaminophen for chronic pain. Diabetic ketoacidosis treatment protocol was initiated with regular insulin drip and frequent monitoring of fluid status and serum electrolytes. Bicarbonate drip was given for metabolic acidosis. Despite above measures, anion gap failed to correct although blood glucose levels returned to less than 200. N-acetylcysteine was started suspecting acetaminophen-related liver toxicity while awaiting urine 5-oxoproline levels. For renal failure and electrolyte disorders, continuous renal replacement therapy was initiated. She continued to stay unresponsive and neuron specific enolase was elevated at 34. Vasopressors (norepinephrine and vasopressin) were started for hypotension refractory to volume resuscitation. Urine 5-oxoproline came back elevated at 8800 µmol/ mol creatinine (reference range: <50).

Conclusions: In severely malnourished patients, chronic ingestion of acetaminophen can cause high anion gap metabolic acidosis secondary to elevated blood levels of 5-oxoproline.

### Hickam's Dictum or Occam's Razor? Use PRN!

Hari Pokhrel, MBBS, Rachel Hawker, MD, FACP; Gundersen Heath System, La Crosse, Wis

Introduction: Decision making in medicine relies a lot upon heuristics. We present a case in which Hickam's dictum was used initially to explain multiple issues the patient had. In hindsight, however, it appeared that Occam's razor would have been more appropriate for explanation.

Case: A 63-year-old woman with a history of alcoholic liver disease, presented to her primary care clinician with concerns for acute mental status changes and inability to perform activities of daily living. She was referred to an emergency department (ED) where she was found to have severe hypercalcemia (corrected calcium: 14.98) and elevated ammonia. She was given intravenous fluids, calcitonin, and zoledronic acid and transferred to our hospital. A thorough evaluation of hypercalcemia did not reveal anything specific. Complete blood cell count (CBC) showed pancytopenia; so did the peripheral blood smear. Serum protein electrophoresis showed a polyclonal gammopathy with normal light chain ratio. Hematology was consulted due to high suspicion for an underlying bone marrow malignancy. Hematology advised that the polyclonal gammopathy was likely a consequence of liver disease and the pancytopenia was likely a consequence of splenomegaly. They further recommended to right upper quadrant ultrasound and screening for liver malignancy due to history of liver cirrhosis. Both these tests were negative. However, the next day, the shifts changed and a different hematologist saw the patient and recommended a bone marrow biopsy to evaluate the cause of hypercalcemia and pancytopenia and rule out underlying bone marrow disorder or lymphoma. The final pathology report for bone marrow biopsy was read as noncaseating granulomas consistent with sarcoidosis. Further evaluation revealed that her sarcoidosis was only limited to her bone marrow. She has been following rheumatology and is being treated with steroids.

Conclusions: Medical decision making is a

complex process and physicians certainly should be aware of the cognitive errors and biases. Although we may be able to explain clinical cases using either Occam's razor or Hickam's dictum, we should certainly be willing to reconsider our preassumptions and challenge ourselves until we find a satisfactory explanation and see actual clinical improvement in our patients.

#### **HSV** in Eczema's Clothing

Christopher R. Lindholm, MA, Sean O'Neill, MD; Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wis

Case: A 20-year-old woman 3 months postpartum with past medical history significant for asthma, allergies, and atopic dermatitis presented to the ED with 2 weeks of fatigue, fever to 103° F, nausea, and a progressively worsening rash involving the face, hands, legs, and back. On presentation, temperature was 99.9° F, blood pressure 82/40 mm Hg, SpO2: 92% on room air, white blood cell count 4.0, C-reactive protein 18.9, and chest x-ray was clear. She was fluid resuscitated and started on ceftriaxone and vancomycin. She was transferred to another hospital 2 days later for continued hypotension increasing oxygen requirements and concern for sepsis secondary to skin and pulmonary source. Chest x-ray now revealed bilateral patchy infiltrates and she was given a single dose of IV acyclovir for concern of herpetic rash. She was transferred to our facility the following day for persistent hypoxemia and specialty care. There, she reported a similar rash all her life, usually limited to face and hands. The rash had worsened during pregnancy for which she received oral steroids within last 3 months but had progressed over preceding 2 weeks. Rash was tender without pruritis. She denied a history of herpes simplex virus (HSV) and had chicken pox as a child.

On exam, thick erythematous plaques with punched out bases and overlying yellow crusts were noted on her forehead, cheeks, nose and chin, and forearms. Her lower legs had many 2 to 3 mm monomorphic vesicles with eroded centers and an umbilicated appearance. Some vesicles coalesced into larger plaques with hemor-

rhagic crusts. HSV1 PCR of fresh lesions was positive and Tzanck was positive for multinucleated giant cells. She was diagnosed with eczema herpeticum and continued on IV acyclovir. Mupirocin 2% ointment was applied for secondary impetigenization and moisturization with white petrolatum was used. Oxygen requirements slowly improved over the course of her 7-day hospital stay, no pathogen was ever identified for her bibasilar pneumonia but she did receive IV zosyn for 5 days. The erosions and plaques eventually sloughed off revealing denuded skin and she was ultimately discharged on oral valacyclovir for 7 days.

Conclusions: This case illustrates eczema herpeticum as one of the dermatological emergencies and the importance of recognizing the characteristic presentation of fever and clusters of pustular vesicles and/or punched out erosions that most often occurs as a complication of atopic dermatitis. It also highlights the importance of prompt lab tests and treatment with acyclovir as this condition has high rates of morbidity and mortality.

#### **Hypertension in a Pregnant Woman**

Ann M. Chodara, MD, Charles A. Weber, MD; University of Wisconsin Hospital and Clinics, Madison, Wis

Case: This case report describes a 25-year-old G3P0020 woman at 36 weeks and 2 days gestation presenting with severe hypertension. She had a 2-year history of hypertension treated with labetalol. She was noted to be hypertensive from the 140s to 170s systolic at multiple office visits starting at 11 weeks. She developed episodes of dizziness, sweating, and tachycardia during her second trimester. Holter monitor showed sinus tachycardia and transthoracic echocardiogram was normal. Testing returned positive for elevated urine normetanephrine, 24-hour norepinephrine and dopamine levels, and normal metanephrine, 24-hour epinephrine and vanillylmandelic acid levels. Twenty-four hour urine protein excretion also was elevated. Of note, she has a positive family history for paraganglioma in her mother. She was started on phenoxybenzamine. Given persistent severe hypertension at 36 weeks, she was admitted to the ICU. MRI abdomen was concerning for extra-adrenal paraganglioma. Nicardipine drip was started, phenoxybenzamine was uptitrated, and propranolol was added on hospital day 2. She underwent a caesarean delivery at 37 weeks and 1-day gestational age. This patient remained inpatient at the time this report was prepared.

Discussion: Catecholamine-secreting tumors are a rare but life-threatening cause of hypertension, particularly during pregnancy. Pheochromocytomas are intra-adrenal masses, while paragangliomas are extraadrenal. Diagnosis is made by measurement of urinary and/or plasma fractionated metanephrines and catecholamines; family history also may be of assistance. Strict blood pressure control is essential, particularly in pregnancy, via obtaining alpha blockade before beta blockade. Untreated, this condition causes maternal and fetal mortality rates of 8% and 17%, respectively. Timing of surgical intervention is more controversial. In this case, caesarean delivery was pursued prior to tumor resection.

### Localized Ocular Amyloidosis: A Case Series

Lindsay Hammons, Anita D'Souza, MD, MS; Pinky Jha, MD; Medical College of Wisconsin, Milwaukee, Wis

Introduction: Immunoglobulin light chain amyloidosis (AL) is a clonal plasma cell neoplasm in which clonal immunoglobulin light chains, either  $\lambda$  or  $\kappa$ , misfold into amyloid and deposit in tissues. The pathogenesis of AL depends on the degree of systemic deposition of amyloid fibrils into vital organs. Localized ocular amyloidosis without systemic involvement is rare.

Cases: (A) A 31-year-old woman presented to eye clinic with left ptosis, watery eyes, a left inner eyelid lesion, and a foreign body sensation (FBS) in her left eye. Physical exam was unremarkable except for left eye ptosis. Laboratory findings were significant for Congo red positive staining on left upper lid conjunctival excision with liquid chromatography-tandem mass spectrometry (LCTMS) positive for AL (lambda) type amyloid deposition. Workup for systemic amyloidosis was within normal limits.

(B) A 49-year-old woman with migraine headaches presented to eye clinic with leftsided proptosis, left-sided FBS, limited eve movement, and binocular horizontal diplopia. Past MRI showed enlargement of left extraocular muscles (EOM) thought to be secondary to orbital pseudotumor and treated with a course of prednisone that did not seem to help. Physical exam was unremarkable except for left eye proptosis, diplopia, and enlarged EOM on left side. Laboratory findings were significant for anterior orbitotomy with medial rectus muscle biopsy and Congo red positive staining with LCTMS positive for AK (kappa) type amyloid deposition. Workup for systemic amyloidosis was within normal limits with the exception of mildly elevated K levels in serum.

(C) A 69-year-old man with history of coronary artery disease, atrial fibrillation, and stroke presented to his primary care clinician with left ptosis for the past month with a change in vision. Physical exam was unremarkable except for left upper lid ptosis with significant visual field changes. Laboratory changes were significant for left orbicularis muscle and full-thickness wedge left upper lid excision with immunohistochemistry subtyping suggestive of AA, however weak staining for  $\lambda$  and  $\kappa$  also was present. Workup for systemic amyloidosis (no serum immunofixation or bone marrow biopsy) was within normal limits.

(D) A 66-year-old man with history of posterior vitreous detachment, cataract, and dermatochalasis of bilateral eyelids presented to eye clinic with new floaters and flashes in left eye with restricted right EOM. Physical exam was unremarkable. Imaging showed right inferior rectus mass and laboratory changes were significant for Congo red positive right inferior rectus biopsy with LCTMS positive for AL (lambda) type amyloid deposition. Workup for systemic amyloidosis was within normal limits.

*Discussion:* Patients with localized ocular amyloidosis do not appear to be at an increased risk of developing systemic involvement; watchful waiting is appropriate.

#### **New Onset Psychosis in Young Man**

Geoffrey Dang-Vu, MD, Amanda Willcox, DO,

Jennifer Schmidt, MD; Medical College of Wisconsin, Milwaukee, Wis

Introduction: Anti-N-methyl-D-asparate receptor (NMDAR) encephalitis is a neurologic syndrome with prominent psychiatric manifestations. This autoimmune encephalitis is often paraneoplastic, post viral, or idiopathic, and leads to limbic encephalitis and frontal lobe dysfunction that can mimic a primary psychiatric disorder. Diagnosis requires a high level of clinical suspicion in order to guide prompt recognition and initiation of appropriate therapy.

Case: We discuss a 23-year-old high functioning graduate student with no significant past medical or psychiatric history who presented to the ED after a diarrheal illness with progressive agitation, psychosis, euphoria, and suicidal ideation. The patient initally was triaged to psychiatry and discharged on olanzapine. He returned to the ED following a suicide attempt. Urine drug screen was negative; lumbar puncture demonstrated >100 white blood cell with lymphocyte predominance with subsequent negative viral serology and bacterial cultures. Magnetic resonance imaging (MRI) showed bilateral temporal lobe hyperintesity and leptomeningeal enhancement concerning for meningoencephalitis. Patient initially was treated for presumed herpes simplex encephalitis with acyclovir despite negative herpes simplex virus polymerase chain reaction (PCR). Two weeks after presentation, cerebrospinal fluid returned a positive NMDAR antibody, confirming anti-NMDAR encephalitis. Patient was started on high-dose steroids and intravenous immunoglobulin (IVIG) with improvement though he continued to experience episodes of agitation, psychosis, and catatonia, alternating with periods of lucidity. During episodes of agitation, he demonstrated Kluver-Bucy syndrome, as he would sporadically become hypersexual and impulsive. Due to continued agitation, he was started on rituximab with significant improvement, though far from his baseline. Patient was discharged to neurocognitive rehabilitation. Primary malignancy was never identified despite extensive radiologic and serologic workup.

Discussion: Anti-NMDAR encephalitis is part of an expanding group of autoimmune

encephalitides that generally affect younger patients (median age of 21 years). Given association with paraneoplastic syndromes, this diagnosis should prompt workup for a primary malignancy. The majority of patients with underlying neoplasm are women with an ovarian teratoma. When present, tumor resection with immunotherapy leads to favorable outcomes. In men, it is common that no tumor is discovered. First-line treatment for those without identifiable tumors is immunotherapy with IVIG, glucocorticoids, or plasma exchange. For those failing first-line treatment, therapy with rituximab or cyclophosphamide showed improved outcomes, as well as significant reduction in relapses. Despite severity of disease, patients often improve with supportive care, immunotherapy, and lengthy recovery with multidisciplinary care.

#### Rapid Dissemination of Blastomycosis in Late Pregnancy

Kenneth Coggins, MD, Pierre Kory, MPA, MD; University of Wisconsin Hospital and Clinics, Madison, Wis

Introduction: Blastomycosis is widely prevalent in the lungs of those living in the Great Lakes region and is widely known to disseminate in the immunocompromised, such as those with AIDS or solid organ transplant recipients. However, in rare cases, a latent infection is activated by the partially immunocompromised state of pregnancy. Given the life-threatening nature of this disease complication, early diagnosis is critical.

Case: A 38-year-old woman at 35 weeks pregnancy presented to a local ED with 2 weeks of right knee pain, a cutaneous left thigh lesion, and new-onset dyspnea. MRI of knee revealed large effusion with findings consistent with tibial osteomyelitis while CT chest revealed bilateral infiltrates. The patient was taken to the operating room for urgent caesarean delivery and incision and drainage of both the right knee and left thigh cutaneous lesion. Postoperatively, she failed to respond to antibacterial therapy and developed severe acute respiratory distress syndrome (ARDS). She was transferred to a tertiary care center, where she underwent bronchoscopy and was diagnosed with pulmonary blastomycosis. Retrospective review of original tibial biopsy confirmed the presence of osteomyelitis secondary to blastomycosis, confirming suspicions of dissemination. She later experienced seizures thought to be due to central nervous system infection with blastomycosis, as MRI findings were consistent with such a diagnosis. She was treated with amphotericin and voriconazole with subsequent improvement. She was discharged with plan to complete 8 weeks of amphotericin and 1 year of voriconazole.

Discussion: This case presents an uncommon primary manifestation of blastomycosis in a pregnant patient. The peripartum state of immunosuppression can lead to rapid dissemination and ARDS. Blastomycosis must be considered in the differential of both native joint osteomyelitis and disseminated ARDS among immunocompromised patients in the Great Lakes region.

#### Successful Treatment of Lupus Mesenteric Vasculitis With Cyclophosphamide

Pooja Kumari, MD, Sonali Khandelwal, MD; Marshfield Clinic-St. Joseph's Hospital, Marshfield. Wis

Introduction: Lupus mesenteric vasculitis (LMV) is one of the most serious gastrointestinal complications in systemic lupus erythematosus (SLE). Steroids are considered as a first-line therapy; in only few steroid unresponsive cases cyclophosphamide has been tried. We present a case of LMV that carried therapeutic challenge with pulse dose steroid with ongoing risk for sepsis, but cyclophosphamide treatment provided symptom improvement.

Case: A 39-year-old man with a past medical history of antiphospholipid antibody syndrome and SLE presented with acute onset abdominal pain and diarrhea. On examination, he had stable vital signs, diffuse abdominal tenderness, no rebound tenderness. The following were normal: CBC, comprehensive metabolic panel, lipase, infectious, autoimmune, and vasculitic workup. International normalized ratio was 4.5. CT of abdomen showed generalized small bowel edema with perienteric fluid around terminal ileum consistent with enteritis, no large vessel thrombosis. Gastroscopy shows severe scalloping and villous loss in duodenum, ery-

thematous friable terminal ileal mucosa with ulcers/exudate and granular colonic mucosa. Histopathology showed mucosal capillary vasculitis and excessive plasma cells in lamina propria, consistent with autoimmune and/or small vessel vasculitis related enteritis. He was started on 1mg/kg/day steroids. He developed worsening abdominal pain, fever, and hypotension. Repeat CT showed no bowel perforation. Repeat infectious workup was negative. After stabilization over 72 hours, he received 1 dose of cyclophosphamide 800mg with concomitant steroids. His symptoms improved within a few days and he was discharged home with plan to continue cyclophosphamide therapy for 3 to 6 months and slowly wean steroids.

Discussion: The relevance of LMV in SLE patients is 0.2% to 6.4%. LMV-related ischemia carries high risk for infarction and mortality. There are no return to clinic recommendations or guidelines in literature regarding LMV treatment; nevertheless, based on high steroid responsiveness in retrospective studies, it has been considered first-line treatment. Cyclophosphamide have been tried in few rare steroid unresponsive situations. LMV carries high risk for gut bacterial translocation and sepsis, and use of pulse dose steroids can be challenging. In that situation cyclophosphamide use can help improve symptoms and mortality.

### Supradiaphragmatic Ectopic Hepatic Tissue

Lauren Richards, MD, Mouhammed Rihawi, MD; Aurora Health Care, Milwaukee, Wis

Introduction: Ectopic liver tissue is a rare developmental anomaly most commonly found incidentally during surgery in intraand retroperitoneal spaces. Only a few cases of supradiaphragmatic ectopias are reported in the literature. Detection of an abnormality by imaging before surgery or autopsy is also unusual. Most of the reported supradiaphragmatic cases are found in neonates causing respiratory distress or hydrothorax. Erroneous dorsal budding of hepatic tissue before closure of the pleuroperitoneal membranes may explain how ectopic liver develops in the thoracic cavity.

Case: A 38-year-old generally healthy woman

presented with a productive cough of 4 days duration with acute dyspnea. She had no chest or calf pain, fever, or chills. Vital signs were stable but she demonstrated decreased breath sounds in the right lung field on exam. Chest x-ray and subsequent CT revealed a right loculated hydropneumothorax with a small fluid component and several nonparenchymal 1.2 to 1.4 cm lesions above the right hemidiaphragm. The patient denied any occupational exposures or travel. Pulmonology contemplated a parapnuemonic fluid collection, hepatic deposits, or catamenial pneumothorax, however unlikely since she had menstruation 3 weeks prior. Infectious Disease did not believe this to be infectious. She underwent video-assisted thoracoscopy with decortication. Pathology was positive for benign liver tissue with hemosiderin. No malignancy or endometrial tissue was seen. α-fetoprotein was normal.

Discussion: This is an extremely rare case of ectopic hepatic tissue. Not only are the patient's age and diaphragmatic ectopic location impressive, but the majority are found incidentally in asymptomatic adult patients; this ectopia caused a symptomatic hydrothorax, making this even more unusual. Most importantly, ectopic deposits have a higher incidence of hepatocellular carcinoma, independent of disease or tumor in the regular liver. Small ectopic liver tissue is thought to have an incomplete functional architecture leading to longer exposure to carcinogenic factors. Awareness of this entity is important for prevention of future malignancies. This patient, therefore, will have close monitoring with consideration for future surgical resection.

#### An Underrecognized Cause of Anion Gap Metabolic Acidosis

Nicholas Torgerson, DO, Vijay Ramalingam, MD, Gurminder Dhillon, MD; Medical College of Wisconsin, Milwaukee, Wis

Introduction: The causes of pure anion gap metabolic acidosis are taught early in medical education through the mnemonic MUDPILES. However, this mnemonic overlooks other causes of metabolic acidosis such as oxoprolinemia. Oxoprolinemia is directly linked to the use of acetaminophen, and its

diagnosis is likely limited by awareness of clinicians and by availability of testing.

Case: A 72-year-old woman with a history of chronic kidney disease stage 3 and chronic back pain presented to the ED with a chief complaint of back pain after running out of hydrocodone/acetaminophen, acetaminophen/codeine, and acetaminophen. The patient's daughter reported that the patient was acting confused and somnolent. Review of medications revealed chronic intake of at least 4000 mg of acetaminophen from 3 different sources per day for the past year. A basic chemistry panel revealed a bicarbonate of 9 mmol/L with a serum creatinine of 1.63 mg/dL, a serum urea nitrogen of 38 mg/dL, and an anion gap of 31. A subsequent arterial blood gas revealed a pH of 7.25, CO2 < 20 mmHg. Her workup was negative for lactic acid, volatile alcohols, or other ingestions; there was no evidence of diabetic ketoacidosis, and a drug screen was negative for salicylates. She was found to be appropriately compensating via Winter's Formula and her Delta-Delta indicated a pure metabolic acidosis. She was started on a bicarbonate infusion, which corrected her bicarbonate but her anion gap remained elevated. A urine sample was sent for organic acid evaluation given her long-term use of acetaminophen and found to be highly positive for 5-oxoproline. She was started on n-acetylcysteine and IV fluids, acetaminophen was held, and her anion gap slowly recovered over 10 days in the hospital, but did not fully normalize for another 7 days after discharge.

Discussion: 5-oxoproline is a byproduct of acetaminophen metabolism that builds up in the blood with continued acetaminophen use. Glutathione depletion and cysteine deficiency occur secondary to chronic use of acetaminophen. Alongside malnutrition, these factors result in the depletion of ATP stores, which leads to the inability to convert oxoproline to glutamic acid. Oxoprolinemia is most likely to be seen in elderly women with chronic kidney disease, and with the increasing prevalence of kidney disease due to diabetes and hypertension, and the ubiquity of acetaminophen-containing pain relievers used daily, it is likely that oxoprolinemia anion gap meta-

bolic acidosis is underdiagnosed due to lack of awareness and access to testing. There is no defined treatment; per case reports n-acetylcysteine is often used given the physiology of glutathione depletion, as well as bicarbonate infusions, with no clear benefit of either. The only proven treatment is abstaining from acetaminophen. High clinical suspicion and awareness remains the key for diagnosis as confirmatory labs tests are not readily available and can take weeks for a final result.

#### **POSTER PRESENTATIONS**

#### 1st Place

### Autoimmune Thyroid Disease: A Rare Presentation of a Common Condition

Lauren Richards, MD, Netsanet Chalchisa, MD, Aijaz Noor, MD; Aurora Health Care, Milwaukee, Wis

Introduction: Hashimoto encephalopathy (HE) is a rare, possibly underreported, autoimmune condition associated with Hashimoto thyroiditis (HT). The association is not well known, but HT is the most common cause of hypothyroidism making this case an imperative demonstration of recognizing a life-threatening and sometimes irreversible condition that can easily be mistaken for other common disorders.

Case: A 67-year-old woman was admitted for worsening altered mental status. She had a 3-week history of mild cognitive decline and complained of headaches. CT and MRI demonstrated no acute ischemia but cerebral atrophy and extensive hyperintense white matter changes were evident. Infectious etiology was ruled out. Thyrotropin was severely elevated at 258. Antithyroid peroxidase antibody (TPOAb) and antithyroglobulin antibody (TgAb) were both elevated at 3,548 and 1,858. She was started on levothyroxine but her mental status continued to worsen. Electroencephalogram showed generalized slowing consistent with moderate diffuse encephalopathy. She developed myoclonus and somnolence. Hyperreflexia was present. Myxedema coma was considered, but she did not demonstrate signs of hypothermia, hypotension, bradycardia, or hypoglycemia. HE was considered and the patient was given IV methylprednisolone; within 24 hours her myoclonus and somnolence resolved, her mentation

improved and she was able to converse again.

Discussion: This case emphasizes the challenge of diagnosing a rare condition in a patient presenting with altered mental status, a common diagnosis in emergency departments nationwide. This was a particularly difficult case because HE does not always present as hypothyroidism; thyroid status varies tremendously. This misled suspicion for other differentials such as severe HT and myxedema coma. Although HE is rare, thyroid dysfunction along with a similar clinical presentation to this patient should cause high suspicion for HE. Mild cognitive impairment persisted after treatment, but it is well documented that HE may take up to 1 year to resolve. In some cases, if left untreated, encephalopathy will not improve making recognition paramount for timely and effective treatment.

#### 2nd Place Steroids and Ritonavir: A Case of Drug-Induced Cushing's Syndrome

Brian Lewis, MD, Bennett Vogelman, MD; University of Wisconsin Department of Medicine, Madison, Wis

Introduction: Managing comorbidities in HIV-infected patients can be complicated given the numerous drug interactions with antiretroviral (ART) medications. Ritonavir (RTV) is a protease inhibitor (PI) that is a potent inhibitor of cytochrome P450 CYP3A4, CYP3A5 and CYP2D6. Glucocorticoid medications are metabolized by the CYP34A enzyme system. Taken concurrently, RTV can increase the area under the concentration versus time curve (AUC) and half-life of glucocorticoid medications resulting in iatrogenic Cushing's syndrome.

Case: A 54-year-old man with 23-year history of HIV, calcium pyrophosphate disease (CPPD) and chronic obstructive pulmonary disease (COPD) presented with an 11-pound weight gain, facial swelling, new onset dyspnea with increased abdominal girth over the past 3 weeks. His HIV was well controlled on darunavir, etravirine, raltegravir, and RTV with a CD4 count of 448 and undetectable viral load. Prior to these symptoms, he received 120 mg intra-articular (IA) triam-

cinolone (TMC) injections in his knees over 2 months relieving his CPPD. Additionally, he was taking beclomethasone nasal spray and formoterol/mometasone. His exam showed facial plethora, moon facies, hoarseness, lateral eyebrow loss, and mild bilateral hand tremor. He had no abdominal striae, an enlarged pannus with internal umbilicus without lower extremity edema. A cortisol level was < 0.8 for 4 months. Over the next 5 months his symptoms resolved and his cortisol remained low at 1.2 with a relatively low corticotropin level of 9 with postcosyntropin cortisol of 6.5. He was placed on anakinra and colchicine for his CPPD, his beclomethasone nasal spray was discontinued, and formoterol/mometasone inhaler dose was lowered to reduce his glucocorticoid exposure.

Discussion: This patient presented with iatrogenic Cushing's Syndrome secondary to the interaction between RTV and TMC injections for his CPPD. The TMC injections required no entry in the electronic medical record prior to use as this was readily available in the clinic, thus evading the drug interaction warning. There are case reports describing similar instances in HIV patients taking glucocorticoids; however, different steroids vary in their metabolism making some safer than others. HIV patients are susceptible to osteoporosis, infection and DM highlighting the importance of this interaction. This case illustrates the importance of monitoring drug interactions in HIV patients on ART and speaks to the systems issue of having the ability to dispense medications and bypass the EMR drug interaction warnings.

#### **3rd Place**

#### 'Experimental' Ingestion of Cerberin

Marvi V. Rijhwani, MD, Dhaval Desai, MD, Joaquin Solis, MD; Aurora Health Care, Milwaukee, Wis

Introduction: Cerberin is an active ingredient found in the seeds of the Cerbera odollam tree, also known as the "suicide tree." Cerberin mimics digoxin and is commonly used as a suicide and homicide drug in South Asia. However, its use is relatively uncommon in the western world.

Case: A 25-year-old-man with a past medical history of depression and prior suicide attempts presented to the ED with confusion, lip numbness, nausea, vomiting, palpitations, and diarrhea. He admitted to ingesting a seed containing cerberin, which he purchased online. He reported experimenting with the seed in the event he was sentenced to prison. In the ED, he was found to have an irregular pulse with heart rate of 106 and blood pressure of 94/55. Electrocardiogram (ECG) revealed sinus tachycardia, Mobitz type I 2nd degree AV block, and T wave inversions in inferolateral leads. His labs were significant for a potassium of 5. His urine drug screen was positive for cannabinoids. Toxicologist at Poison Control recommended Digibind, a digoxin-specific antibody. The patient's overall condition remained stable. A repeat ECG 24 hours later was normal sinus rhythm.

Discussion: Cerberin ingestion is responsible for 50% of plant poisonings in South Asia. Since cerberin poisoning is uncommon in the western world, its diagnosis presents a challenge to physicians. Cerberin and digoxin are cardiac glycosides that inhibit the Na-K-ATPase pump in the myocardium. Overdose may present with a variety of systemic symptoms including nausea, vomiting, diarrhea, and any dysrhythmias of which AV block is more commonly seen. Physicians must suspect cerberin poisoning in patients with unexplained digoxin-overdose like presentation. Management includes appropriate administration of Digibind and monitoring on telemetry for any further arrhythmias.



*WMJ* (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

 $\ \, \odot$  2017 Board of Regents of the University of Wisconsin System and The Medical College of Wisconsin, Inc.

Visit www.wmjonline.org to learn more.